UNIVERSITY OF STIRLING

Why laterality matters in trauma: *sinister* aspects of memory and emotion

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To Alexander & Jade

my left handed twins

Abstract

This thesis presents an eclectic mix of studies which consider laterality in the context of previous findings of increased prevalence of Posttraumatic Stress Disorder (PTSD) in male combat veterans with non-consistent right hand preference. Two studies extend these findings not just to civilian populations and women, but to left handers and find that left, rather than mixed, handedness is associated with increased prevalence of PTSD in both general population and clinical samples, and to severity of symptoms in the former. To examine issues relevant to the fear response in healthy populations, a movie excerpt is shown to be theoretically likely to target the emotion of fear and to generate subjective and physiological (skin conductance) responses of fear. The film is used as a laboratory analogue of fear to examine possible differences in left and right handers in memory (for events of the film) and in an emotional Stroop paradigm known to produce a robust and large effect specifically in PTSD. According to predictions based on lateralisation of functions in the brain relevant to the fear response, left handers show a pattern of enhanced memory for visual items and poorer memory for verbal material compared to right handers. Immediately after viewing the film, left handers show an interference effect on the Stroop paradigm to general threat and film words and increased response latency compared to right handers, approaching performance of previously reported clinical samples with PTSD. A novel non-word Stroop task fails to show these effects, consistent both with accounts of interference as language processing effects and compromised verbal processing in PTSD. Unexpected inferior performance of females in memory for the film, contrary to previous literature, may also be amenable to explanations invoking compromised left hemisphere language functions in fear situations. In testing one theory of left handedness as due to increased levels of *in utero* testosterone, the 2D:4D (second to fourth digit ratio) provides mixed evidence in two samples. A possible association of more female-like digit ratios in males with PTSD is a tentative finding possibly relevant to sex differences in prevalence of PTSD. A critique of existing and inadequate theoretical accounts of handedness concludes the thesis and proposes a modification of the birth stress hypothesis to one specifically considering peri-natal trauma to account for the above findings. This hypothesis remains to be empirically tested.

Papers

The following is a list of papers that have resulted from this thesis

Choudhary, C. J. & O'Carroll, R. E. (2007). Left hand preference is related to Posttraumatic Stress Disorder. *Journal of Traumatic Stress, 20,* 365-369. [Included at Appendix 24]

Choudhary, C. J., Alexander, D.A.A., Forbes, D., Creamer, M., Huntley, Z., Fuchkan, N., Brewin, C.R., Durham, R.C., O'Carroll, R. E. (2008) (submitted). Left hand preference is related to Posttraumatic Stress Disorder, but not to other anxiety disorders. *Psychological Medicine.*

Choudhary, C. J., & O'Carroll, R. E. (in preparation). Left handers differ from right handers in memory for events of a fearful film in ways similar to deficits in memory found in PTSD. *Learning & Memory.*

Choudhary, C. J., & O'Carroll, R. E. (in preparation). Unexpected sex differences in memory for events of a fearful film: females perform worse than males, but not on a standard test of verbal memory. *Learning & Memory.*

Choudhary, C. J., & O'Carroll, R. E. (in preparation). Left handers show Stroop interference after viewing a fearful film to general threat and film- related words. *Journal of Experimental Psychology: General.*

Choudhary, C. J., & O'Carroll, R. E. (in preparation). Mixed evidence for theories implicating *in utero* testosterone in left handedness, but do males with PTSD show a more female-like digit ratio? *Evolution and Human Behavior.*

Choudhary, C. J., & O'Carroll, R. E. (in preparation). Historical considerations of PTSD in the context of DSM-V. *Psychological Medicine.*

Choudhary, C. J., McIntyre, A., Hancock, P.J.B., O'Carroll, R. E. (in preparation). It's not what you study, but when you recruit: results depend on whether students want to participate. *The Psychologist.*

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Declaration

I declare this thesis to be my own written work and based upon research carried out by me. The following contributed as follows:

Provision of clinical data for the collaborative study reported in Chapter 4; all subsequent analysis was my own work:

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Chapter 1

Introduction

1.1 Introductory remarks

The starting point for this thesis was two papers (Spivak et al., 1998; Chemtob & Taylor, 2003) describing findings in male combat veterans (of the Vietnam War) that suggested that an increased prevalence of Posttraumatic Stress Disorder (PTSD) was associated with mixed hand preference (for manual tasks such as writing) rather than a consistently right handed preference. The aim of this chapter is to introduce the reader to the disorder which is PTSD and to aspects of lateralisation and asymmetry of the brain that may be relevant factors underpinning this observed relationship. These issues set the context for the experimental chapters which comprise the substance of this thesis.

PTSD is a mental disorder which has an environmental aetiologic component: exposure to an extreme stressor or trauma which threatens life or physical integrity and which is experienced with extreme fear and helplessness. Symptoms of the disorder, which must persist for at least a month, form three clusters, re-experiencing, avoidance and arousal, and need to be present to the extent that they affect normal functioning in everyday life. These are the descriptive criteria for the disorder according to the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, or DSM-IV (American Psychiatric Association, 1994) shown in Table 1.1.

Table 1.1 DSM-IV criteria for PTSD

A. The person has been exposed to a traumatic event in which both of the following were present:
   (1) the person experienced, witnessed, or was confronted with an event or events that involved actual or threatened death or serious injury, or a threat to the physical integrity of self or others
   (2) the person's response involved intense fear, helplessness, or horror

B. The traumatic event is persistently re-experienced in one (or more) of the following ways:
   (1) recurrent and intrusive distressing recollections of the event, including images, thoughts, or perceptions
   (2) recurrent distressing dreams of the event
   (3) acting or feeling as if the traumatic event were recurring (includes a sense of reliving the experience, illusions, hallucinations, and dissociative flashback episodes, including those that occur on awakening or when intoxicated)
   (4) intense psychological distress at exposure to internal or external cues that symbolise or resemble an aspect of the traumatic event
   (5) physiological reactivity on exposure to internal or external cues that symbolise or resemble an aspect of the traumatic event

C. Persistent avoidance of stimuli associated with the trauma and numbing of general responsiveness (not present before the trauma), as indicated by three (or more) of the following:
   (1) efforts to avoid thoughts, feelings, or conversations associated with the trauma
   (2) efforts to avoid activities, places, or people that arouse recollections of the trauma
   (3) inability to recall an important aspect of the trauma
   (4) markedly diminished interest or participation in significant activities
   (5) feeling of detachment or estrangement from others
   (6) restricted range of affect (e.g., unable to have loving feelings)
   (7) sense of a foreshortened future (e.g. does not expect to have a career, marriage, children, or a normal life span)

D. Persistent symptoms of increased arousal (not present before the trauma), as indicated by two (or more) of the following:
   (1) difficulty falling or staying asleep
   (2) irritability or outbursts of anger
   (3) difficulty concentrating
   (4) hypervigilance
   (5) exaggerated startle response

E. Duration of the disturbance (symptoms in Criteria B, C, and D) is more than one month.

F. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

The introduction to PTSD follows an historical perspective in section 1.2, which shows it to have been subject, like the disorder itself, to various episodes of historical amnesia and re-experiencing. Conceptions of the disorder from a century ago are introduced as relevant to current views of the biologically based, wide ranging effects of overwhelming trauma. Amidst some debate when it was first included in the DSM in 1980, PTSD is currently classified as an anxiety disorder but this does not fully reflect its nature. In the context of reviews in preparation for a revised DSM V, emerging knowledge suggests PTSD is a disorder of fear conditioning, of dissociation and of memory. These phenomena are associated with lateralisation of structure and function within the brain, particularly in relation to emotion, language and memory. Although the work of this thesis is not neurobiological in nature, the reader is introduced to the neurobiological underpinnings of the disorder in section 1.3, since they relate to lateralisation of these functions in the brain. As such, they are relevant to hypotheses proposed, and interpretations of findings, in the experimental studies reported, particularly in Chapter 5 and Chapter 6.

There are sex differences in prevalence of PTSD: a ratio of 2:1 in women compared to men, and section 1.4 considers some of the possible reasons for this, as these are not currently fully understood. Any study, therefore, of factors possibly relevant to PTSD needs also to consider possible sex differences and this theme inevitably runs alongside considerations of lateralisation throughout this thesis.

A review of the literature on handedness in relation to PTSD follows in section 1.5, and this is extended by the work reported in Chapters 3-4. Other potential risk factors for the disorder are outlined here also.

A brief introduction to the issue of handedness and laterality follows in section 1.6. Whilst in an everyday context this might appear to be simply a matter of which hand is used for writing, this is not necessarily so; methodological issues in the definition and measurement of handedness are considered in Chapter 2. The fundamental question of why only 10% of the population is left handed is currently not understood and this and issues arising from it are introduced in section 1.6; the work presented in Chapter 7 tests one theory of left handedness and the final chapter, Chapter 9, returns to these issues in conclusion to this thesis after Chapter 8 which summarises and discusses results from the studies presented here.

Section 1.7 introduces the research questions the experimental studies of this thesis were designed to answer and outlines the structure of the thesis.

1.2 Posttraumatic Stress Disorder (PTSD): a new disorder?

PTSD was first conceptualised as such in the DSM-III (American Psychiatric Association, 1980). This is not to say that PTSD has only existed as a disorder since this time. The effects of trauma have been described throughout recorded history. Perhaps the earliest account of symptoms consequent on trauma is recorded on a Sumerian cuneiform tablet describing the attack on the city of Ur between 2027 and 2003 B.C. (Ben-Ezra, 2001; 2002). Also in antiquity, Homer’s account of Achilles in the Iliad deals with reactions of men in battle relevant to more recent experiences of war (Shay, 1991). The diary of Samuel Pepys in 1666 records in detail the development of his own posttraumatic reactions to the Great Fire of London (Daly, 1983).

In the more recent past, during the American Civil War (1861-1865) Da Costa, a physician treating casualties of the war, described symptoms of increased arousal, irritability and elevated heart rate in soldiers exposed to combat. This was considered to be a physiologic reaction to combat stress and gave rise to the descriptions "Soldiers Irritable Heart" or "Da Costa's Syndrome" (Da Costa, 1871; cited in Saigh & Bremner, 1999). The widespread construction of railways as a means of mass transport during the 19^{th} century resulted in the first major study of the effects of trauma – as a result of railway accidents – and recognition of the consequences of trauma:

> "We know of no clinical picture more distressing than that of a strong and healthy man reduced by apparently inadequate causes to a state in which all control of the emotions is well-nigh gone; who cannot sleep because he has before his mind an ever-present sense of the accident; who starts at the least noise; who lies in bed almost afraid to move; whose heart palpitates whenever he is spoken to; and who cannot hear or say a word about his present condition and his future prospects without bursting into tears."
>
> Page (1883) p172-3; quoted in Brewin (2003) p 26

The cause of these symptoms was generally thought to be some physical lesion of the brain or part of the nervous system as a result of the accident, and this presentation came to be known as "railway spine". This was typical of medicine of the time, which sought to find some physical or organic cause of the injury, even though one was not immediately apparent. Page's opinion, however, was more typical of modern views, ascribing the symptoms to "general nervous shock" caused by extreme fright, and combined both psychological and physiological levels of explanation.

The events precipitating these historical accounts of symptoms recognisable as PTSD today were traumas of combat, disaster and accidents. However, at the end of the 19^{th} century, most of the descriptions of symptoms now recognised as posttraumatic arose from the study of the psycho-neuroses, particularly of hysteria, a condition, as the derivation of its name suggests, which was thought, originally at least, to affect only women. The diagnosis of hysteria no longer exists and is now subsumed within the dissociative, personality and posttraumatic disorders in the DSM (van der Hart & Friedman, 1989). Perhaps most relevant to current perspectives on PTSD, although the most disregarded until recently, is the work of Pierre Janet (1859-1947) on *désagrégation* or dissociation. Part of the reason for this disregard is that many of his major works were never translated from French; this is still the case for his first major work, *L'Automatisme Psychologique* [Psychological Automatism] (Janet, 1889) his thesis for the doctorat ès-lettres, which introduced his dissociation theory, based on several years of work with patients he saw in Le Havre. It was not until publication of Ellenberger's extensive work, *The Discovery of the Unconscious* (Ellenberger, 1970), that Janet's work was made more widely known; many contemporary interpretations of the relevance of his work to PTSD were made in 1989 on the centenary of the publication of *L'Automatisme Psychologique* (e.g. van der Hart & Horst, 1989; Nemiah, 1989; Putnam, 1989; van der Hart & Friedman, 1989; van der Hart et al., 1989; van der Kolk et al., 1989; van der Kolk & van der Hart, 1989). Janet's contributions to our understanding of other mental disorders are not considered here.

L'Automatisme Psychologique was produced while Janet was professor of philosophy; he then undertook medical studies, obtaining his MD in 1893. In his theory of the mind, Janet distinguished two functions: activities that preserve and reproduce the past (memory) and those that are directed towards synthesis and creation (or integration) which aid the organism in maintaining equilibrium with environmental changes in the present (action). Action and memory are fundamental in Janet's theory; successful action on the environment results in successful integration of memories. Memory is seen as a creative act occurring for the most part automatically: new experiences and skills acquired are automatically integrated into existing schemes of knowledge. These *automatisms* [automatic adaptations] are actions triggered by ideas and accompanied by emotions and form rudimentary elements of consciousness available to awareness and conscious control.

These notions are similar to Piaget's concept of adaptation of an organism to its environment by assimilation and accommodation: new information is added into existing schemas - structures which organise past experience - by the process of assimilation. If the new information is inconsistent with existing schemas, then the schema is modified to include the new information by the process of accommodation. Piaget was no doubt influenced by the ideas of Janet, as he had briefly been his student (van der Kolk et al., 1989).

van der Kolk et al (1989) consider the interplay between memory and action as fundamental to Janet's psychology. The process of memory is dynamic: "memory is an action: essentially it is the action of telling a story" (Janet, 1919, p 661). To be appropriate this action needs to include a verbal representation of the experience: "It is not enough to just be aware of a memory: it is also necessary that the personal perception 'knows' this image and attaches it to other memories" (Janet, 1911, p 538) (both citations from van der Kolk et al (1989), p 368).

The healthy reaction to stress is the mobilisation of adaptive action to integrate the experience. When an event is encountered which overwhelms a person's capacity to take action to protect themselves from threat, and because it may not fit into existing schemas, this integrative function fails. Traumatic experiences and the "vehement emotions" arising from them and which are biologically encoded, result in an unassimilated, or dissociated, event separated off from consciousness, interfering with proper memory storage, existing rather at a subconscious level and forming an *idée fixe* [fixed idea]. Janet here introduces the notion of the "subconscious", prior to Freud, who later used the alternative term "unconscious" (Ellenberger, 1970). The subconscious fixed idea serves to organise the sensory, affective and visceral elements of the memory, while keeping them from conscious memory; this unintegrated, or dissociated, memory may later return as fragmentary reliving of aspects of the trauma (as what would now be considered flashbacks or intrusive phenomena). Janet recognised that there may be differences in temperament which make their own contribution to vulnerability to environmental stressors, but identified a traumatic precipitant in 257 of the 591 cases studied in his first four major works (Crocq & Verbizier, 1988; cited in van der Kolk et al., 1989).

The wealth of Janet's expositions and insights has been only briefly explored here. Janet never described a posttraumatic syndrome as such; however, his observations on effects of trauma are closely aligned to contemporary understandings of the effects of trauma considered below in section 1.3.

Although Janet and Freud (1856-1939) possibly met at the International Congress of Psychology in Paris in 1889, there is no record of their meeting (Ellenberger, 1970) and according to Ernest Jones (Freud's biographer from within the psychoanalysis movement), Freud maintained that they had never met when he rudely refused Janet's request to visit him in 1937 (Jones, 1961, p 633). A quote from a paper by Breuer and Freud in 1893 (Ellenberger, 1970, p 486), makes it clear that they were aware of Janet's theory of subconscious fixed ideas and therapeutic approaches prior to this publication of their own preliminary theories. However, Jones makes it clear that he, and by implication Freud, considers Freud owed nothing to Janet's ideas (Jones, 1961, p 70-1).

Perry & Laurence (1984) provide a factual consideration of the disputes between Janet and Freud and point out that Jones is erroneous in the refutation of Janet's prior claims, not just by a consideration of chronology, but also because each did acknowledge the work of the other even though there was often animosity between them.

It is not the intention here to consider Freud's work in detail, but only to mention the direct impact of his ideas on what was to become the study of PTSD. In 1896 Freud gave a paper on 'The aetiology of hysteria' to the Society of Psychiatry and neurology in Vienna which was subsequently published with Breuer (Jones, 1961). Up to this point, Freud's work with patients with hysteria led him to believe that early sexual trauma (such as incest) in the lives of these (female) patients was the cause of their hysterical symptoms.

> "According to Freud, the paper was met with an icy reception. Krafft-Ebing, who was in the chair, contented himself with saying: "It sounds like a scientific fairy tale"."
>
> (Jones, 1961, p 232)

Although at first apparently convinced of the truth of his patients' experiences, during his correspondence with Fliess over the next year it is apparent that Freud became frustrated that the (psycho)analyses of the eighteen cases on which he had based his paper and claimed, by implication, as cured, still seemed incapable of reaching a conclusion: they were not cured. By the following year, his ideas had completely changed. In 1897 he wrote to Fliess of "the great secret of something that in the past few months has gradually dawned on me" (Jones, 1961, p 233). This dawning was the "realisation" that the childhood seductions on which he had built his theory had in fact not occurred but had been imagined.

In this letter to Fliess, Freud gives four reasons for his doubts (Jones, 1961). First was the failure to bring the analyses of his 18 patients to a proper completion and cure, which left the scientific and theoretical outcomes imperfect. Second, were the implications of the prevalence among so many Viennese fathers of the abuse of their daughters. Third, his belief that the unconscious possessed no criterion of reality, rendering it unable to distinguish truth from fiction (which differs significantly from Janet's conception of subconscious fixed ideas being dissociated fragments of reality) and fourth, because memories of incestuous sexual abuse did not surface in delirious states of the more severe psychoses, this suggested they might never have actually occurred (Jones, 1961). According to Freud, writing retrospectively about this period: "I was at last obliged to recognise that these scenes of seduction had never taken place, and that they were only fantasies which my patients had made up or *which I myself had perhaps forced on them*…" (emphasis added: Webster, 1996, p 210), although he goes on to discount this possibility.

Freud developed his theory of infantile sexuality and repression to fill the theoretical gap left by this about turn in his thinking[‡]. In this view sexual fantasies developed in infancy; these wishes were in conflict with morality and so became actively repressed in the unconscious. Instead of actual sexual abuse, what existed in these women's minds were sexual fantasies and thus sexual fantasy and psychic reality came to be substituted for objective reality.

However, the quote from Webster at the end of the penultimate paragraph gives a clue that perhaps Freud's apparent initial starting point that all cases of hysteria originated in actual sexual trauma, was not as it seemed. Whilst some patients encountered by Freud may have suffered sexual abuse, in his 1896 paper, Freud makes it clear that when they

‡ Freud's basis for this theory was Haeckel's now discredited biogenetic law which stated that ontogeny (the development of the individual) recapitulates phylogeny (the evolutionary history of the species); while Haeckel considered that this happened during the development of the embryo in the womb, Freud applied it to development in infancy.

came to him, his patients did not come with memories of incest: "before they come for analysis, the patients know nothing of these scenes". It was part of his therapy to prepare them for the uncovering of such events, to which patients usually reacted with indignation that there was nothing to uncover – but how were they then persuaded? In Freud's words again: "only the strongest compulsion of the treatment can induce them to embark on a reproduction of them" (Webster, 1996, p 516).

Freud had created a theory which would effectively silence any reality of sexual trauma. In its original form, since the cause of all hysteria was held to be sexual trauma, then Freud set out to recover these memories in his patients to make sense of the symptoms and associations he identified in their presentation, as only by reproducing these pathogenic memories could there be a cure (hence his frustration that the analyses were not proceeding to cure). Once this idea was discarded, the theory in its second form, which held that all memories of sexual abuse were repressed sexual fantasies, also denied the reality of any sexual abuse. This state of affairs is an issue which recurs in the recovered memory debate arising in the late 20th century, although not considered within the scope of this thesis.

The contributions of Janet were increasingly overshadowed by Freud and the psychoanalysis movement; unlike Freud, Janet had worked independently and had not held a post where he would have taught his clinical findings to medical students. Ellenberger (1970) also cites the *Zeitgeist* of the early 20th century as widening the gap between Janet and the concerns of the younger psychiatrists.

Psychiatry was not well prepared for the events of the First World War and the enormous scale of the psychoneuroses which resulted from it (Rivers, 1920). In the

First World War, as in the case of railway accidents, the tendency was for psychiatry to ascribe a physical, organic, cause to the psychological sequelae of combat.

> "In accordance with the general materialistic tendency of medicine the first stage of this branch of the medical history of the war was to ascribe the psycho-neuroses of warfare to the concussions of shell-explosion, an attitude crystallised in the unfortunate and misleading term "shell-shock" which the general public have now come to use for the nervous disturbances of warfare."
> (Rivers, 1920, p 1)

Once it was realised that the causes were mental, rather than physical, there was no ready model to explain them. Freud's focus on the sexual as the primary cause of psychoneurosis had not been generally accepted and had been the grounds for great hostility and ridicule within medicine (Rivers, 1920), and had precluded any consideration of possible explanatory factors within the model relevant to understanding war neuroses. Rivers (1864-1922) was Medical Officer at Craiglockhart War Hospital (Edinburgh). On the basis of his clinical experiences with men returned from the trenches for recuperation and rehabilitation, River's assessment of Freud's theory was that the objective conclusion to be reached was that in the vast majority of cases sexual factors were not implicated as causal factors. In his own classic text, *Instinct and the unconscious. A contribution to a biological theory of the psycho-neuroses*, Rivers proposes that a more fundamental instinct, that of self-preservation in the face of danger, is responsible.

Rivers considers the "danger-instincts" as the possible mechanism for suppression (of affect and memory) in fear responses. Of these, he identifies flight as perhaps the most deeply seated of the behavioural responses to danger threatening existence or integrity. Along with aggression and "manipulative activity" (a response involving often complex activity to avoid the danger, as in discharging a weapon, or manoeuvring a car or aeroplane, and which he considers the normal reaction of healthy man), these responses involve purposeful activity. Contrasted with these is immobility – the complete cessation of movement (and vocalisation) to conceal the animal (or human) from the threat of a predator or attacker, whose visual system is particularly primed to respond to perceptions of "biological motion" (Johansson, 1975). Finally, is collapse, a response associated with terror and accompanied by tremors of movement which are not purposeful activity and expose the individual to any attacker; this state represents a failure of the self-preservation instinct. Of these responses, it is proposed that immobility is most associated with suppression of memory for the traumatic event into the unconscious. It is this response which is perhaps most closely aligned with modern conceptions of the role of feeling trapped, powerless and helpless in the causation of PTSD.

In relation to his theory, Rivers makes a careful distinction between suppression and repression (Rivers, 1918; 1920). Suppression is the unwitting process, by which some part of the traumatic experience becomes separated from normal consciousness, and which he considers closely resembles the term "dissociation"; he considered this responsible for the fugue states as a response to trauma, rather than for the symptoms of hysteria, although in other parts of his work he does consider hysteria as a variant of the immobility instinct, leading to suppression. Repression is described as the active or voluntary process which attempts to remove experience from memory; it is not considered pathological in itself, but only when it fails to adapt the individual to their environment. Rivers considered repression of war memories unhelpful and responsible for many of the symptoms; his approach to treatment was to identify them through talking with the patient, working back through triggers and reminders, until the layers of experience responsible were uncovered. It is possible that suppressed memories were also uncovered in this way.

Rivers states that: “One of the most frequent features of the hysteria of warfare is mutism.” (Rivers, 1920, p 132). This is in fact a matter of common knowledge: in common parlance we speak of one being “struck dumb with terror”. This is explained in the context of the immobility response to danger: if a group adopts immobility, then any cry (which frequently accompanies flight to alert conspecifics to the presence of threat) becomes totally inappropriate, as this too serves to expose the whole group to an attacker. In this way, Rivers clearly sees mutism as adaptive and part of the suppression or dissociation response.

Rivers’ approach, like Janet’s, was a talking cure, working with the patient until they could verbalise the memories that had become suppressed, or dissociated. Not all clinicians took this approach. A traditionalist view perceived sufferers of war neurosis as morally inferior, or as malingerers and cowards. On this basis treatment consisted of shaming, threats and punishment. The British psychiatrist Yealland was a typical proponent of this view; mutism was treated by strapping a patient in a chair and applying electric shocks to the throat, for hours if necessary, until they finally spoke (Shephard, 2001). This was the approach typically taken in Germany, where following the war there was no diagnosis equivalent to PTSD and symptoms were recast as a failure of will (van der Kolk et al., 1996b). Freud considered war neuroses as promoted by a conflict in will: between the old peacetime ego and the new warlike ego. The old ego responds by a flight into illness to escape from the dangers of war. He considers a precondition for this state to be a national [conscript] army: “there would be no possibility of their arising in an army of professional soldiers or mercenaries” (Freud, 1920/1955, p 209). Events of contemporary war experiences have clearly proved otherwise. Freud was called upon to give an expert opinion by the Austrian War Ministry on the alleged brutality of army doctors. He states:

> "It seemed expedient to treat the neurotic as a malingerer and to disregard the psychological distinction between conscious and unconscious intentions, although he was known not to be a malingerer. Since his illness served the purpose of withdrawing him from an intolerable situation, the roots of the illness would clearly be undermined if it was made even more intolerable to him than active service …. for this purpose painful electrical stimulation was employed, and with success."
>
> (Freud, 1920/1955a, p 213)

"Success" was in terms of restoring the soldier to service, not in a cure; as Freud goes on to say, the effects of the electric current were not lasting. As to its negative consequences, Freud acknowledges that the strength of the current used was high and that it was well known that in German hospitals there were deaths as a result of the treatment as well as associated suicides.

Freud ends his report:

> "But with the end of the war the war neurotics, too, disappeared – a final but impressive proof of the psychical causation of their illnesses."
>
> (Freud, 1920/1955a, p 215)

Any further influence Rivers may have had was curtailed by his death not long after the end of the First World War, in 1922. However, it is clear that the "war neurotics" did not disappear. Abram Kardiner (1891-1981) was one of the few individuals who underwent analysis by Freud himself as a student-patient in 1921-2 (Kardiner, 1977). On his return to the USA, Kardiner took up a post at the Veterans Bureau, working with the chronic cases of "shell shock" from the war. As a result, he wrote the classic *Traumatic Neuroses of War* in 1941, and then reformulated this book as *War stress and* *neurotic illness* after the Second World War, to incorporate experience of acute cases with his collaborator, Spiegel (Kardiner & Spiegel, 1947).

Based on this experience, there is recognition that many circumstances (such as fatigue, pain or, in opposition, morale and leadership) will influence the point at which an individual is overwhelmed by trauma. The acute onset may be very different in different circumstances. However, Kardiner (1947) recognised that once established, the war neuroses:

> "…[firstly] are characterized by an unusually small number of symptoms and an uncommon stereotypy. Every case is almost like all the others. [Secondly]… the psychic elaboration of these neuroses is extremely limited …. The situations feared and avoided by the patient are the actual ones under which he broke, not symbolic extensions of the basic trauma."
>
> (Kardiner & Spiegel, 1947, p168)

Kardiner sees trauma as an external factor which initiates an abrupt change in previous adaptation. In a manner reminiscent of Janet's concept of action in memory and in integration and synthesis of experience, Kardiner considers the roles of perception and execution in ongoing adaptation to events; the fear encountered in trauma – the perception of danger and threat – disrupts the executive functions that normally deal with accommodation to the external world. There is a "neurotic alteration of adaptation" (Kardiner & Spiegel, 1947, p187) or rupture of the equilibrium between the individual and the outside world: increased sensitivity to the danger situation leads to avoidance, which is not curative and which is in any case futile since "the subject carries the traumatic situation with him at all times, and cannot rid himself of it. He may succeed …. while he is awake, but when he attempts to sleep, the distressing nightmares with the content of annihilation continue to terrify him." (p 189). At the same time there is "a repressive factor operating" (p191) which results in amnesia for at least a part of the trauma. He also notes disturbances of sensory and/or motor functions, which suggest the patient is re-living experience of the traumatic environment, and of the autonomic nervous system (ANS), hence his use of the term "physioneurosis" as the core of the disorder.

His long experience with chronic cases leads Kardiner to suggest that ongoing reduced functioning in the activities of living is not uncommon and is not amenable to treatment; the optimum intervention is in the acute phase, but is not always successful. On the other hand, probably from his psychoanalytic training, he still holds on to the idea of secondary gain to the patient from the illness (drawing on notions of repression) and these two opposing views lead him to some discussion of the problems of compensation that are still relevant today. On the one hand he is clearly of the opinion that there is an intractable "physioneurosis", which changes the whole personality and greatly reduces functioning; on the other hand he sees a danger in there being no incentive to recover if compensation is allowed. He considers this situation is exacerbated by the lack of both recognition of the disorder and any understanding of its psychopathology, and of psychiatrists trained in recognising and dealing with the disorder and the fact that the disability is hidden and not easily demonstrable in court.

The descriptions of failure of adaptation and the resulting symptoms both reflect present day criteria for the disorder and bear some similarity to Janet's observations. However, while Janet was clear about the role of dissociation, Kardiner struggles to find any explanatory account of war neuroses. He believes any theory should be derived from the data and be consistent with it and, since the neurosis is the same as that encountered in response to civilian trauma, that the theory should therefore apply to all cases of trauma induced neurosis. He is unable to apply Freud's theory of sexual instinct;

neither can he transform this theory to fit the observed responses to trauma. Even writing in retrospect, he says:

> "My efforts to create a theory for the war neuroses proved impossible. Working with the concepts of the libido theory, which are based on instinctual energies, phylogenetically programmed stages of development, and a predetermined Oedipus complex, left little room to explain the response to a traumatic experience, whether in war battle environments or any other situation offering an immediate threat to survival. But I tried …. and then abandoned the project."
>
> (Kardiner, 1977, p 111)

Once again, the revelations of a clinician working for many years with chronic cases of PTSD had little impact on a psychiatry framed by psychoanalytic theory, a theory which could not be made to fit the facts of the observed responses to the reality of external events in the world; once again the consequences of trauma were ignored at the end of the war. This was despite repeated evidence that vulnerability could not be identified *a priori*, and that clinical opinions on who would survive war psychologically unscathed were equally unreliable. The Americans, particularly, had tried to learn from British experience and to actively screen out potentially vulnerable young men from the armed forces when they entered World War II, an attempt that was a total failure (Shephard, 2004). Not only were large numbers of applicants excluded, generating questions about "the state of the nation's manhood", but rates of psychological breakdown were not reduced. It still remains not possible to predict post war psychological disorder (Rona et al., 2006). Section 1.5 returns to consider the extent to which there may be individual risk factors for PTSD.

It took another war, the Vietnam conflict of the 1960-70's, and a particular set of political circumstances for the next rediscovery of the effects of warfare to lead to the formulation of PTSD as an accepted diagnosis in the DSM. [This war passed by Britain and Europe, being fought by the USA, although there was involvement from commonwealth countries geographically close to south-east Asia, such as Australia and New Zealand.] This time, the imperative was not from psychiatry or the military, but from the efforts of the soldiers themselves. In previous wars at least soldiers had been treated as heroes. With the war still in progress there was a growing anti-war movement amongst both civilians and the soldiers themselves. "Rap groups" organised by the veterans, to enable them to share their experiences of war and to raise public awareness, proliferated, supported by sympathetic psychiatrists. Their pressure led to the establishment of the Veterans Administration; the studies by this body once again described the disorder of PTSD.

At the same time, the rise of the feminist movement in the 1970's was bringing to public awareness the reality and extent of rape experienced by women, and of child abuse, and rape crisis centres also proliferated, again outside of established mental health system; a centre for research on rape was created in 1975 at the National Institute of Mental Health (Herman, 2001). The movement redefined rape as a crime of violence, countering the old established views, based on Freudian ideas, of rape as wish fulfilment of women's inner desires. As both groups created descriptions of the syndromes with which soldiers and raped women presented, it was recognised that they were describing the same disorder.

> "The implications of this insight are as horrifying in the present as they were a century ago; the subordinate condition of women is maintained and enforced by the hidden violence of men. There is war between the sexes. Rape victims, battered women and sexually abused children are its casualties. Hysteria is the combat neurosis of the sex war."
>
> (Herman, 2001, p 32)

The working groups on the DSM III included these syndromes together and named them as Posttraumatic Stress Disorder (American Psychiatric Association, 1980). As one "new" controversial illness was added to the DSM III, so an old controversial illness, homosexuality, was "cured" and dropped from the DSM. Critics object that these political forces have created in PTSD not a true disorder, but a social construction of the 20th century (e.g. Summerfield, 2001; 1999; Jones et al., 2003); the counterpoint to this view is that it confuses social construction with the empirical facts of the disorder. Simply because a fact is socially constructed does not mean that it has no real existence (Rechtman, 2004).

It seems that, historically, knowledge of the consequences of trauma is not sufficient to guarantee ongoing study of the resultant disorder. Commentators (e.g. Herman, 2001; McFarlane & van der Kolk, 1996) observe that the ordinary response to atrocities is to want to ignore and deny them; to bear witness to someone else's trauma is to acknowledge that one is not invulnerable either. Denial, suppression and dissociation operate at a societal as well as an individual level to all sorts of trauma, perhaps notably in respect of the events of the Holocaust.

> "Society's reactions to traumatized people are rarely the results of objective and rational assessments. Rather they are primarily the results of conservative impulses in the service of maintaining the belief that the world is essentially just, that "good" people are in charge of their lives, and that bad things only happen to "bad people. Although people are capable of profound bursts of spontaneous generosity to victims of acute trauma, the continued presence of victims as victims constitutes an insult to the belief (at least in the Western world) that human beings are essentially the masters of their fate. Victims are the members of society whose problems represent the memory of suffering, rage, and pain in a world that longs to forget."
>
> (McFarlane & van der Kolk, 1996, p28)

These authors argue that since it is difficult to be objective and impartial about the effects of trauma, the way forward is in a scientific approach to study of the biological and psychological effects of trauma, based on empirical data. The inclusion of PTSD within the DSM at least provided recognition of the disorder and an organised basis on which to move forward. The next section (1.3) considers some of the progress made in this direction on matters relevant to the experimental work of this thesis.

A series of historical individuals who worked with victims of trauma and war recognised the importance of physiology: in the arousal symptoms (Criterion D: Table 1.1) (Da Costa, 1871; Page, 1883), and that physiology lay at the core of the disorder (Janet, 1889; Rivers, 1920; Kardiner & Spiegel, 1947). Recent application of neuroimaging techniques are contributing to increased understanding of the neurobiology of PTSD (e.g. Pitman et al., 2001; Hull, 2002; Grossman et al., 2002; Liberzon & Martis, 2006). Rivers (1920) identified the helplessness of the immobility response as important, now recognised by Criterion A2; Kardiner (1947) recognised the stereotypy of symptoms (criteria B,C &D) provoked by different traumas; Page (1883) described the inability to function as a consequence of the disorder which now constitutes Criterion F.

In other respects, these historical figures identified factors which presage current understanding emerging from neurobiology: that language functions may be compromised in people with PTSD (Rivers, 1920) and that this is important to memory: that verbalisation is involved in re-integrating fragmented traumatic memories which have become dissociated as a result of “vehement emotions” (Janet, 1911). These relationships, between fear-arousal-language-memory, are not only becoming increasingly understood in neurobiological terms, but as involving functions lateralised in the brain. The fear response and its biological and psychological effects are introduced in Section 1.3 and explored by the experimental work of this thesis in relation to handedness – another lateralised function which appears to be relevant in PTSD.

1.3 PTSD as a disorder: of emotion, dissociation and memory

This section will first outline the prevalence of PTSD as a disorder. At its core there appear to be biological changes as a result of an extreme fear response; these are outlined and the implications explored, particularly in respect of significant alterations to neuropsychological functioning and because lateralisation of functions in the brain increasingly appears to be relevant to the experience of emotion, to memory and the disorder.

The DSM-III diagnosis of PTSD referred to above was formed by a committee compiling signs and symptoms evident in war veterans and abused women, by reference to the literature, particularly Kardiner, and as part of a political process (van der Kolk et al., 1996b). A separate committee of researchers and clinicians had been formed to consider the diagnostic system for dissociative disorders; initially neither was aware of the work of the other or of the relevance of dissociation in trauma (based particularly on Janet's work). Despite subsequent recommendations from both committees that their work, and the diagnostic categories, should be combined, PTSD was categorised as an anxiety disorder (van der Kolk et al., 1996b). It remains so categorised despite recommendations at both DSM-IIIR (1987) and DSM-IV (1994) revisions that this be re-considered (Brett et al., 1988; Davidson & Foa, 1991, respectively), or indeed that PTSD should form a new diagnostic category based on its aetiology (Davidson & Foa, 1991; Brett, 1996). These arguments will not be pursued in detail here, other than to point out that one of the main objections to the current classification of PTSD as an anxiety disorder is that it does not focus on the unique and distinctive aspects that have to do with memory.

DSM-III required the traumatic stressor to be one that would "evoke significant symptoms of distress in almost everyone" and deemed to fall "outside the range of usual human experience". DSM-IV redefined the stressor, acknowledging that some precipitating stressors were actually common; the stressor now has to involve actual, or threat of, death or serious injury and can be vicariously experienced, but has also to be experienced with intense fear, helplessness or horror (now included as criterion A2). DSM-IV also added the requirement (criterion F) that significant distress and impairment in daily functioning had to be present in some form for at least one month. There are ongoing controversies over the scope of potential traumatic stressors (e.g. McNally, 2004) but these are not considered further here.

Experience of trauma is a common phenomenon. The (US) National Comorbidity Survey (NCS; Kessler et al., 1995) found that approximately 60% of men and 50% of women experienced at least one trauma in their lifetime and estimated lifetime prevalence of PTSD was 7.8%. Although men were more likely to experience trauma than women, more women than men had lifetime PTSD (10.4% *vs* 5.0%); sex differences are considered further in section 1.4. In approximately one third of cases, PTSD became chronically unremitting, whether or not treatment had been received. In a replication of the NCS, rates of 12 month prevalence of PTSD were 3.5%, with 36.6% of these considered severe cases (Kessler et al., 2005b); lifetime prevalence was estimated at 6.8% overall, but was higher in ages 30-44 and 45-59 at 8.2% and 9.2%

respectively (Kessler et al., 2005a). DSM-IV widened the criterion A1 definition of trauma, but by imposing the subjective element in criterion A2 and imposing a criterion of functional impairment, criterion F, may have led to a narrowing of the definition overall. Lifetime exposure to traumas which may precipitate PTSD was found to have increased to 77.6% as a consequence of widening criterion A1, and the conditional probability of developing PTSD after a trauma meeting A1 and the subjective A2 criterion was found to be 12% (Breslau & Kessler, 2001) compared to an earlier estimate of 9.2% (Breslau et al., 1998); events not involving A2 rarely resulted in other criteria for PTSD being met.

These prevalence rates may, however, be underestimates, particularly in certain subsets of the population. In a study of 275 patients receiving public health services for severe mental illness, Mueser et al (1998) found that 98% of these reported at least one lifetime trauma. Rates of PTSD were high: 43% of patients were found to have PTSD, but only 2% had received this as a diagnosis. Similarly, in a study of psychiatric inpatients, McFarlane et al (2001) found that 61% of patients reported at least one lifetime trauma and 28% met criteria for lifetime PTSD; only one of the 141 patients actually had a formal diagnosis of PTSD recorded in their case notes. High rates of PTSD, often unidentified, have also been found in prison populations; prevalence rates for PTSD recorded in a New Zealand prison for the preceding month were 16.6% for women and 9.5% for men (Brinded et al., 2001).

Indeed the NCS-R (Kessler et al., 2005a) identifies four possible sources of bias, all of which render estimates conservative. First, people with mental illness may be less likely to participate, either due to sample frame exclusions (of, for example, the homeless), differential mortality or reluctance. Second, and similarly, there is a bias against reporting embarrassing behaviours, whether by survey or in a clinician interview. Third, assumptions in estimating lifetime risk assume constant conditional risk across age groups, but in fact cohort effects seem likely: prevalence appears higher in more recent cohorts. Fourth, age at onset may be recalled incorrectly; either by telescoping events to the more recent past or by age related failure to report past disorders, thus creating the false appearance of a cohort effect. Taken together, Kessler et al (2005a) suggest that estimates of lifetime prevalence and projected risk are likely to be conservative.

Interpersonal violence is the most inherently trauma producing event (Frederick, 1984; cited in Adams et al., 1998); combat and rape are the most potent events in precipitating PTSD. They are also most often experienced in adolescence and early adult life. Herman (2001) points out that the average age of the Vietnam combat soldier was 19; of women who are raped, half are aged 20 or under, and three-quarters are aged between 13-26 at the time of the rape. Indeed a recent review of the literature considering age of onset for all mental disorders found that approximately half of all lifetime disorders start by the mid-teens and three quarters by the mid-20's (Kessler et al., 2007); for PTSD age of onset at the 50th percentile is 23 years and at the 75th percentile is 39 years (Kessler et al., 2005a). This is relevant to considerations of the prevalence of PTSD in the student samples in the experimental chapters which follow; students are not immune from experiencing trauma by their relatively young age, but rather may be at an age particularly vulnerable to experience major trauma.

PTSD carries with it a high comorbidity of other mental disorders, particularly substance abuse, which is considered further below in relation to sex differences (section 1.4), and depression; in the NCS, 47.9% of men and 48.5% of women had comorbid depression while 51.9% of men and 27.9 % of women had co-morbid alcohol abuse (Kessler et al., 1995). Substance abuse may occur as an attempt to control arousal symptoms (van der Kolk et al., 1996a) as indicated in Figure 1.1 below (p 29). Major epidemiological studies suggest that PTSD is the primary disorder more often than not (Kessler et al., 1995) and that it is unlikely that this is due to separate pathways to each disorder (Breslau et al., 2000). In a clinical study of psychiatric inpatients, PTSD was found to be the incident disorder in 50% of cases, and preceded depression in 83% of cases (McFarlane et al., 2001).

PTSD also carries with it a high risk of suicide, perhaps unsurprisingly, for a disorder where a third of cases may become chronic and unremitting. There are established findings of high risk for suicide associated with combat situations (e.g. Adams et al., 1998) and in women who have been raped, where nearly one in five may attempt suicide (Steketee & Foa, 1987). In a sample of civilian patients with chronic PTSD, more than half (56.4%) reported some aspect of suicidality; 38% reported ideation, 8.5% had made plans and 9.6% had attempted suicide since experiencing trauma (Tarrier & Gregg, 2004). McFarlane (2004) reports higher odds ratios for various aspects of suicide in PTSD than depression in the Australian National Mental Health and Wellbeing Survey. A recent assessment of 12 month prevalence estimates of suicide ideation, plans and attempts were 2.6, 0.7 and 0.4 % respectively (Borges et al., 2006). Both PTSD and experience of victimisation through sexual or physical abuse (after controlling for depression) were identified as significant risk factors for suicidal ideation and attempts in a large (n=4023) national probability sample of adolescents (Waldrop et al., 2007), the first study to specifically consider the presence of suicidal behaviour in adolescents meeting diagnostic criteria for PTSD. The prevalence of

PTSD and its associated comorbidity therefore constitutes a major public health problem.

The development of PTSD is a progressive process, unfolding over time, with multiple mechanisms involved. Increased understanding of this process raises questions about how the symptoms associated with PTSD should be viewed. At present, a diagnosis of PTSD depends on the presence of a minimum number of symptoms from three clusters: one re-experiencing (criterion B), three avoidance (criterion C), and two arousal (criterion D). It has been suggested that symptoms in the avoidance cluster are not coherent as a construct – several are dissociative (emotional numbing, amnesia) and others behavioural (avoiding reminders, feeling cut off from others and diminished participation) (Bremner, 1999a). In the absence of numbing responses, symptomatic of peri-traumatic or secondary dissociation (discussed below), then all remaining symptoms must be endorsed to meet criterion C; individuals may have high symptom scores in the other criteria, yet fail to meet this one, and escape a PTSD diagnosis (North et al., 1997).

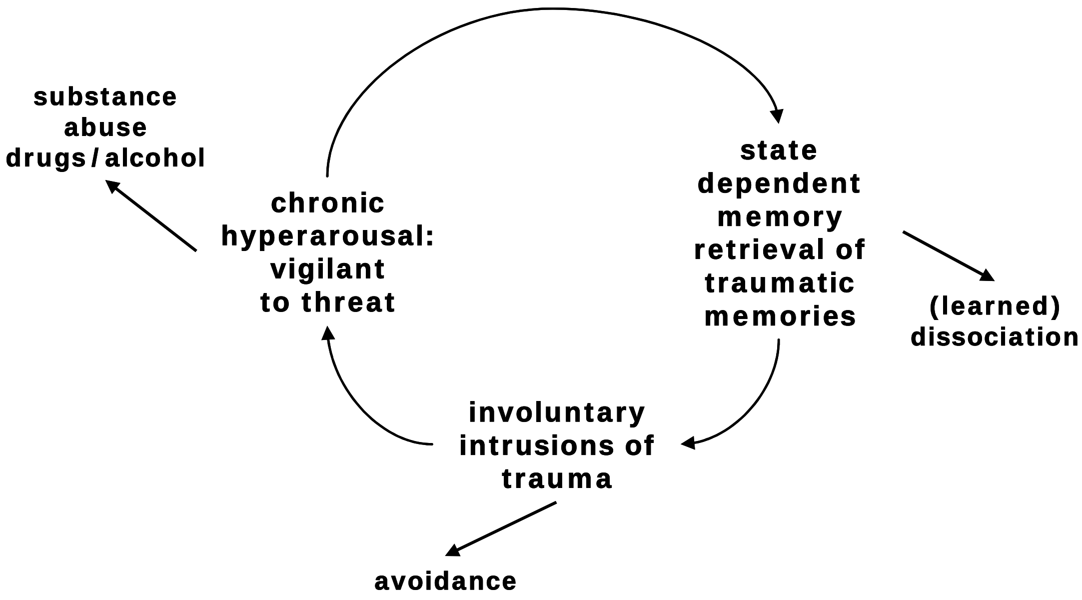
In addition, longitudinal studies suggest that avoidance symptoms may not directly relate to the aetiology of the disorder. McFarlane (1992) found, using path analysis, that the intrusion subscale score of the IES (Horowitz et al., 1979) [which does not include arousal symptoms] accounted for the link between a natural disaster (extensive bushfires) and posttraumatic disorders in fire-fighters; avoidance had no direct relation with onset of symptoms. Neither intensity of exposure nor property loss, predicted the onset of disorder; the only significant aetiological path was from property loss only at 4 months, plus exposure at 11/29 month follow up, via intrusion symptoms to disorder. Avoidance symptoms were predicted only by the severity of intrusive memories at these time points post-disaster. Similarly, symptoms in the avoidance cluster appeared only over the course of time in a follow-up study of a mass shooting (North et al., 1997).

These findings suggest that avoidance is not directly related to trauma, or PTSD, but rather occurs as a defence reaction to the intrusive memories of the trauma. This is contrary to the common idea of alternating states of intrusions and avoidance; Koren (1999) found that symptoms plateau and remain constant rather than alternate in cases of PTSD in road traffic accident (RTA) victims. In a neuroimaging study assessing symptom responses to script driven imagery, only re-experiencing and avoidance scores were correlated (and positively) providing further support for direct links between these symptom clusters (Hopper et al., 2007).

The arousal cluster of symptoms (criterion D) may therefore be those crucial to developing PTSD; while some form of re-experiencing is common after trauma, the phenomena which typically distinguish those who will develop PTSD are the emergence of arousal symptoms (McFarlane, 1998). Physiological responses, such as elevated heart rate, immediately following trauma have been found to predict later emergence of PTSD (Shalev et al., 1998). Arousal symptoms were found to be most prevalent at both time points in the mass shooting study mentioned above (North et al., 1997). The pattern of symptom responses to trauma and common ways of coping, with substance use as self-medication to control arousal symptoms, can be outlined as in Figure 1.1 below, based on van der Kolk et al (1996a).

Although PTSD is currently classified as an anxiety disorder, it is fundamentally a disorder of emotion, specifically fear. It is becoming clear that the emotions are distinct from one another and mediated by different brain systems (LeDoux, 1999; Schulkin et al., 2003; Adolphs et al., 2003; Phan et al., 2004); fear is one of the basic emotions

Figure 1.1 Diagrammatic representation of the vicious cycle of responses to trauma and common ways of coping (based on van der Kolk et al., 1996a)



(fear, anger, disgust, sadness, surprise and happiness) which are distinguished by different autonomic responses and physiology (Ekman et al., 1983; Ekman, 1992). It has long been observed that recognition of these emotions is cross-cultural, universal in humans and recognisable in animals and is considered instinctual, or innate, rather than learned (Darwin, 1872). Since identifying and escaping danger is important to all organisms in order to survive, the underlying, biologically based, emotional functions are likely to be preserved across species. Self-preservation, as Rivers (1920) observed, has to be the most fundamental instinct of all and some of the oldest parts of the brain are involved in fear (and self-preservation) responses and do not require involvement of evolutionary more recent cortex. The (basolateral) amygdala is particularly involved in the experiencing of fear and in triggering responses to fear. Feelings of fear arise from conscious awareness of the behaviours resulting from the operation of this defensive system and involve the prefrontal cortex (PFC) (LeDoux, 2000); such feelings are not the primary function of the fear system in the brain (LeDoux, 1999).

1.3.1 Lateralisation in emotion

At this most fundamental level, lateralisation of the brain is implicated. The right hemisphere is involved in the experience of emotion, particularly the negative emotions and fear, and in spatial awareness. The left hemisphere, specifically Broca's area, is involved in language functions. Differences in hemispheric organisation arise developmentally via a right to left maturational gradient between the hemispheres: pre- and post-natally, the right hemisphere develops sooner than the left hemisphere. Since the brain is a three-dimensional structure lateralised development interacts with other axes: anterior-posterior (primary-secondary motor and sensory zones through to tertiary association areas) and ventro-dorsal (from basal to superior, or lower to upper) gradients. The effect of a growth vector across these dimensions results in a counter-clockwise torque evident in the developing and adult brain: the left hemisphere appears twisted rearward and dorsally while twisting in the right hemisphere is forward and ventral (Best, 1988). The forward extension of the left prefrontal areas is one of the last developments of the hemispheres and associated with later-emerging characteristics. Thus there is early right hemisphere appraisal of emotion in speech utterances, and discrimination for musical notes at two months while the beginnings of speech-related discrimination does not occur until three months post-natally, (Best, 1988). These right hemisphere functions reflect the importance of emotion early in life in establishing bonds with caregivers. This topic is revisited in Chapter 9.

There is neuropsychological (Gainotti, 1972), perceptual (Dimond et al., 1976), neuroimaging (Canli et al., 1998) and non-human primate (e.g. in monkeys: Hauser, 1993) evidence that suggests that the right hemisphere of the brain is differentially involved in the experience of emotion, particularly negative emotion such as fear. Feelings of emotions can be generated by voluntary contractions of the appropriate muscles in the left side of the face (Schiff & Lamon, 1989) and the right hemisphere is activated in neuroimaging studies of facial mimicry of emotional expressions (Lee et al., 2006; Esslen et al., 2004) and assessment of facial emotion (Nakamura et al., 1999). Besides responses to visual material, the right hemisphere is activated in response to angry prosody irrespective of the attended ear and task in hand (Grandjean et al., 2005).

Davidson and colleagues have investigated behaviours associated with manipulations of affect. Negative affect (e.g. fear, disgust) is accompanied by withdrawal reactions, such as turning away from a stimulus or fleeing and is associated with frontal right hemisphere activation (besides involvement of the amygdala), while positive stimuli and approach behaviour are associated with frontal left hemisphere activations (Davidson et al., 1990; Davidson & Sutton, 1995). Pre-frontal asymmetries in individuals are posited to result in differences in affective style along this approach-avoidance dimension (Davidson, 2001; Davidson, 2003) and other models have also proposed links between hemisphere activations and states of arousal and personality traits (e.g. Heller, 1993).

Asymmetries in cerebral organisation occur across species and several examples of species invariance are striking. At least in birds and mammals, there is selective involvement of the right hemisphere in spatial tasks. In *all* vertebrate classes, as in studies with humans noted above, the right hemisphere is associated with escape, attack and sexual behaviour, while the left hemisphere is associated with species-specific vocalisation and with processing of temporal acoustic information across species (Vallortigara & Bisazza, 2002). Discussions in respect of handedness as lateralised behaviour, and comparative perspectives, are considered in Chapter 9 and are not pursued further here.

LeDoux (2000) has argued that increased understanding of "emotions" will only come through operationalising these in more precise ways amenable to experimentation and by separating the basic emotions for study: in fear this has been done by focussing on neural circuits of a mechanism responsive to threat or danger, rather than the mechanism by which fear is subjectively experienced. By studying fear, the emotion relevant to PTSD and this thesis, much has been learned and is introduced here. LeDoux (2000) also makes the important point that similar approaches to the other basic emotions will be required, before generalisations about "emotions" can be attempted. This is important in the consideration of methods required to investigate phenomena which may be relevant to PTSD and is pursued further in Chapter 2.

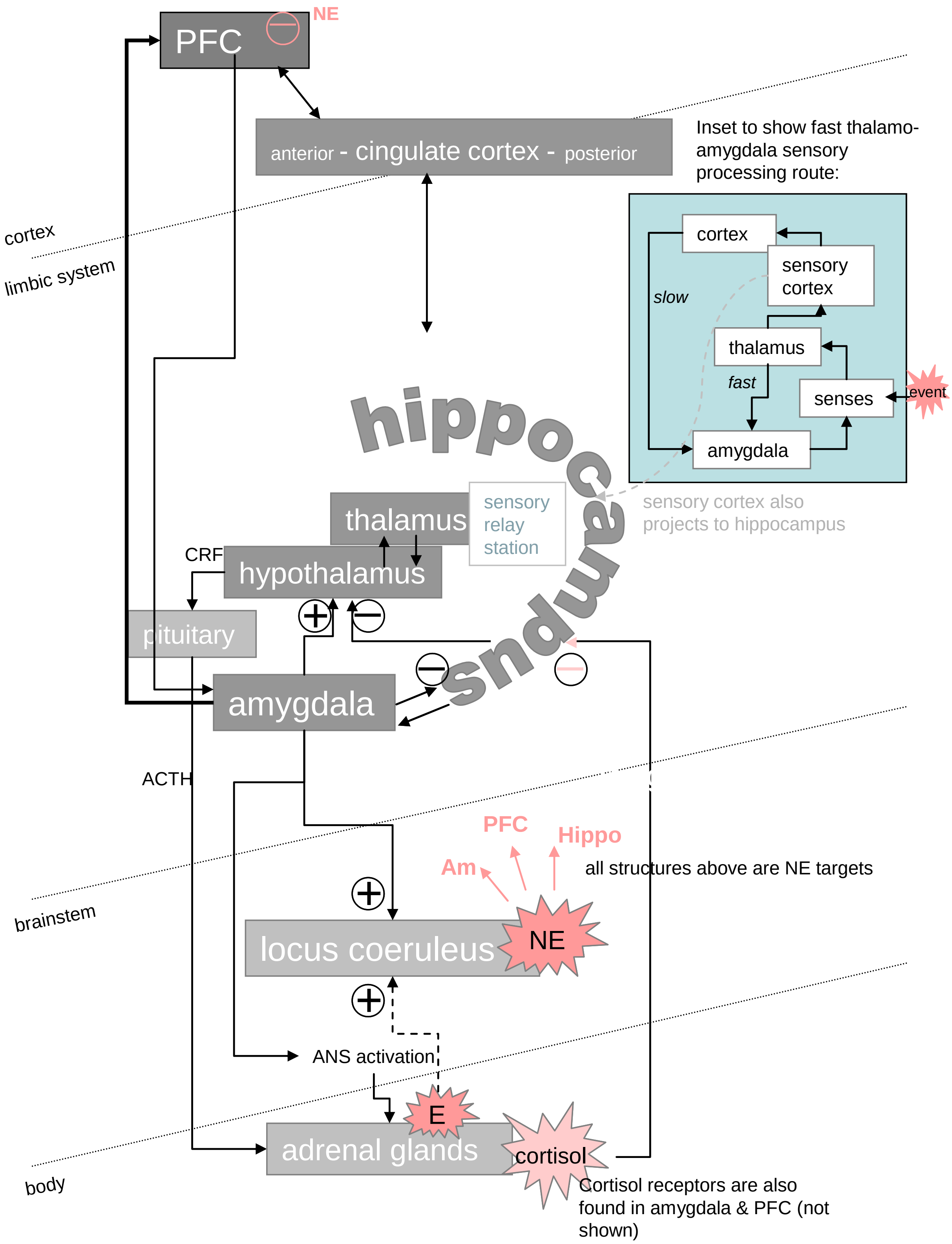
There are also ethical difficulties in carrying out experimental research in fear responses in humans; much of what is known is based on animal models of fear, but results suggest that these translate to human experiences in PTSD (e.g. Rosen & Donley, 2006; Phelps & LeDoux, 2005; Delgado et al., 2006). There has been a long history of using animal models in studying depression, such as "learned helplessness" as a model (Seligman & Maier, 1967); such studies invariably subject animals to an extreme and inescapable stressor. Bremner et al (1999) point out that these studies, designed to be indirect models for depression are actually direct models for PTSD, as the diagnosis requires exposure to an extreme, typically uncontrollable stressor.

1.3.2 The fear response

The amygdala dependent fear response to threat or danger is set in motion when an externally occurring event is perceived by the organism through one or more of the senses. Sensory information passes through the thalamus before passing to the sensory cortex (though olfactory stimuli pass to the entorhinal cortex, an ancient part of the cortex and which is associated with the hippocampus (*q.v.*); olfactory stimuli also pass directly to the amygdala). The thalamus acts as a relay station and projects to the amygdala; blocking this pathway results in a failure of fear conditioning (LeDoux, 1999). Although sensory information also passes to the cortex which ultimately feeds back to the amygdala, this is a slower route. The amygdala initiates the fear response without involvement of the cortex, thus enhancing chances of survival by effecting immediate reactions to danger (Liddell et al., 2005). Figure 1.2 below outlines the structures and processes involved and which are discussed below.

Understanding of the fear response outlined in Figure 1.2 is increasingly seen as important in understanding the disorder of PTSD and the consequences which adversely affect normal functioning. Not only that, but the structures and functions involved are shown to be lateralised in the brain. This may therefore be important in understanding why handedness may be a relevant factor in PTSD. In left handers, there has been a switch of dominant hand motor control to the right hemisphere, but this does not mean that left handers are a mirror image of right handers (discussed further in Chapter 9); the majority (70%) of left handers retain language functions in the left hemisphere. There is no easy way to distinguish language lateralisation, so it has to be acknowledged that any group of left handers will be more heterogeneous than right handers in this respect. In order to set the context for the evidence which may be important in understanding relationships between lateralisation and PTSD, the fear response and its consequences is first outlined in relation to Figure 1.2. The remainder of this section then considers the evidence in relation to this outline and the structures and functions of the brain which are lateralised and implicated in PTSD.

Figure 1.2 Outline of relationships between structures involved in the fear response, maintaining approximate neuroanatomical relationships between them and with inset summarising the subcortical, thalamo-amygdala fast processing route. Diagonal lines indicate broad divisions of parts of the brain and are named in the left margin.



The fear response is instigated without conscious awareness by the amygdala, setting in motion a cascade of neurotransmitter (chiefly norepinephrine, NE, from the locus coeruleus) and hormonal responses (via the hypothalamic-pituitary-adrenal axis: HPA-axis) which are excitatory in nature and catabolic in terms of preparing the body for action in surviving the threat through "fight or flight".

Since it is vital for continued survival that an organism remembers the source of danger, fear conditioning is a form of associative learning that is sufficiently powerful that it occurs in response to a single event. This is how memory processes come to be crucially involved in PTSD. This learning occurs in the amygdala (Blair et al., 2005; Wilensky et al., 2006; Schafe et al., 2008). The PFC (which includes Broca's area in the left hemisphere) is bidirectionally connected to the amygdala; although the PFC is implicated in extinction (of fear conditioning), its inhibitory connections in this direction (to the amygdala) are weaker than those from the amygdala to the PFC. High levels of circulating NE, instigated by the amygdala in response to fear, can inhibit function of the PFC and thus "take out" the mechanism responsible for extinction. This makes evolutionary sense for survival, since it ensures that strong fear-related memories are not extinguished and forgotten.

Thus key parts of the brain implicated in PTSD are the amygdala and the PFC. The hippocampus is also bidirectionally connected to the amygdala and affected in PTSD. The hippocampus acts as part of a negative feedback control system on the HPA axis which ultimately secretes glucocorticoids and epinephrine, but in chronic fear situations can be adversely affected, failing to control HPA-axis output, to the extent that there is neuronal degeneration and reduced hippocampal volume has been found in people with PTSD (e.g. Bremner, 1999b; Bremner et al., 2003; Lindauer et al., 2006) although methodological issues have been raised (Jelicic & Merckelbach, 2004). The hippocampus is also implicated in declarative memory processes, and these become relevant to PTSD, although evidence is suggesting the hippocampus may be less important in this respect than formerly assumed, since it appears that hypoactivation of PFC functions are more relevant to PTSD.

As mentioned above, the amygdala sets in motion a cascade of neurotransmitter and hormonal responses which are excitatory in nature and affect both higher (via NE output of the locus coeruleus) and lower brain regions (via the hypothalamus). The hypothalamus releases corticotrophin releasing factor (CRF) which has two effects. Firstly, it causes the pituitary gland to secrete adrenocorticotropic hormone (ACTH) which is carried in the bloodstream to the adrenal glands which secrete adrenaline/epinephrine, noradrenalin/NE and corticosteroids or glucocorticoids (cortisol in humans) (Clow, 2004). Secondly, CRF containing neurons project to the locus coeruleus. CRF release increases the rate of firing of the locus coeruleus and the rate of release of NE. The amygdala also projects to other brainstem areas which instigate the different aspects of the ANS response. The central NE system is one of the few systems with widely dispersed projections; alterations in the NE system may therefore impact widely on the activity of neurotransmitters and brain systems (McFarlane, 1997). NE containing neurons project back to the PFC and structures of the limbic system including the hypothalamus, and thus stimulate the release of more CRF by the HPA-axis.

These two systems are thus interconnected and together are responsible for the fear response driven by the sympathetic branch of the ANS, but can be dissociated and are not equivalent (Clow, 2004). Enhanced NE functioning, directly, and through dysregulation of the HPA-axis and amygdala feedback to the locus coeruleus, is thought to be responsible for the re-experiencing and hyperarousal symptoms of PTSD (O'Donnell et al., 2004). The hemispheres appear to be asymmetrically involved in these physiologic processes in regulation of autonomic activity with right hemisphere control of arousal (Wittling, 1998). Concentrations of NE, involved in upregulation of arousal, have been shown to be consistently higher in the right hemisphere as are concentrations of serotonin, involved in downregulation of arousal. Dopamine is involved in co-ordination of motor responses with sensory input and in view of population right hand dominant motor control would be expected to show increased concentrations in the left hemisphere, and indeed, this is the case. The complementary nature of these systems in arousal and activation functions is discussed in detail by Tucker & Williamson (1984). Although NE clearly has a role in taking the PFC "off-line", there is evidence that dopamine systems may also be implicated in relation to stressors. A loud noise, to which people with PTSD seem to be especially sensitive (van der Kolk, 1996), affected performance on a spatial working memory task dependent on the PFC in monkeys, via a hyperdopaminergic mechanism. This relatively minor, and neutral stressor, was also able to take the PFC "off-line", and suggesting that more automatic, lower brain areas may regulate behaviour in this context also (Arnsten & Goldman-Rakic, 1998).

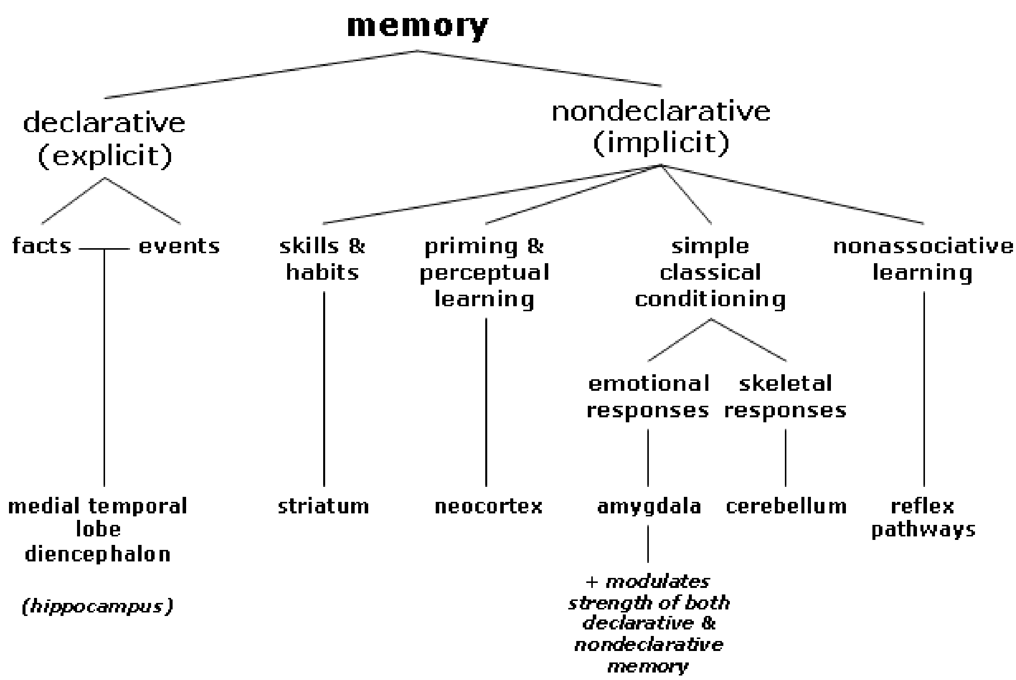
Aside from neurotransmitters, the hormonal system, via the HPA-axis, is the second main control system for the body and as noted above there are reciprocal influences between the two systems. Wittling (1998) suggests there is evidence of right hemisphere primary control of cortisol secretion in response to negative stimuli, irrespective of subjective emotion, although differential involvement of the hemispheres in other immune responses. Control of heart rate by both sympathetic and parasympathetic ANS is predominantly through right rather than left pathways, although control of contractility and atrioventricular conduction is by predominantly left autonomic pathways. Parasympathetic control of heart rate is thought to be impaired in individuals with right-brain damage. Experimental evidence in humans also suggests that pain sensitivity is higher in the right hemisphere.

Wittling (1998) suggests that brain asymmetry is a universal phenomenon, not only in cognitive and emotional states, but in the control of body processes, and is observed at all levels of the nervous system. In summary, the right hemisphere seems to be primarily involved in the control of functions relevant to survival and in coping with external challenges, whereas the left brain is involved in control of motor behaviours and higher integrative functions, and in regulation of defence responses against invading agents. This assumes that lateralisation of such control functions remains lateralised during successive hierarchical stages in processing and that descending pathways involved in autonomic control processes project ipsilaterally, at least within the brain, with no interhemispheric transfer. This is consistent with brain anatomy, and other evidence from detailed reference to visual processes, suggests that interhemispheric transfer via the corpus callosum is slow, particularly when aspects of a constantly changing stimulus have to be continually transferred, and induces errors, and thus is not relevant in these control processes.

The right hemisphere therefore plays a key role in responses to fear and perhaps not surprisingly, is thought to be particularly integrated with the amygdala (van der Kolk et al., 1997); presentation of a negative emotional stimulus appears to automatically access right hemisphere resources and transiently interfere with ongoing right hemisphere function (Hartikainen et al., 2000).

If the fear response is to be of ongoing survival value, then it must be remembered. A fundamental distinction can be made between declarative, explicit memory – a conscious recollection of facts and events – and non-declarative, implicit memory, which includes a variety of learning capacities expressed through performance including reflexes, skill learning, priming and perceptual learning and classical conditioning (Squire & Knowlton, 2000). A taxonomy of mammalian memory systems is shown in Figure 1.3 below.

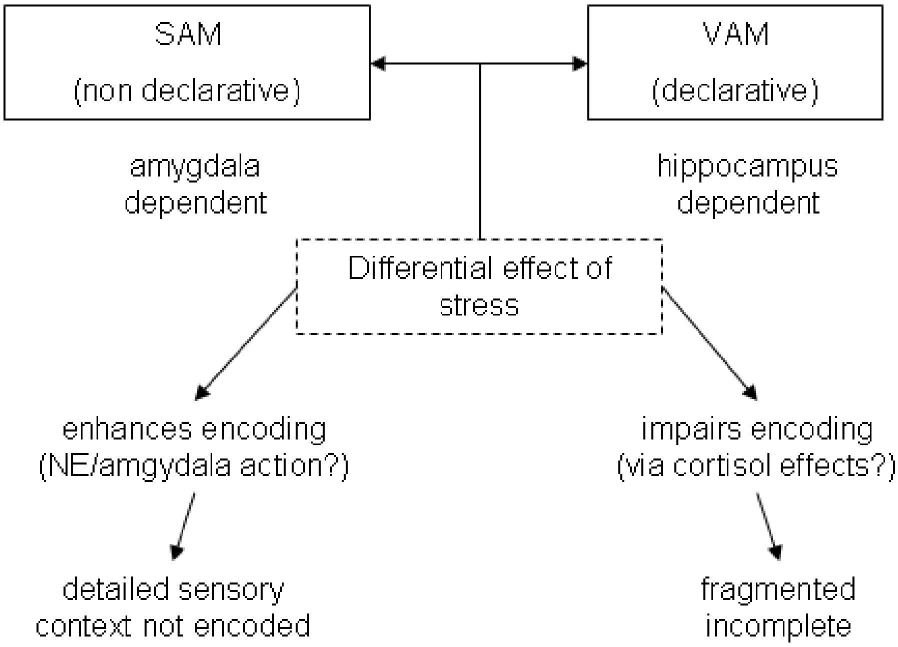
Figure 1.3 Taxonomy of mammalian long-term memory systems listing the brain structures thought to be responsible for each form of memory (from Squire & Knowlton, 2000; p776)



The amygdala (implicit), hippocampus and PFC (declarative) are all involved in memory functions and are affected in PTSD. There are bidirectional pathways from the amygdala to the hippocampus, which is particularly involved in contextual memory - the spatial and temporal aspects of memory - relevant to the sense of time or place which form the basis of episodic or autobiographical memory (Eichenbaum, 1999). Though based on animal studies, these findings appear to translate to human memory functions (Kesner & Hopkins, 2006). The hippocampus integrates information from the sensory processing areas of the cortex and provides contextual information to the amygdala which processes, and responds to, the emotional significance of stimuli. Fear conditioning involves the amygdala and is considered first below. LeDoux (1999) refers to these implicit memories of fearful events as *emotional memories*, and conscious, or explicit memories as *memories about emotions*; these are mediated by a medial temporal lobe system involving the hippocampus and related areas (Squire, 1992). The role of the hippocampus is temporary, binding together sites forming a memory until a more permanent memory is gradually established elsewhere, probably in neocortex (Eichenbaum et al., 1996). If the hippocampus is adversely affected by cortisol output in PTSD, hippocampus mediated conscious memories of a traumatic event may fail to form, whereas amygdala mediated implicit fear conditioning is strongly developed. Declarative memory is considered further below.

Understanding of the neurobiology of the fear response may help to refine cognitive models. Dual representation theory (Brewin, 2001; Brewin et al., 1996) posits situationally accessible memories (SAM's) with high perceptual detail, possibly equivalent to amygdala based fear conditioning and verbally accessible memories (VAM's) which are suggested to be mediated by the hippocampus. The model is outlined in Figure 1.4 below. This model does not address dissociative responses (*qv*) as such (Hopper & van der Kolk, 2001) and is not considered further here.

Figure 1.4 Brewin's dual representation model



1.3.3 Fear conditioning and the amygdala

The amygdala stores conditioned fear memories and these are retrieved involuntarily by trigger stimuli. Storage was originally thought to occur in the hippocampus, but it is becoming clear that this occurs in the amygdala (Blair et al., 2001; Blair et al., 2005; Wilensky et al., 2006; Schafe et al., 2008). The amygdala and hippocampal memory systems are doubly dissociable (Bechara et al., 1995): damage to the amygdala prevents fear conditioning but not memory for the context, that is, which conditioned stimuli were used, while damage to the hippocampus interferes with knowledge of these facts but not with fear conditioning. Bilateral damage to both structures prevents acquisition of conditioning and the facts.

Fear conditioning is a form of associative learning that is sufficiently powerful that it occurs in response to a single event. That such indelible effects of exposure to one event may occur should not be surprising. The phenomenon of taste aversion (Garcia, 1966; Gustavson et al., 1974; Schafe & Bernstein, 1996) is also one which reveals persistent learning from a "one-off" experience, which once established is very difficult to overcome, being resistant to extinction (Garb & Stunkard, 1974). Taste aversion can also be acquired despite the animal being anaesthetised when the aversive agent is delivered (Bermudez-Rattoni et al., 1988). Survival of exposure to a life threatening event, whether through a trauma or a digested potential toxin, serves to potentiate the organism to avoid these circumstances in the future.

Fear conditioning is a useful model to describe some of the effects seen in PTSD (Rau et al., 2005). Much of the work in relation to fear conditioning has been in animal studies, but the neural systems underlying emotion, particularly fear, appear to be consistent across species (Phelps & LeDoux, 2005), as might be expected in relation to behaviour fundamental to survival. When a conditioned stimulus (CS, a neutral stimulus, in animal studies usually a tone or light) is repeatedly paired with an unconditioned stimulus (US, a stimulus such as a footshock that will cause a fear response), the CS alone will come to generate the fear response (a conditioned response, CR) including behavioural (increased freezing and startle responses) and ANS responses (LeDoux, 2000).

Fear conditioning learning in the amygdala is rapid and persistent and is proposed to involve cellular mechanisms (voltage gated calcium channels and N-methyl-D-aspartate (NMDA) receptors) which act together on associative neural pathways specific to the CS and US to cause long term potentiation in these neurons within the lateral amygdala

(Blair et al., 2001; Kalisch et al., 2008). The amygdala, however, also projects to perirhinal and entorhinal cortices which form the interface between the hippocampus and the neocortex, where memories are stored. Thus the amygdala is able to mediate memory storage processes supporting declarative memory organised by the hippocampus and rhinal cortices (McGaugh et al., 1996; Squire, 1992). This may explain how the amygdala can influence declarative memory about emotional events (*qv*) as well as being crucial to the experience and storage of fear conditioning as the emotional memory itself (Paz et al., 2007).

Other features of conditioning, such as generalisation and sensitisation, are also important in understanding what happens in PTSD. The CR may generalise to other sensory stimuli which happen to be present with the CS and these will also come to evoke stress responses. In PTSD, many perceptual reminders of the situation experienced at the time of a trauma may trigger a fear response through generalisation, and chronic hyperarousal may lead to sensitisation effects (van der Kolk & McFarlane, 1996).

In classical conditioning paradigms, the strength of a reflex usually decreases on repetition of a stimulus. In fear conditioning, in a state of arousal, the opposite - sensitisation - occurs: an aversive event, such as footshock, potentiates a fear response, such as the startle response, increasing the magnitude of response, rather than causing expected habituation (Davis, 1989). This is also known as kindling, from an animal paradigm used to invoke seizures: repeated subthreshold stimulation over time results in a full-blown seizure and thus behavioural output increases, rather than decreases, with repetition of the inducing event. In this way the associations learned in conditioned fear appear to be “indelibly burned into the brain’s hardwiring” (LeDoux, 1999) and operate irrespective of any amnesia for the traumatic event (Rau et al., 2005). This mechanism is considered to have temporal similarities to the way in which memories emerge over time as flashbacks; kindling in the amygdala is thought to result in a complex "spatiotemporal cascade of neurobiological events" which also involve changes in gene expression (Post et al., 1997). In this way an extreme stressor can induce psychobiological changes. That kindling over time is relevant to PTSD is reflected in the development of the disorder, which is progressive and emergent and does not necessarily depend on maladaptive immediate responses to trauma (McFarlane, 1998). Even when symptoms remit, re-exposure to trauma may cause re-activation of PTSD due to sensitisation (McFarlane, 1997).

Animal, neuropsychological and neuroimaging studies suggest the amygdala is fundamental in processing negatively valenced stimuli (see Davis & Whalen, 2001; Lang et al., 2000 for reviews). The amygdala is highly responsive to threat; extremely brief presentations of threatening stimuli, such as angry faces, which are subliminal and beyond conscious recall result in (right) amygdala activation (Morris et al., 1999) suggesting that the sub-cortical fast processing pathway responsible for fear conditioning is involved. Nonconscious viewing of fearful pictures can also potentiate the eye blink startle response (Ruiz-Padial & Vila, 2007). The (left) amygdala is responsive to linguistic representations of fear in an emotional Stroop task (Isenberg et al., 1999) and to a verbal link to an aversive event and amygdala activation was correlated to arousal measured by skin conductance (Phelps et al., 2001). These findings are relevant to the experimental work in Chapter 6 using an emotional Stroop paradigm.

While activated in response to direct threat (e.g. angry faces), the amygdala is particularly sensitive to uncertainty in anticipation of fearful or painful stimuli. Greater amygdala activation is seen to fearful faces than to pictures of attacks, explosions or mutilations (Hariri et al., 2002). Davis & Whalen (2001) suggest that a fearful face is more ambiguous as to the origins of the observed fear. There is therefore a need to gather more information about biologically relevant environmental stimuli and the amygdala is well placed to do this: the amygdala receives inputs from late stages of cortical processing from all sensory modalities via the thalamus, but projects back to cortical sensory processing areas and not the thalamus (Amaral et al., 1992; cited in Armony & LeDoux, 2000). In this way it can regulate the inputs it receives from sensory areas; the amygdala can also influence this process indirectly through projections to the various "arousal" networks, including the locus coeruleus noradrenergic system which innervates widespread areas of the cortex. These processes form neurobiological bases for the increased vigilance to threat found in PTSD.

1.3.4 Extinction and the PFC: fear memories may be forever (LeDoux, 1999)

In classical conditioning paradigms, extinction occurs as new learning, rather than by erasure of the conditioned fear response in the amygdala (Bouton, 2002). This is supported by recent evidence for cellular changes in the amygdala that correspond to behavioural extinction (Barad et al., 2006; Lattal et al., 2006). The expression of extinction, once learned, may depend on contextual factors (implicating hippocampal inputs to the PFC) and PFC inputs to the amygdala. The ventromedial PFC (which includes Broca's area in the left hemisphere) is bi-directionally connected to the amygdala and receives input from areas of sensory cortex. Although less well understood than amygdala involvement in conditioned fear, there are several strands of evidence that the PFC is involved in extinction (Kim & Jung, 2006; Milad & Quirk, 2002; Quirk et al., 2000).

However, the PFC role in extinction appears impaired by stress (Izquierdo et al., 2006) and both the amygdala and NE are implicated in inhibition of the PFC. Activation of the amygdala to consciously viewed (Kilpatrick & Cahill, 2003) or subliminal primes of angry faces was found to be inversely related to activation of the PFC, but not in cases of neutral priming conditions (Nomura et al., 2004). High levels of circulating NE also inhibit vmPFC function (Arnsten, 1998). It seems extreme fear resists extinction by taking out the mechanism responsible and it is suggested that the perseveration of fear conditioning observed in the absence of vmPFC control (Sotres-Bayon et al., 2006) may be equivalent to the cognitive perseveration apparent in individuals with lesions in the dorsolateral PFC (Morgan et al., 2003).

1.3.5 A fear conditioning model of PTSD

Some of the earliest neuroimaging studies of people with PTSD exposed to their trauma narrative showed there was extensive right hemisphere activation of the amygdala and sensory areas and hypoactivation in Broca's area (in the left vmPFC) (Shin et al., 1997; Rauch et al., 1996), that is, there are lateralised effects consistent with the evidence suggesting (1) right hemisphere activation to threat, (2) activation of sensory, particularly visual areas, consistent with amygdala-driven sensory input from the environment and (3) hypoactivation of left hemisphere PFC and consequently language functions. This pattern of activation is important and relevant to the hypotheses of this thesis and interpretation of results.

These are consistent findings, though not all reviews of neuroimaging studies in PTSD include a consideration of the lateralisation of brain areas implicated (e.g. Phan et al., 2004). Electrophysiological evidence also supports right hemisphere activation associated with arousal symptoms in PTSD (Metzger et al. 2004) and during recall of traumatic memories (Schiffer et al., 1995). A meta-analysis of neuroimaging studies suggests that people with PTSD show greater amygdala responses than healthy control subjects, a finding common with some other anxiety disorders and similar to the experience of fear in healthy individuals, but only people with PTSD show hypoactivation of the vmPFC (and anterior cingulate cortex, ACC; Etkin & Wager, 2007). This pattern of activation extends to negative stimuli not directly related to trauma, for example angry faces (Williams et al., 2006) suggesting that PTSD involves not just an exaggerated fear response, but that trauma causes a dysregulation in normal amygdala and PFC (and ACC) responses. A model of PTSD characterised by exaggerated amygdala responses and deficient hippocampal and frontal cortical function is consistent with neuroimaging studies of people with PTSD, but neuroimaging studies using direct fear conditioning and extinction paradigms to assess the neural correlates underlying these processes in healthy participants and those with PTSD remain for future research to establish definitively (Rauch et al., 2006). A recent study of combat veterans with exposure to traumatic events and focal brain injury found that damage to either the amygdala or the vmPFC resulted in a substantially lower rate of PTSD in these individuals, suggesting these two areas are critically involved in the pathogenesis of PTSD, and that the role of the vmPFC may not be entirely inhibitory (Koenigs et al., 2008). There was no evidence that hippocampal damage affected the development of PTSD.

1.3.6 Is PTSD an anxiety disorder?: fear is not equivalent to anxiety or stress

Evidence presented above suggests that a state of fear arises from sensory perceptions of the environment, resulting in amygdala activation and consequent inhibition of the hippocampus and PFC.

Catherall (2003) suggests that normal hippocampal (and PFC) functioning, without amygdala activation, is a state of non-anxious rumination, cognitive in nature and including verbal states; anxiety occurs when the amygdala is activated to some extent, but the hippocampus and PFC are both active, and is conceptually induced. In anxiety a threat is not immediately present, but is cognitively represented: as true thought about a threat. Anxiety may be concerned with thoughts about experiencing fear, but is not the same state, either biologically or in terms of the structures involved. For example, Heller et al (1997) found that anxious worry (typical anxiety) was associated with greater left frontal EEG activity (compared to controls), whereas anxious arousal, characterised by physiological hyperarousal (and typical of PTSD) was associated with greater right hemisphere parietal activation in an emotional narrative task.

Catherall (2003) goes on to suggest that a potentially feared event, generating anxiety may move along a continuum to become an actual event at which fear is experienced. As the *concept* of potential danger becomes a *percept* of actual danger, there will be a point of transition from top-down conceptual driven processing to bottom-up perceptual processing. The switch from normal, hippocampal/PFC functioning to hypoactivation as a consequence of hyperactivation of the amygdala in response to an immediate, true threat, may be the point at which dissociation, in the sense that Janet (1889) used the term, occurs (and dissociation is considered further below). The linguistic memory about the emotional event, that is declarative, hippocampally mediated, and verbalised in the PFC, cannot form; what exists are the perceptual, sensory inputs stored in the amygdala as fear conditioning to the overwhelming threat. Perceptual and conceptual memory have been shown to invoke separate areas of the brain consistent with these patterns of activation (Blaxton, 1999).

These dynamic processes, which differentiate fear and anxiety, likely have implications for treatment of PTSD. People with PTSD will frequently enter states where they re-experience (parts of) the trauma; however, this is not cathartic and occurs without any resolution of the traumatic memory which remains unintegrated into coherent narrative memory (van der Kolk et al., 1996a). Too much exposure to fear may only *sensitise* the fear response still further and too much emphasis on cognitive restructuring without accessing the conditioned fear may have no impact. What may be crucial is the balance between accessing the fear memory, with its sensory elements and, with the help of a trusted therapist to find the words, beginning the process of verbalising the experience and forming a conceptual and meaningful coherent narrative, that is no longer so perceptually biased (Catherall, 2003).

Elzinga & Bremner (2002) caution that exposure therapy may only be useful in situations where NE and cortisol are low, otherwise exposure will aggravate fragmentation of memories, rather than their synthesis. Exposure may also make the traumatic memory more indelible, if the PFC is “off-line” and cannot facilitate extinction. This may also help to explain how psychological debriefing, intended as an early intervention to prevent PTSD, may, by re-exposing people to their traumatic memories, actually cause the disorder to develop (Bisson et al., 1997; Rothbaum & Davis, 2003; Maren & Chang, 2006) and thus current guidelines are that the practice of debriefing should cease (Cochrane Review: Rose et al., 2003).

However, there is also some doubt about how well exposure treatments undergone in a therapist's office generalise to the real world outside or whether they remain specific to this context (Bouton et al., 2006). Extinction is new learning, not unlearning and appears to be less stable and persistent than the original learning, and far more context specific in terms of external (perceptual) and internal (e.g. mood, drug state) cues and of temporal context than is fear conditioning itself (Bouton, 2002; Bouton et al., 2006).

It has been suggested that one possible explanation for the apparent rapid treatment effects of EMDR (Eye Movement Desensitisation and Reprocessing (Shapiro, 1989; Shapiro & Forrest, 1997), a controversial treatment, whose basis is not yet understood) is that the protocol "provides a powerful blend of the best ingredients of different therapies" (Servan-Schreiber, 2000). Elzinga & Bremner (2002) indeed suggest that facilitation in therapy of associations to related events, specifically included within the EMDR protocol, may re-integrate all aspects in declarative memory. For a successful treatment outcome it seems that the implicit memories stored within the amygdala need to be recovered and changed, or integrated into declarative memory, before they can be resolved and become a memory about the emotional event. Treatment is not considered further here.

Not only is fear not equivalent to anxiety, neither is it the same as psychosocial stress. The amygdala is crucially important in assessing sensory stimuli indicative of threat and instigating the fear response. A recent imaging study using a psychosocial stressor (mental arithmetic with social evaluative threat components), found apparently similar increases in HPA-axis activity and elevations of cortisol but these were associated not with amygdala activation but with reduced activity in the hippocampus which consequently reduced its inhibitory action on the HPA-axis (Pruessner et al., 2008).

This suggests that while end effects on the HPA-axis may appear similar to amygdala activations in fear, fear and stress are distinct mechanisms and show different patterns of activation Though presently speculative, Pruessner et al (2008) suggest that if supported by future work, this will have implications for the type of stressor used in laboratory research. Psychosocial stressors may not equate to the environmental stressors that result in fear and may therefore be less relevant in understanding responses important to PTSD. Interpretations of studies using psychosocial stressors may require re-evaluation in this context. This point is directly relevant in respect of methods used in this thesis and is discussed further in Chapter 2.

1.3.7 The nature of traumatic memories

Laboratory studies have attempted to investigate the effects of “emotion” on memory. Both NE and cortisol can affect memory processes; these relationships are, however, complex and incompletely understood. Generally, memory for emotional, compared to neutral, events is enhanced by their action (e.g. Cahill et al., 1994; Cahill & McGaugh, 1995; Buchanan & Lovallo, 2001), but memory can also be impaired by glucocorticoids (e.g. de Quervain et al., 2000; de Quervain, 2006; Oei et al., 2007). Factors modulating neurohormonal effects on memory may be related to: the state of arousal when material is presented (Gore et al., 2006; Anderson et al., 2006a); at which stage (encoding, storage or retrieval) manipulations of arousal occur (Cahill & Alkire, 2003; Het et al., 2005; Dolcos et al., 2005; Payne et al., 2007); precisely where (amygdala/hippocampus) agonists or antagonists are administered (LaLumiere & McGaugh, 2005; Ramos et al., 2005); interactions of NE/cortisol with amygdala activation (van Stegeren et al., 2005; van Stegeren et al., 2007; Kilpatrick & Cahill, 2003; Anderson et al., 2006b; Roozendaal et al., 2006) and whether material to be remembered is verbal or non-verbal in nature (Newcomer et al., 1999). These issues, along with those which follow in relation to memory for central or peripheral items, are complex and extensively considered in the literature; they are acknowledged here, but the complexities are not considered further in this thesis. In addition, there are two problems in interpreting some of this work: psychosocial stressors may not prove helpful in understanding PTSD as discussed above and it is becoming clear that "emotion" is not something that is generalisable: if the effects of fear are to be understood then they must be investigated with specifically fearful situations.

There is also a considerable debate in the emotional memory literature about whether items presented centrally or peripherally are better remembered *per se*, and in relation to arousal and emotional memory (e.g. Adolphs et al., 2005). Experimental studies invariably present static pictures, or slide shows, not dynamic, veridical views of the world. Generally, it is suggested that central items in a scene, or gist, in a narrative, (compared to peripheral details appearing in a picture or mentioned in a narrative), are better remembered in states of arousal, but see Laney et al (2004) who question whether such visual presentations of "central" items are not just "attention magnets" which are selectively remembered, rather than emotion selectively improving memory for central items. The amygdala seems preferentially involved in memory for gist rather than detail of emotional material; both damage to, and decrease in volume of, the amygdala are inversely related to memory for gist (Adolphs et al., 2005).

These models originate from the much quoted "Easterbrook Hypothesis" (Easterbrook, 1959). The fundamental proposition is that emotional arousal consistently acts to reduce the range of cues an organism uses, defined by reduced use of peripheral cues while maintaining the use of central and immediately relevant cues. This is associated with improvement, or at least maintenance of, performance under stress. This may be the case in the examples discussed, which are to do with maintenance of (perceptual) concentration to different cues in proficiency in skilled, or precision motor performance tasks in different conditions of motivation (e.g. by the offer of bonuses or rewards) and alterations in performance associated with loosely defined concepts of drive or specific instances (e.g. of thirst).

However, this premise is counterintuitive to situations of threat or danger and to considerations of the hypervigilance observed in PTSD. There are strong arguments specifically against a narrowing of attention: if a predator appears outside of a narrowed focus of attention this would not serve the best interests of the organism; the source of danger would not be detected until too late (LeDoux, 2000; Armony & LeDoux, 2000). Armony & LeDoux (2000) argue that an organism is able to attend to threats *outside* the focus of attention, via the thalamo-amygdala pathway which operates as an attention independent channel, enabling sensory information to be detected outside (as well as inside) a focus of attention. This point becomes relevant to the emotional Stroop paradigm used in experimental work reported in Chapter 6 and is pursued there. Laboratory situations that do not produce amygdala activation may therefore produce different effects. Memory for traumatic events may thus be different to any kind of peripheral-central distinctions theoretically established in non fearful situations and the following case study example illustrates this.

Even from within the memory literature, direct generalisation of these central/peripheral effects to real life is cautioned by Christianson (1992) summarising a case study by Christianson & Nilsson (1989) of a woman, C.M., who was raped while out jogging. C.M. initially showed amnesia for both the trauma and her previous life, but remembered some isolated details of "bricks along a path"; Christianson comments that it might be difficult to determine what is central or peripheral outside the laboratory, in real life, and that few (of the memory researchers in this field) would have predicted that this, an apparently non-central detail, would be remembered. In the context of what is known about the neurobiology of PTSD, this makes perfect sense: what is being remembered are sensory elements of the conditioned fear memory stored in the amygdala (see sections 1.3.2 and 1.3.3 above). Global amnesia consequent on trauma is not uncommon, but is insufficiently understood (van der Kolk & Fisler, 1996).

Christianson (1992) reports that on being escorted back through the area, C.M. felt uncomfortable at certain places, and could not explain why the thoughts of bricks and the path were the only ones recalled; on seeing some crumbled bricks on a path, she experienced severe "unbearable" anxiety and associated these feelings with the scene and felt that something must have happened at this location. A rapist had confessed to the police a few days earlier; this was where she had been attacked before being dragged to an adjoining field and raped.

C.M.'s amnesia remained for 16 weeks, until the first time she went out running again; the recovery of the memory demonstrates how learning and subsequent memory can be state dependent, which may be particularly important in PTSD, and triggered by stimuli that match elements associated with the trauma (van der Kolk & Fisler, 1996). C.M. was reminded of the location of the trauma by similar perceptual cues (a country environment with brush, a gravel track with pieces of bricks, and a pile of bricks) while in the same internal state (the physiological state from running: motor activity, increased respiration and heart rate) experienced immediately prior to the trauma. The other memories relating to the rape could only begin to return in the physiological state in which they were encoded.

Researchers within the PTSD field also caution against simple central/peripheral distinctions; Ehlers et al (2004) includes examples from extensive clinical experience in discussing intrusive re-experiencing in PTSD. In their example 15, a rape victim initially failed to remember that she had been threatened with a knife by her assailant, something which memory theory debates on "weapon focus" would consider a central element, likely to be remembered (Loftus et al., 1987). Instead Ehlers et al (2004) suggest that, in PTSD, the intrusive, implicit sensory memories are not random fragments, but likely to be stimuli that signalled the onset of the trauma, or stages where a situation suddenly got worse for the victim, that is, just prior to when fear conditioning occurred. Stimuli temporally associated with significant parts of the trauma may be implicitly associated with the fear memory, but the individual may not remember, explicitly, what these warning signal triggers are, even when an intrusive flashback occurs: they seem to occur "out of the blue" whilst experienced with a sense of impending current threat, as originally experienced. The determination of significance will be idiosyncratic to the individual and situation and can not be objectively determined. Indeed, if memory dysfunction in PTSD is dependent on physiological factors, then no psychological, or intended factors are necessary to explain disturbances of memory (Elzinga & Bremner, 2002). Thus we return to early conceptualisations of the dissociation of (traumatic) memory being subconscious (Janet, 1889) and unwitting (Rivers, 1920). There is no need for Freud's notion of repression as an active process and indeed, Elzinga & Bremner (2002) comment that assigning intentions of deliberate forgetting to PTSD patients may be harmful to them.

The above considerations have demonstrated how increased understanding of the neural circuits and neurobiological underpinnings involved in fear conditioning, and which appear dysregulated in PTSD, are suggesting that it is not an anxiety disorder. Indeed, as a result, there is renewed debate about where PTSD should be classified; the DSM-V working group is considering classifying PTSD as a "stress-induced fear circuitry disorder" at present (Friedman & Pitman, 2007). Where does this leave considerations of PTSD as a dissociative disorder?

1.3.8 PTSD as a dissociative disorder

Janet (1889) viewed dissociation as at the core of PTSD, and our understanding of the effects of trauma on fear memory systems, reviewed above, still support this view. The term "dissociation" has, however, come to be used for different phenomena. van der Kolk et al (1996a) distinguish three phenomena. The failure to integrate all elements experienced at the time of the trauma, due to the fear mechanisms (discussed above) operating, is referred to as primary dissociation and characteristic of PTSD; memories intrude as elements dissociated from normal, declarative, memory as flashbacks, nightmares and intrusive recollections of the trauma, often somatosensory in nature, with little narrative component (van der Kolk & Fisler, 1996).

Secondary dissociation (or peri-traumatic dissociation: Marmar et al., 1994) occurs when, in the context of trauma, a further disintegration occurs within the individual and there is a sense of disengagement and observing the trauma as if from a distance, as a spectator. Alterations in the experience of time, place or person are commonly reported in many forms of trauma: these include out of body experiences, altered pain perception and body image, bewilderment, disorientation, confusion, disconnection, detachment, tunnel vision, derealisation and depersonalisation. This form of dissociation renders people out of touch with their feelings and emotions at the time of the trauma but is not considered an active process; however, if used previously in response to threat, it is likely to re-occur. Contrary to some views of secondary dissociation as protective, by engendering a safe sense of distance from the trauma, this response is an important risk factor in predicting PTSD (van der Kolk et al., 1996a) and is considered fundamental to a diagnosis of Acute Stress Disorder (ASD) immediately following a trauma, and which was introduced as a disorder in DSM-IV (APA, 1994). People with ASD may or may not go on to develop PTSD. In survivors of road traffic accidents (RTA's), of the 13% developing full ASD and 21% developing sub-clinical ASD, 75% and 60% respectively went on to develop PTSD (Harvey & Bryant, 1998) although lower rates (32% with PTSD) have been found at 1 year follow-up of RTA victims (Koren et al., 1999) and there is ongoing debate about whether ASD and PTSD are distinct diagnoses (e.g. Brewin et al., 2003). ASD is not further considered here.

Tertiary dissociation refers to distinct ego states which contain the traumatic experience, while allowing other ego states to function normally. This is typical of the identity fragments in Dissociative Identity Disorder, in which chronic sexual and/or physical abuse at a very early age is known to be a potent causal factor (Braun & Sachs, 1985; Frischholz, 1985; Kluft, 1985). Tertiary dissociation will not be further considered here.

Interestingly, recent neuroimaging studies are revealing two main subtypes of responding to trauma experiences in chronic PTSD as well as the acute responses identified above and that these have different neurobiology (Lanius et al., 2006). The majority of patients (70%) report an intense reliving as primary dissociative flashbacks with increased arousal, while 30% report phenomena of secondary dissociation, and with no increases in heart rate to symptom provocation paradigms; these two types of responding had previously been suggested as different routes to chronic PTSD (Bremner, 1999a).

However, it is being established that a substantial minority of people with PTSD respond to symptom provocation with a secondary dissociative response, that is, with detachment from the re-lived trauma, and show a different neural pattern of response, not just from controls, but also from those with PTSD who respond with a flashback response (Lanius et al., 2002). Autonomic responses are also different: secondary dissociation is associated with no increases in heart rate or skin conductance. In response to symptom provocation, increased activation was seen in the thalamus, part of the temporal and parietal lobes, areas of the PFC (dorsolateral and ventromedial), occipital lobe and ACC and was lateralised to the right hemisphere. Temporal lobe activation is consistent with reports of dissociative phenomena in temporal lobe epilepsy and of depersonalisation experiences on direct stimulation of these areas during neurosurgery (Penfield & Rasmussen, 1957; reported in Lanius et al., 2006). The areas activated in parietal and occipital cortex are involved in the hierarchy of sensory processing and may affect integration in higher levels of cortex. Activation of prefrontal areas, with inhibition of the amygdala, may explain the sense of detachment without arousal and may still impede extinction, as amygdala inhibition precludes sufficient emotional engagement with the conditioned response (Hopper et al., 2007).

In Lanius' (2002) study of those showing a secondary dissociation response, all of the participants had histories of chronic sexual, physical and emotional abuse beginning in childhood and all reported that dissociation had been used as a defence to escape traumatic experiences throughout their lives. This is consistent with other evidence suggesting that early trauma may be related to right lateralised responses and is considered further in Chapter 9, the final chapter.

Neuroimaging studies commonly use a subtraction method: for example, activations on exposure to an individual's trauma narrative are compared to activations on exposure to a neutral event narrative by subtracting activation strengths in the target to the neutral condition in regions of interest. Recent studies have begun to explore the neural networks associated with PTSD symptoms. Functional connectivity analysis allows correlational analyses of regional activity in response to a task (e.g. recall of traumatic memories) that covaries with a seed voxel - an area activated in both groups being compared. Using a seed voxel in the right ACC, differences were found between PTSD subjects showing flashback responses (primary dissociation) and controls consistent with different phenomenological experience of memory. The PTSD group experienced their memories as primarily visual images, whereas the control group recalled memories in narrative form. In a functional connectivity study of PTSD patients showing a (secondary) dissociative response, activation patterns differed from both those showing a flashback response and traumatised controls without PTSD (Lanius et al., 2005). Different patterns of connectivity from a seed voxel in the left thalamus, thought to be implicated in temporally binding experiences into a constructed reality in cortical areas to which it projects, are possibly indicative of altered conscious experience in the dissociating PTSD group. It has also been reported that stimulation of the left thalamus results in disruption of language abilities; thus both PTSD groups experienced a *non-verbal response* in comparison to control groups whose experience was of a normal autobiographical memory. Associated changes in connectivity in respect of the insula, thought to be involved in the experience of emotions (Damasio, 2000) could also be relevant to dissociative experience.

In summary, then, neuroimaging studies are beginning to identify neural underpinnings for different sub-groups within PTSD and these appear to be linked to different forms of dissociation, but both sub-groups experience traumatic memories as non-verbal through either disruption to or hypoactivation of language areas. However, it seems that secondary dissociation stems from earlier trauma, particularly childhood abuse, so both forms of dissociative response are still rooted in trauma.

Exposure to previous trauma may also be implicated in dysregulation of the HPA-axis and cortisol levels. Although acute reactions to stress involve increased cortisol levels (Sapolsky, 1998), although findings are mixed, and not considered in any detail here, findings of hypocortisol have been consistently, but not universally, found in PTSD, consistent with enhanced negative feedback inhibition of the HPA-axis and dysregulation (Yehuda, 2002; Yehuda et al., 2006). It appears that this can be intergenerational: offspring of Holocaust survivors were found to have low basal cortisol levels even though not exposed to trauma themselves (Yehuda et al., 1995; Yehuda et al., 2000). It is becoming apparent, that exposure to a previous stressor, while not producing PTSD, may underlie changes in the HPA-axis response (Ganzel et al., 2007) such that consequent exposure, with resultant PTSD may result in low cortisol levels, whereas an initial response to a stressor may produce high levels of cortisol (Resnick et al., 1995); this may also be relevant when considering differences in child and adult cortisol levels after trauma (Ostrowski et al., 2007) and the effects of childhood trauma (Santa Ana et al., 2006). This again suggests the importance of considering prior exposure to trauma, including early abuse, in investigating patterns of biological responses in PTSD.

1.3.9 PTSD as a disorder of memory: memory functions are also lateralised

Much of the discussion so far has alluded to problems with memory of traumatic events, and a model of PTSD as a disorder of memory has been proposed (Elzinga & Bremner, 2002). However, it is becoming increasingly clear that neuropsychological deficits in people with PTSD include general memory functions, although these may be subtle rather than generalised deficits. Deficits have been found in tests of verbal fluency (Uddo et al., 1993) and verbal memory (Bremner et al., 2004a), including the AVLT (Auditory Verbal Learning Test: Rey, 1958) used as a measure of standard memory in the experimental work reported in Chapter 5 (Vasterling et al., 1998; Vasterling et al., 2002; Uddo et al., 1993) and in similar variants of this test (Veltmeyer et al., 2005). These deficits have also been found in children and adolescents with PTSD (Yasik et al., 2007). Although some reviews have commented on possible relations to hippocampal functioning to explain memory deficits (e.g. Horner & Hamner, 2002; Buckley et al., 2000), it seems that it is prefrontal areas that are implicated, converging with the neurobiological findings discussed above (Vasterling & Brailey, 2005). Lindauer et al (2006) found that memory deficits were not directly correlated to reduced hippocampal volumes and conclude that memory impairments in PTSD do not seem to be a direct consequence of any effects of PTSD on the hippocampus. The type of deficits observed in PTSD seem to be related to very specific functions of prefrontal areas, rather than on standard neuropsychological tests of frontal functioning (Koenen et al., 2001).

Deficits in recall, but not cued recall or recognition tasks have been reported (Jenkins et al., 1998; Vasterling et al., 1998). Hippocampal dysfunction would be expected to result in generally impaired retrieval; in contrast, consistent with these findings, imposed structure (in recognition contexts) enhances memory performance in prefrontal dysfunction (Shimamura, 1996; cited by Vasterling & Brailey, 2005). Qualitative measures of errors in the Block Design subtest of the Weschler Adult Intelligence Scale-Revised (Weschler, 1981) in combat veterans with PTSD produced a pattern of errors consistent with performance of patients with documented left hemisphere lesions (Kaplan et al., 1991; cited in Vasterling et al., 2000) indicative of relative left hemisphere hypofunction but not implicating right hemisphere function (Vasterling et al., 2000). A meta-analytic review (Brewin et al., 2007) concludes that memory deficits in people with PTSD are robust and common across types of trauma and different populations. Deficits affect verbal rather than visual memory and do not seem to be confounded with possible effects of traumatic brain injury, likely to be a consequence of a general motivational problem or the result of any one comorbid condition. These findings may be relevant in the experimental studies comparing memory performance of right and left handers reported in Chapter 5.

There are also reports of overgeneralised autobiographical memory retrieval to cues in people with PTSD (e.g. McNally et al., 1994). This is a finding previously associated with suicide and depression: when people are asked to provide a specific memory to a cue word prompt, negative or positive in valence, they fail to provide a specific memory and instead respond with a memory that comprises a category of responses, a so-called overgeneral memory. However, a recent reviews suggests this also seems to occur in people with PTSD, but not in other anxiety disorders (Williams et al., 2007; Moore & Zoellner, 2007). This effect is not associated with trauma exposure, but with PTSD symptoms. At present existing, cognitive models, for example, functional avoidance theory, are unable to fully account for observed findings. It is interesting however, that trauma and PTSD may be more implicated than depression: Hermans et al (2004) found production of overgeneral memories was linked to a history of physical abuse, in depressed inpatients, but did not correlate with severity of depression on any of the three measures used. There are currently several possible attempts at explanations, none of which satisfactorily explain why overgeneral memory occurs in PTSD (Schönfeld et al., 2007) but further discussion of these is beyond the scope of this thesis. Inter-relationships between depression and PTSD as they might relate to the overgeneralised memory phenomenon remain to be determined.

So far, deficits in memory in PTSD appear to relate to the underlying neurobiology of the disorder where the right hemisphere is activated and amygdala activation compromises left frontal language functions. From the point of view of the taxonomy of memory presented in Figure 1.3 above (see p 29), these discussions about the relevance of lateralisation to PTSD have related to implicit fear conditioning, but processes underlying declarative memory are also lateralised within the brain.

Distinctions can be made between different types of declarative memory. A distinction can be made between semantic memory, for facts, and episodic memory, for events, or episodes, but in practice these are difficult to differentiate as memories for facts will be stored in an episodic context, for example, retrieving a fact from semantic memory will also encode this as a novel event in episodic memory (Tulving et al., 1994; Cabeza & Nyberg, 1997). Within episodic memory a distinction can be made between retrieval using recall, which can be free recall or cued recall to specific cues, and recognition which is more structured and presents information to the participant who then chooses between alternatives. Episodic memory refers to memory for specific events experienced at a specific time and place and includes the “miniature events” used in laboratory tests of memory (Cabeza et al., 1996). Autobiographic memory refers to memory for past events in one's life and is a complex reconstructive process, likely to include qualitative, aspects such as emotion (Cabeza & St Jacques, 2007). Both episodic and autobiographical memory can be seen as points on a continuum of complexity (Daselaar et al., 2008). Considerations of these different types of memory are relevant to the experimental work in Chapters 5 and 6 of this thesis.

Neuroimaging techniques offer useful tools to understand the functional neuroanatomy of cognitive processes including memory. Early reviews of literature, found consistent patterns of lateralised activation, despite differences in the nature of episodic memory tasks (Cabeza & Nyberg, 1997; Tulving et al., 1994), and consistent differences in recall and recognition tasks (Cabeza et al., 1996). While similar right frontal activations occurred in both recall and recognition, suggestive of general retrieval processes, recognition was associated with activation in parietal cortex, suggesting a larger perceptual component in recognition tasks. The differences in episodic encoding and retrieval activations were first described as "hemispheric encoding/retrieval asymmetry" (Tulving et al., 1994) and have come to be known as the HERA model. Such studies require that the reference condition for an encoding task is a retrieval task and vice versa and they point out that it is hemispheric asymmetries in the differences in activity between encoding and retrieval that are important, rather than absolute levels of activity.

The asymmetry refers to differential prefrontal involvement in encoding and retrieval revealed by positron emission topography (PET) studies. While prefrontal regions are part of a network involved in remembering, left prefrontal regions appear to be preferentially involved in the retrieval of semantic memory and the simultaneous encoding of novel aspects of the retrieved memory into episodic memory, whereas the right prefrontal regions are preferentially involved in retrieval of episodic memory. Specific regions activated within frontal areas may vary according to the nature of the materials and method used.

Ongoing debates about the HERA model have centred around whether nonverbal encoding is in fact left lateralised (e.g. Kelley et al., 1998); the model has been more precisely reformulated in terms of the kind of data are relevant to it to avoid claims based on simple observed associations (Habib et al., 2003). For example, in order to compute proper differences it is essential that the reference condition for an encoding task is a retrieval task and vice versa and they point out that it is hemispheric asymmetries in the differences in activity between encoding and retrieval that are important, rather than absolute levels of activity. If there are differences in asymmetry driven by materials, or other factors, in addition to processes, then they need to be explored but only by systematic manipulation of both factors. Material-specificity may occur independently of process-specificity, but reveal the same underlying pattern proposed by the HERA model when this is done (e.g. Nyberg et al., 2000; cited by Habib et al., 2003).

Patterns of activation can be summarised as follows. Left PFC is involved in (1) retrieval of information in semantic memory and (2) encoding of information into episodic memory, at least as far as verbal material is concerned, to an extent that the right PFC is not. Right PFC, but not left PFC, is involved in (1) retrieval of information in episodic memory and (2) to an extent not observed for retrieval of semantic information. It is recognised that other components of the memory network include medial temporal lobe structures and more posterior areas.

A later extended review (Cabeza & Nyberg, 2000) reached similar conclusions in support of the HERA model. The use of neuroimaging techniques is preferred compared to traditional lesion studies, with neural reorganisation consequent on a lesion, in that normal functions in healthy populations can be examined and the processes of encoding and retrieval considered separately (Nyberg et al., 1998). These authors also point out that the model is a probabilistic pattern, based on meta-analytic reviews, and that single studies can provide exceptions to the pattern. Ongoing work will increasingly refine differential patterns within prefrontal areas, perhaps associated with factors such as the nature of material being remembered in laboratory studies and the mode of response, semantic processing or intentional learning, and encoding strategies used. If semantic encoding is left lateralised in parts of the PFC which are hypoactivated by the amygdala and NE during states of high arousal, this may be another reason why semantic, verbal memories of the events are not formed in people with PTSD and remains to be directly investigated.

Autobiographical memory is more complex and more difficult to study than laboratory manipulations of memory which can be standardised across subjects (Cabeza & St Jacques, 2007). A recent study used fMRI to investigate networks of brain regions activated during the accessing and re-experiencing of an unrehearsed autobiographical memory as it unfolded naturally over time, but time locked to the point where the memory was brought to mind (Daselaar et al., 2008). Patterns are consistent with accounts presented above. Accessing the memory activated right PFC (consistent with the HERA model) and areas of the medial temporal lobe, consistent with amygdala and hippocampal involvement in accessing emotional intensity of the memory, and retrosplenial posterior cingulate cortex. Once the memory had been retrieved, areas associated with visual imagery, and auditory cortex were activated indicative of sensory re-experiencing and as the memory was (internally) elaborated and kept in mind; finally, areas of the left PFC were activated consistent with successful recognition and working memory elaboration.

1.3.10 Summary: back to a behavioural account

This section has provided an extensive outline of the main processes that appear relevant in understanding PTSD as a disorder, not of anxiety, but of dysregulation of processes involved in fear, one of the basic emotions which has been extensively studied in animals and humans. This has consequences for phenomena of dissociation and memory and lateralisation with asymmetrical organisation is fundamental to many of these functions. Right hemisphere functions are implicated in PTSD to the detriment of left hemisphere language and memory functions. Converging evidence confirms the earliest conceptualisations of PTSD as a neurobiological disorder; having considered at length the neurobiological underpinnings as they are currently understood, we return to a behavioural account.

Rivers' (1920) theory considers in some detail the response options available to an animal (human or otherwise) in response to danger. His discussion of the freeze or immobility response is perhaps particularly relevant to PTSD in several ways.

Rivers' theory was based on his extensive experience as a military medical officer during World War I. His methods were particularly enlightened compared to the traditionalist methods of some of his colleagues discussed above, and involved *listening to*, and pursuing with his patients their experiences, uncovering repressed and suppressed layers of experience and meaning, rather than denying their experiences. His theory is likely to be based on the reality of the experience of those he treated.

Rivers considered that the immobility response was particularly relevant to the origin of the reactions to trauma that he saw in his patients. The immobility response occurs so as to conceal the animal from the source of danger. In some animals this is accompanied by other physiological processes which aid concealment, such as a change in the distribution of pigment within the skin. Rivers carefully makes the point that if a group of animals choose to make this response, then they all must be fully committed to this response. Any one of the group who moves, immediately destroys the safety of the whole group, particularly as the visual system of all animals, including humans, seem particularly able to detect movement in the environment, particularly of biological motion, which appears instantly recognisable as such to the observing animal (Johansson, 1975). If movement must be totally suppressed, so must all sound, as the auditory senses are particularly alerted by danger and threat, and reflected in the fact that people with PTSD are especially sensitive to noise (van der Kolk et al., 1996a). In flight, or fight, it seems self-serving to cry out, either to alert others to the threat (in flight) or in an attempt to threaten the other (in fight). In immobility, all members of the group must be equally committed to the absence of sound. There is thus an extremely strong requirement for suppression of all language, and, stemming from this argument, perhaps particularly in situations of being trapped and helpless when it is not possible to engage physically active responses. These are precisely the conditions among the most likely to precipitate PTSD. Blascovick & Katkin (1993) suggest that: "One of the most toxic dimensions of stressful stimuli is uncertainty relating to lack of predictability or control of threatening events" (quoted in Adams et al., 1998, p 1688). Here then, we have a behaviourally based rationale for the absence of language in extreme fear, which corresponds to what is now understood of the psychobiology of PTSD.

The next two sections will go on to consider two particular risk factors for PTSD, sex differences and handedness, which set the context for the research questions of this thesis; other known risk factors for PTSD are also briefly considered.

1.4 Sex differences in PTSD

One of the prime movers in securing PTSD as a diagnostic category in the DSM was the feminist movement who were publicly recognising the effects of rape on women, the victims of the sex war (Herman, 2001). Rates of PTSD have consistently been found to be twice as high in women as men. The (US) National Comorbidity Survey (NCS; Kessler et al., 1995) found that while approximately 60% of men and 50% of women experienced at least one trauma in their lifetime and men were more likely to experience trauma than women, more women than men had lifetime PTSD (10.4% *vs* 5.0%) and that this was the most common anxiety disorder in women. Sex differences were even greater in relation to conditional risk: 20.4% of trauma exposed women but 8.2% of men developed PTSD. The NCS replication (Kessler et al., 2005a) does not consider sex differences by disorder. PTSD apparently persists longer in women: a large community study in Detroit found the median length of the disorder to be 48.1 months in women versus 12.0 months in men (Breslau et al., 1998).

The reasons for this are not fully understood. Rape carries one of the highest conditional risks for PTSD (e.g. 65% in men compared to combat 38.8% in men; in women, 45.9%, second only to 48.5% physical abuse: Kessler et al., 1995) and more women than men report rape, sexual assault and molestation, and child abuse. Men are more likely to report being threatened with a weapon and physical assault (and combat). In summarising major studies carried out in different areas of the world, Norris et al

(2002) conclude that there is no exception to the rule that females experience sexual violence far more often than males and since this is associated with higher conditional risk, then this may account for some, but not all, of the difference. It is also suggested, in respect of the A2 criterion (see Table 1.1), comparable events seem to be experienced by women as more threatening, (with greater terror, horror and helplessness) than by men.

In terms of aetiology, possible differences have been found in relation to substance abuse, the most common co-morbid condition in men, present in about half of men with PTSD and second most common (to depression) in women, occurring in one third of women; in the majority, PTSD is the primary disorder (Kessler et al., 1995). A study of chemically dependent adolescents found that in males, substance abuse preceded the development of PTSD, suggesting that possible risk taking behaviour consequent on drug use was implicated in some cases of PTSD, whereas in women the opposite occurred and PTSD seemed to be the incident disorder (e.g. Deykin et al., 1997). This issue is revisited in Chapter 7 in relation to testosterone. This finding is consistent with substance abuse, particularly in women, being an attempt to self-medicate and gain symptom relief from arousal symptoms, and reciprocal relations between the two conditions may complicate treatment unless both are considered together (Stewart et al., 2002).

Most of the research of neurobiology in PTSD has been in men, possibly since much funding on research has been via the (US) Veterans Administration, and thus on male combat veterans (Rasmusson & Friedman, 2002). While our understanding of the neurobiology of PTSD increases, investigating possible neurobiological differences between women and men is problematic. Animal work suggests interactions of hormonal systems may be both gender and species specific and little real progress has been made in researching these complex issues in women (Rasmusson & Friedman, 2002). The sex hormone systems interact in a complex way with NE and HPA-axis systems and more recent research suggest that in women the HPA-axis is more sensitised than in men (Olff et al., 2007). In addition, in women variations across the menstrual cycle and according to use of oral contraceptive, in pregnancy and at the menopause seem to affect HPA-axis responses and it is speculated that these differences may reflect evolutionary pressures to protect the foetus from adverse effects of maternal stress (Kajantie & Phillips, 2006).

There has also been a variety of suggested sex differences in brain structures implicated in emotional memory and PTSD and which may affect emotion and cognitive functions differently in men and women. There have been mixed findings in relation to the amygdala. Lateralisation of the amygdala (left in women and right in men) in emotional memory has been proposed (Cahill et al., 2004), but while a functional dissociation was found in the formation (right) and retrieval (left) of memory for fearful faces, the sex difference was not substantiated in another study (Sergerie et al., 2006). Gender is, however, often ignored in neuroimaging studies, despite possible sex differences in functioning being identified in structures including the hippocampus and amygdala which are likely to be relevant to our understanding of disorders including PTSD (Cahill, 2006) and in brain activation patterns to emotional stimuli (e.g. Hofer et al., 2007).

There are other psychological factors that may interact with neuroendocrine responses to trauma. Olff and colleagues' (2007) review suggests that women may experience higher perceptions of threat and loss of control and show more severe emotional responses and greater rates of peri-traumatic dissociation than do men, while being unable to access sufficient social support. In a study of victims of violent crime, negative responses in support were correlated with PTSD symptoms six months post crime and these impacted more on women than men (Andrews et al., 2003). Women may also be socialised to use more passive, or avoidant, and emotion focussed coping responses while males are socialised to use active behaviours and these may also influence neuroendocrine functioning in the stress response (Olff et al., 2007).

Since the reasons for sex differences in prevalence of PTSD are not yet understood, sex differences are separately considered in relation to the main variables in the experimental chapters of this thesis.

1.5 Studies of lateral preference in PTSD: a new risk factor?

When the current programme of research was proposed two studies had considered lateral preference in PTSD, both in male combat veterans. Spivak et al. (1998) found significantly more PTSD patients than controls had mixed lateral preference, and a significantly lower rate of right hand preference. They suggested that individuals with mixed lateral preference may have an altered balance between the hemispheres with a more active role for the right hemisphere in perceptual and cognitive processing. Chemtob & Taylor (2003), in a study of right handed combat veterans, found that those with mixed lateral preference were more likely to have PTSD than those with consistent right preference. This study also found that those having a left handed parent were more likely to have PTSD. Although the number of participants having parental left handedness and mixed lateral preference themselves was small (n=5), 100% of them had PTSD. The results of these studies also support an earlier finding (Chemtob et al.

2001) in a nonclinical population of adolescents exposed to a life-threatening natural disaster; those with mixed handedness had increased trauma symptomatology and more symptoms of depression.

These studies, in the absence of sufficient left handers in the sample populations used, could do no more than suggest that perhaps mixed handedness, rather than strong lateralisation to right or left *per se*, was a risk factor for PTSD. This is potentially a large effect in the context of possible risk factors other than gender (considered above). The studies reported in Chapter 3 and Chapter 4 of this thesis seek to extend these findings to civilian populations, including women, and by recruiting large samples, to include sufficient numbers of left handers to examine which aspects of lateralisation may be important. The remainder of this section considers other risk factors for PTSD while section 1.6 which follows, introduces issues relevant to the study of handedness.

Although there is ongoing debate about criteria used for the nature of the trauma that has to be experienced (e.g. McNally, 2004), PTSD develops consequent on a traumatic experience, an event that is often random and unpredictable, but not everyone experiencing a trauma develops PTSD. Section 1.2 has considered the historical amnesia for the concept of PTSD; it served military leadership to see these issues as individual weakness. In this way they became not the responsibility of the military, and avoided implications of poor leadership on morale and bad decision-making (McFarlane, 2000). In PTSD, it serves to blame the victim in order to preserve a sense of invulnerability (Andrews et al., 2003; Brewin, 2003); for the victim this intensifies feelings of guilt and self blame. A search for consistent vulnerabilities on the part of the individual has produced several factors, but none of these seem to exert large effects (Brewin, 2003).

An inverse relationship between education levels and rates of PTSD is sometimes found (e.g. Green et al., 1985), but in combat this may be linked to higher exposure to frontline combat of those with lower education (Green et al., 1990). The NCS found that once sex, age, marital status and their interactions were controlled, there was no residual association of PTSD with level of education (Kessler et al., 1995).

Previous psychiatric history seems to contribute to risk, but increasingly investigations of depressed, anxious and suicidal populations (summarised in Nemeroff et al., 2006) are revealing high levels of early trauma through childhood abuse or other adverse events. Nemeroff et al (2006) contend that biological effects of early life stress on the developing brain and functioning of the HPA-axis have likely been confounding factors in research on the biology of depression and these authors observe that "although prevalence estimates [of early trauma] are extremely approximate, they are indeed sufficient to account in part for the high prevalence of depression and anxiety disorders among the general population" (p7). Childhood adversity in itself predicts PTSD. Also, in children, trauma threatening not only self but family integrity, as in witnessing domestic violence is predictive of PTSD (Silva et al. 2000). That childhood abuse and other adverse events are risk factors is perhaps unsurprising since previous exposure to trauma is an important risk factor for PTSD (Steketee & Foa, 1987).

In a meta-analysis, relatively larger effects were found for variables relating to the severity of the trauma itself and the period afterwards, particularly lack of social support (Brewin et al., 2000; Andrews et al., 2003; Zoellner et al., 1999; Green et al., 1985). Dissociation at the time of trauma has been considered an important risk factor (e.g. Marmar et al., 1994; Bremner et al., 1992; van der Kolk & van der Hart, 1989; van der Kolk et al., 1996a) but inevitably relies on retrospective reports, which may be open to distortions of memory (Candel & Merckelbach, 2004); prospective studies are difficult to do not least because of the randomness with which trauma occurs (McFarlane & Yehuda, 1996).

Post-trauma social support appears protective, and negative social responses are associated with poorer outcomes (Brewin, 2003; Brewin et al., 2000). A recent meta-analysis (Ozer et al., 2003) suggests that peritraumatic processes rather than individual vulnerabilities are more important in predicting PTSD. Family and self history of psychiatric illness and previous trauma had small predictive effects, whereas perceived life threat and experience of intense negative emotion at the time of the trauma, and an (inverse) relation with perceived social support had larger predictive effects and peritraumatic dissociation the largest. Testing of a model of risk and resilience factors in a large sample (n=715) of police officers, produced five significant predictors in a regression analysis; risks were greater peritraumatic distress and dissociation, greater work stress and lack of social support while use of problem solving coping was helpful (Marmar et al., 2006). Once again these factors point to the importance of responses to the trauma rather than prior vulnerabilities.

That social support is protective may be consistent with the apparent importance of verbalising a trauma experience: if individuals are able to revisit the trauma in an environment of positive support and talk over what has happened, this may represent successful resolution, whereas negative social responses, such as blaming the victim, or taking control of their decisions (Ullman et al., 2007) may be equivalent to re-traumatisation in the same way as debriefing may exacerbate symptoms (Bisson et al., 1997) as discussed in section 1.3.6 above.

Much is made in the PTSD literature of how individuals experiencing the “same” trauma do not all go on to develop PTSD. However, detailed examinations of individual experience reveal many factors operate during the event that possibly preclude a “same” experience. An example is the study of 117 survivors of the Beverley Hills Supper Club Fire in 1977, involving over 2500 patrons, many of whom were trapped by inadequate fire exits and in which 165 people died (Green et al., 1985). Apart from measures of other risk factors considered above (such as previous and subsequent life events, coping, social supports, subjective stress and assessment of symptoms) many other detailed measures were included including bereavement, life threat and post-fire experiences.

Bereavement was rated by how close the relationship was with the lost person or persons. Life threat included the extent of any warning, the closeness of contact with smoke and difficulty in exiting; extent of any injury was rated on a three point scale. Separate records were made of immediate post-fire experiences such as helping to pull out dead bodies, or visiting the temporary morgue set up in a nearby armoury, as well as the length of time spent waiting for news of a friend or loved one.

At this level of detail, it becomes clear that even arbitrary factors such as one’s spatial location within the club is likely to greatly affect the extent of fear and helplessness experienced and the particular lived experiences through the event. These “stress-at-fire”, objective measures were those most highly correlated with primary outcome measures and in a regression analysis explained 45.1% and 29.6% of the variance in affective distress and symptoms respectively one year after the fire. In keeping with more recent studies, other significant predictive factors of symptoms were prior life events (10.8% of variance), demographic factors (9.0%) and subjective stress (6.2%).

Interestingly, at two years post fire, while the "stress-at-fire" measures were still significant and accounted for 34.8% of the variance in affective distress, these measures also accounted for almost a third (27.1%) of the variance in substance abuse, an important co-morbid condition with PTSD, which appeared most related to trying to rescue people. Green et al (1985) conclude that "the most striking finding …. is the extent to which individual differences in people's objective experiences during the fire were predictive of their later psychological functioning, particularly with regard to primary stress response symptoms" (p 677) and that the effects of different aspects may vary over time. This fire and the associated research occurred prior to the inclusion of PTSD in the DSM, so does not use current conceptions of the disorder. Nevertheless, this serves to remind us that at a micro-level, everyone's location in space and time is unique and that the events of a trauma will impact differently as a consequence, irrespective of the other more commonly identified risk factors for PTSD.

1.6 Handedness and laterality

This section outlines basic observations in respect of asymmetry of hand use, or handedness. There are complex issues in the definition and measurement of handedness and these are pursued in Chapter 2. There are empirical facts which current theories of left handedness can not explain; neither do current theories speak directly as to why left handers may show increased prevalence of PTSD. Issues in respect of lateralised hand use are introduced here and Chapter 9, a final theoretical chapter, returns to these issues. While the work presented in Chapter 7 tests one theory of handedness, outlined in Chapter 2, a full consideration of proposed theories of handedness remains for Chapter 9.

The human body, and indeed the bodies of most other multicellular organisms, appears to be organised symmetrically about the midline, with most organs paired to either side. It has generally been considered that many of these organs are also functionally symmetrical, and that human handedness is an exception (e.g. Corballis, 2003; Bishop, 1990a). However, lateralisation in brain functions has been considered above in section 1.3 and it is becoming increasingly evident that functional asymmetry is widespread and occurs across species. For present purposes, the functions of most interest are the paired sensory organs (in humans the major sensory organs are the eyes and ears) and the limbs which effect the major motor responses of the body. The use of the term handedness without qualification is used here to refer to the hand used for writing.

The majority of humans are right handed but approximately 10% of the population is left handed. Motor control is effected by the contralateral hemisphere, that is the left hemisphere in right handers. There is evidence that the left hemisphere is superior in guided motor tasks. Performance of hemiplegic children on a variety of motor tests, showed a significant superiority in the right hand of left hemiplegics compared with the left hand of right hemiplegics; if the two hemispheres were equipotent in terms of motor performance, this result would not be expected (Hiscock et al., 1989; Peters, 2000). There are excitatory and inhibitory connections across the corpus callosum, which unites the two hemispheres, and there are delicate balances in functional coupling between the hemispheres. Connectivity between homotopic areas of the motor cortex is mainly inhibitory in nature; in right handers unilateral hand movements are associated with ipsilateral deactivation of the cortex, such that the dominant left hemisphere inhibits the right hemisphere. However, in left handers this pattern is also observed, suggesting that the left pre-motor cortex modulates neural activity in bilateral primary sensorimotor cortices irrespective of the moving hand. It would appear that the left pre-motor cortex/right hand combination is superior in motor control *per se* and/or in the performance of sequential tasks (Pollok et al., 2006).

Predominant right handedness could suggest either an adaptive advantage over ambidexterity - the use of either hand according to circumstance - which may appear preferable (Bishop, 1990a) or that handedness is not adaptive in itself and is a by-product of some other characteristic (such as language (e.g. Corballis, 2003) which is not further considered here) or the operation of some consistent environmental process.

Bishop (1990a) suggests that handedness may be most apparent in highly skilled, stereotyped pre-programmed movements. In learning a motor skill, initial performance is relatively poor: muscles are poorly co-ordinated and feedback is actively monitored to improve performance, until over time, a motor programme is formed that co-ordinates the sequence into a pre-programmed whole. Whilst practice, through frequency of use, may influence stereotypy, the speed and precision required will also be important; to achieve accuracy, instantaneous ballistic movements such as throwing, where feedback is minimal, have to be pre-programmed. Handedness may also be beneficial in bimanual tasks, so that both hands do not have to learn dual roles. None of these actions need necessarily be the most commonly performed actions.

To test this hypothesis, Bishop (1990a) used available performance data for a large (n=934) sample of male students on a variety of manual tasks (Provins & Magliaro, 1993) and rated these activities according to six characteristics: strength, precision, speed, whether instantaneous, and whether bilateral coordination and mirror-reversible movements were involved A rough estimate was made of the frequency each of the performance tasks would be carried out on average. Regression analysis showed that the strongest predictor of hand preference for a task was the precision of the movement, the next being movements with complementary action by the two hands (such as tool use) or which were ballistic actions (such as throwing); frequency of performance of the action seemed unimportant (Bishop, 1990a).

Though this was acknowledged as an informal analysis, a study using rats is supportive of this analysis. The pattern of learning observed in rats trained to reach a food sphere from a narrow tube with one paw, showed a gradual reorganisation from attempts with either hand, consistent with innate alternating excavatory movements with both paws which would be used in digging, to consistent use of one hand for this learned new skilled precision movement (Stashkevich & Kulikov, 2007). Similarly, in wild chimpanzees observed termite fishing, a skilful one-handed task requiring object manipulation, those who exhibited a consistent hand preference were found to be more efficient, gathering more prey per unit effort, suggesting there is benefit in lateralisation of skilled manipulative tasks (McGrew & Marchant, 1999). It seems then that motor skills requiring precision are those most likely to show a consistent hand preference and this may be relevant in comparative studies a topic revisited in Chapter 9.

If humans are predominantly right handed, this raises several fundamental questions. Why should there be a preference for use of one hand rather than using either equally for tasks? Why is it that the right hand should be preferred by the majority of humans, rather than the left and why do some humans prefer to use their left hands at all? The fact that the population distribution of handedness is not 50-50 suggests that a factor (or factors) other than chance are operating. If so, what are the mechanisms that underlie the observed distribution of right and left handedness? At present, there are incomplete answers to these questions and Chapter 9 will consider them further.

1.7 Structure of the following chapters

This thesis presents an eclectic mix of experimental work, investigating phenomena which are relevant to PTSD and which have lateralisation implications. Of prime importance is the work extending previous findings of an association of non-right hand preference with increased prevalence of PTSD by using samples of left handers.

Chapter 2 describes methods which are common to most, if not all, of these studies. These include standard instruments used as a diagnostic measure of possible PTSD (in the absence of a clinician assessment) and for assessment of lateral preference. The latter raise considerable methodological issues in the definition and measurement of handedness and these are fully discussed. The second to fourth digit ratio (2D:4D) is a measure putatively indicative of *in utero* levels of testosterone, one of the mechanisms proposed to account for left handedness. As it is apparently relatively simple to collect, this measure is included in most of the experimental studies and Chapter 2 considers the status and methods of this measure, noting that an apparently simple methodology is not in fact as simple as it seems. Two of the experimental chapters (5&6) use a film excerpt as a laboratory analogue of fear and Chapter 2 also discusses the rationale for this methodology.

The experimental chapters which follow answer the fundamental research questions of this thesis. Chapters 3 and 4 were designed to answer two questions. Firstly, does the finding of non-right handedness associated with increased prevalence of PTSD extend to civilian populations and to women? Secondly, is it left or mixed preference which is important? Chapter 3 presents findings from non-clinical, general population groups recruited from two different sources in order to recruit sufficient left handers to make analysis possible: students and staff of the University of Stirling and members of the general public who were weekend visitors to the Glasgow Science Centre, a hi-tech "hands on" science-based tourist attraction. Chapter 4 uses pooled data from an international, clinical collaborative study to address the same issues in populations known to have a clinical diagnosis of PTSD, compared to clinically assessed individuals exposed to trauma but without PTSD, and with anxiety disorders other than PTSD. Both of these chapters hypothesise that left handedness, rather than mixed handedness, is associated with increased prevalence of PTSD and with symptoms of the disorder.

Chapter 5 is one of two experimental chapters which use ostensibly healthy, student population samples of left and right handers to investigate whether they differ in emotional processing and memory in ways characteristic of people with PTSD. Chapter 5 reports two experimental studies. The first was designed to test whether film excerpts, intended for use as a laboratory analogue of fear in experiments reported in the second part of Chapter 5 and in Chapter 6, were able to elicit subjective self-report measures of fear and to provoke physiological arousal, as measured by skin conductance response (SCR), known to be part of the autonomic response to fear. The second part of Chapter 5 investigates whether memory for events of the fearful film differs in left and right handers. This represents a laboratory test of memory perhaps more ecologically valid to traumatic events than typical tests of episodic memory using word lists or similar stimuli, and the procedure includes a standard test of verbal memory for comparison purposes. The film is intended to specifically target the emotion of fear in a dynamic way veridical to real world experience and the rationale for how the film medium may do this is examined in detail in respect of this film. Both of these experiments also consider possible sex differences in responses, in the context of higher prevalence of PTSD in women compared to men.

Chapter 6 presents an experiment which has three aims. Firstly, the study compares the performance of left and right handers using an emotional Stroop colour naming paradigm in which there is known to be a robust interference effect in people with PTSD. This is made situationally relevant by including film-related words as the target condition. Secondly, since much of what is known about PTSD implicates verbal functioning, a novel type of Stroop paradigm was constructed to be non-verbal in nature to further investigate and compare interference effects in a between-subjects design. Thirdly, a recognition test of memory for the words used in the (word) Stroop task is used to investigate processing of stimuli during the task.

Chapter 7 tests one theory about a possible causal factor for left handedness: the hypothesis that left handedness is linked to *in-utero* testosterone. This is afforded by an apparently simple indicative measure, the 2D:4D and this is assessed in the large community populations participating in the study reported in Chapter 3 and the other experimental, student samples in the studies of Chapters 5&6.

Chapter 8 concludes the experimental work of the thesis with a summary and review of findings. Results are discussed in relation to the main theme of this thesis which is of lateralisation of functions relevant to PTSD. Possible implications and suggestions for further work are also presented in this chapter.

Chapter 9 is an integrative, theoretical chapter which returns to the question of possible causes of left handedness and the inadequacies of present theories in accounting for all the empirical findings in respect of handedness. Evidence in the literature is also reviewed which provides support for revisiting an old hypothesis, that of birth stress, but refining it to hypothesise that peri-natal experience of events specifically traumatic to the neonate may precipitate changes in lateralisation that result in left handedness.

This is shown to be theoretically consistent not only with empirical evidence in respect of handedness, but may also account for the observed relationships between left handedness and PTSD established in Chapters 3&4 and for the findings from the experimental studies in Chapters 5&6 in respect of left hander's behaviour on the component tasks. This remains as a hypothesis to be empirically tested.

Chapter 2

Methodological Issues

This chapter describes the methods that have been used in the studies within this thesis for assessing PTSD, handedness, a state measure of perceived stress and the second to fourth digit ratio (2D:4D), a measure indicative of *in utero* testosterone. This chapter also includes a rationale for the use of fearful films as a stimulus in the experimental studies.

2.1 Posttraumatic Diagnostic Scale (PDS)

The Posttraumatic Diagnostic Scale (PDS: Foa et al., 1997) included at Appendix 1, is a self-report measure, and is structured to map directly onto DSM-IV criteria for diagnosis of PTSD. It provides both a provisional diagnosis and a measure of symptom severity. In the context of the present study the PDS provides an easy to administer instrument for assessing possible PTSD; the absence of an interview-based clinical assessment is a limitation and means that a diagnosis cannot be made with certainty. Nevertheless, the PDS questions cover all DSM-IV criteria. Limitations with respect to other measures used in studies of PTSD have been summarised by Foa et al (1997) and are shown in Table 2.1 (for clinician interview) and Table 2.2 (for self-report instruments). The sensitivity of a measure is the proportion of individuals with a positive diagnosis who have a positive test result; specificity refers to the proportion of individuals with a negative diagnosis who have a negative test. Against a SCID diagnosis of PTSD, there was 82% agreement and the PDS showed sensitivity of .89 and specificity of .75 indicating a satisfactory level of agreement (Foa et al., 1997).

Table 2.1 Diagnostic instruments for PTSD using clinical interview (text in boxes indicates where instruments are unsatisfactory)

(1) Clinical Interviews	Diagnosis?	Symptom severity?	all DSM criteria?	reliable & valid?
Diagnostic Interview Schedule: **DIS** (Robins & Helzer, 1985)		No		? all trauma
Structured Interview for PTSD: **SI-PTSD** (Davidson et al., 1989);				? all trauma
‡ The Structured Clinical Interview for the DSM-IV: **SCID** (Spitzer et al., 1995)		No		? all trauma
Clinician Administered PTSD Scale: **CAPS** (Blake et al., 1995)				? all trauma
The PTSD Interview: **PTSD-I** (Watson et al., 1991)				? all trauma
PTSD Symptom Scale – Interview: **PSS-I**; (Foa et al., 1993)				? all trauma

The instruments listed in Table 2.1 were in the main developed and tested in studies of male combat veterans and thus reliability and validity was related to this group rather than for all types of trauma. Some of the self report measures in Table 2.2 are designed to fit the conceptual underpinnings of PTSD, rather than being empirically formulated and not all directly correspond to the symptoms forming the diagnostic criteria in DSM-III-R or DSM-IV. In these cases, studies in trauma populations have attempted to derive cut-off points to determine diagnosis. This has the disadvantage that the critical score used to indicate presence or absence of PTSD may vary with the type of sample used in these studies. None of the other self-report instruments listed in Table 2.2 can stand alone in assessing all DSM-IV criteria and thus providing a diagnosis of PTSD.

‡ The SCID is the most widely used measure against which other, self-report, inventories have been compared and validated.

Several do not provide a measure of symptom severity. The PDS was developed to rectify the limitations of the previously available instruments.

Table 2.2 Self report diagnostic instruments for PTSD (text in boxes indicates shortcomings of the measure)

(2) Self-report Measures	Diagnosis?	Symptom severity?	all DSM criteria?	reliable & valid?
Impact of Events Scale: **IES** (Horowitz et al., 1979)	No	No	No	
Revised Impact of Events Scale: **RIES** (Weiss & Marmar, 1997)	No	No	No	
Minnesota Multiphasic Personality Inventory: **MMPI** (Hathaway & McKinley, 1951) and revision: **MMPI – 2** (Butcher et al., 1989) Derived: Keane PTSD Scale: **PK** Scale (Keane et al., 1984) PTSD Scale: **PS** (Schlenger & Kulka, 1989)	No		No	No empirical cf conceptual ∴ vulnerable to sample
Millon Clinical Multiaxial Inventory – III: **MCMI-III** (Millon, 1994)	No		No	ditto ? valid
Mississippi Scale (Keane et al., 1988)	No	No	No	vulnerable to sample
The **Penn Inventory** (Hammarberg, 1992)	No	No	No	only males
PTSD Symptom Scale – Self Report: **PSS-SR** (Foa et al., 1993) = precursor of **PDS**	No		only DSM-III-R	
Posttraumatic Diagnostic Scale: **PDS** (Foa et al., 1997)	Designed to remedy these limitations + DSM-IV + assessed on a diverse sample of trauma plus information on nature of trauma + information on degree of impairment			

In the context of this thesis, the PDS was used in all studies to assess possible PTSD, except in some of the contributing datasets in the collaborative study reported in Chapter 4 which had used clinician assessments of PTSD.

Even the best measures are not without problems. A common difficulty is that where effects of a trauma are probed further, usually by focussing on the ‘worst’ event (including the PDS), this may potentially lose information in respect of any other traumas. This may result in significant underestimation of PTSD rates (Cusack et al., 2002). In any case, it may be difficult for a person with PTSD to separately assign the symptoms they feel to one of a variety of traumas. It is also considered important, particularly when interviewing women, to use behaviourally specific wording when asking about sexual assault and rape, rather than using these labels, as the latter may reduce reporting. Many instruments, including the SCID, fail to use behaviourally specific or sensitive wording and Cusack (2002) suggests this is "likely to result in many respondents 'skipping out' of the PTSD portion of the instrument" (p161). In using the PDS these limitations are acknowledged; PTSD may be underdiagnosed and diagnosis is suggestive rather than definitive in the absence of interview-based clinician assessment.

2.2 Measurement of handedness

> "It is by no means a simple matter to diagnose left-handedness."
> (Newman, 1928b; p301)

At first sight it might seem easy to determine right and left handedness. In everyday life this distinction is made on the hand used for writing and indeed McManus (1984) considers that handedness should be considered as a binary categorical variable. However, factors may operate to change hand use; for example, cultural pressures may operate against use of the left hand for writing. It is also possible that injury to the dominant hand may also force a change, which may persist. Assessment of handedness here therefore included a question concerning whether hand use had ever changed.

Using only one categorical measure as a basis to investigate matters of interest with respect to laterality seems unsatisfactory: researchers have considered that degree of preference, or consistency in the use of one hand, and for different types of activity, may be important as well as direction. It is here that problems of definition and measurement emerge.

First, there is a fundamental distinction between *preference* and *performance*. Annett (1985) considers handedness to be a continuous variable best measured by proficiency, or performance, of a task, and developed a peg-moving task which uses a relatively skilled action but one unlikely to be contaminated by practice in everyday experience. Scores on a laterality index, 100(R-L)/(R+L), calculated by relative speed of the two hands to perform the task, are normally distributed. Preference scores, measured by questionnaire, on the other hand, produce a J-shaped distribution: a majority of right handers, a minority of left handers and few in between with reduced preference. Correlations between the two are relatively low at around 0.7 and have been argued to be orthogonal dimensions (Porac & Coren, 1981; cited in Bishop, 1990a). The latter author shows that this may not be the case. If there is a direct relationship between the probability of using the preferred hand and the difference in proficiency, such that when both hands are equally proficient then neither is preferred, but as one increases in proficiency then the probability of using this hand increases, then using a simulation it can be shown that a J-shaped distribution of preference scores can be derived from the normal distribution of performance scores (Bishop, 1989).

Measurement of hand preference, typically by questionnaire, is, however, usually used rather than performance, and has advantages of time and cost in administration, being readily used with large samples. The Edinburgh Handedness Inventory (EHI: Oldfield,

1971) is one of the most widely used and, in the context of this thesis, is one of the two measures used by Spivak et al. (1998) in the first study investigating lateral preference in PTSD. The EHI (Appendix 2) consists of 10 items (plus two additional questions about foot and eye use). In the original version, participants are asked to indicate by a ++ if preference is so strong they would never use the other hand and otherwise by a + in the appropriate left/right columns; no preference is indicated by a + in both columns. Other variations of the questionnaire separate the response section into five columns and use headings such as "always", "usually", "seldom" and "never" to indicate strength of preference. Scoring can be done by use of a laterality quotient (LQ: 100(R-L)/(R+L) with range -100 to +100) or by a summing method, whereby a unit score is allocated to each column (e.g. -10, -5, 0, 5, 10 respectively) and scores summed over the 10 items to give a laterality score (LS, with range corresponding to the unit score, in this instance -100 to +100). While a handedness questionnaire may appear to be a simple instrument, it results in considerable methodological difficulties.

Any five column Likert scale first of all generates problems of semantic interpretation and estimation in responding to the column headings. It has been reported that males are more likely than females to answer "usually" rather than "always" (Bryden, 1977). Another objection is that the items in a list are all accorded the same value, though they may vary considerably in skill required (Annett, 1985) and items can be idiosyncratic across different instruments (Bishop, 1990a). Assessment of handedness may therefore vary depending on which types of item are included. A more fundamental problem is that direction and degree of handedness are hopelessly confounded (for details of examples see: Schachter, 2000; Bishop, 1990a). To illustrate briefly here, someone scoring -10 on half the items and +10 on the other half, indicating an inconsistent, but strong preference in hand use would score the same as someone scoring -5 on half of and +5 on the other items (weak, inconsistent preference) and as someone scoring 0 throughout, indicating no preference.

The scoring method used is also relevant. While both the LQ and LS will be sensitive to overall direction and will separate individuals above and below a score of 0, the LS is more sensitive to degree of handedness. For example: a subject1 "usually" using their right hand for all tasks and scoring +5 on every item will have the same LQ (+100) as subject2 scoring +10 ("always" - clearly a stronger preference) on every item, whereas the LS would be +50 for the former and +100 for the latter. Subject3, always using their right hand for 9/10 items and usually the left for 1/10, would have a LQ score of +89, which is lower than the score for subject1 and a counterintuitive result. These problems are intractable, but are minimized by collapsing the five columns to three (left/either/right) by ignoring always/usually distinctions (Bishop et al., 1996; Schachter, 2000) and using an LS, not LQ method (Schachter, 2000). This is the method used in the original study of lateral preference in PTSD (Spivak et al., 1998). Many studies in the handedness literature use a five column LQ, as this is the method originally described by Oldfield (1971), and clearly results are affected by the method used.

There is also a problem in defining what constitutes right/left handedness. Is it 100% performance on all items? If not, what cutoff point should be used? Should there be two categories (above/below zero as Oldfield suggested?) or three, to include a group of weak, or inconsistent, handers which may be of theoretical interest? Peters (1992) asks if it is reasonable to consider together as "non right-handers" a subset who use the left hand for fine manual skills but the right hand for gross motor skills such as racquet sports and a subset who use the left hand consistently for a variety of activities. If three groups are desired, at which point then, does right/left handedness become weak or mixed handedness? There is no agreement on these issues.

When highly conservative criteria (100% on all items) are used to define right/left handedness, a longer inventory provides more opportunity for less than 100% answering. This results in right handedness being inversely related to the number of items comprising the inventory; using this criterion, in the same participants, a 60-item questionnaire can yield less than 1% right handers and a 4-item questionnaire over 80% (Peters, 1992). In the same study, separation at the midpoint of 0 into two classes did not separate clearly those who wrote with their right and left hands: around 24% of left handers for writing had an average score above the midpoint. Indeed, when considering neuropsychological variables in relation to handedness, the setting of cut-off points, particularly post-hoc, can generate misleading results (Bishop, 1990b). Not only that, but due to the fact that left handers make up such a small proportion of the population, the size of experimental and control groups may not have sufficient power to detect a difference in the variable of interest (Schachter, 2000; Bishop, 1990a).

Unless tests or tasks are repeated, there is only a between task assessment of handedness; what may also be important, in respect of understanding factors related to laterality, is stability of preference on the same task, a measure of *ambiguous* handedness. An separate inventory of items for assessing ambiguity is widely used (Soper et al., 1987), but as this is a behavioural rather than a self-report measure it is not used here.

In recognition of these methodological problems, handedness was assessed in all studies in this thesis using the EHI scored as follows. Responses were allocated one point, +1 for right, -1 for left hand (or 0 for either) and summed to give a handedness score

(Oldfield 10) ranging from -10 (consistent left hand preference) to +10 (consistent right hand preference). An additional two questions relate to use of the foot in kicking and eye preference. These were scored in the same way and summed to give a lateral preference score (Oldfield 12) ranging from -12 to +12.

In addition to measuring hand dominance, foot, eye and ear preference are additionally assessed in a behaviourally validated inventory (Coren et al., 1979). This asks 13 questions relating to preference in the use of hand (four questions) foot, ear and eye (each three questions) in performing certain tasks. Responses are also allocated one point, +1 for right, -1 for left hand (or 0 for either) and summed to give scores ranging from -4 to +4 for hand preference and -3 to +3 for foot, ear and eye preference (with minus scores indicating left preference and plus scores right preference). Scores were also summed to give an overall lateral preference score ranging from -13 to +13.

Foot preference might suggest itself as a measure of laterality less likely subject to possible cultural biases in acceptable hand use and to the right world nature of most tools, which often results in left handers learning to use their right hands to operate them. However, an immediate problem is the fundamental question of which foot is to be considered dominant: the one performing an action (such as in kicking, or the leading foot in climbing onto something – a mobilising factor) or the one providing postural control by remaining grounded – a stabilising factor (Gabbard & Hart, 2000). Consensus is that the mobilising limb should be considered the dominant limb, when defined in this bilateral context (Peters, 1988); hopping, for example, does not have a bilateral context, and hence determination is indistinct. Humans have been suggested to be predominantly right footed for mobilisation and left footed for stabilisation, although this may turn out to be dependent on the relative complexity of the two types of task and whether there is in fact a dominant limb can be questioned (Gabbard & Hart, 2000). The majority (83-88%) of humans are right footed (for mobilisation) (Coren, 1993). Lateral preference in use of the paired sensory organs appears to be independent of limb preference (Porac et al., 1980).

There are suggestions that irrespective of personal handedness there may be an effect of familial sinistrality (on neuropsychological variables), which is usually taken as an indication of genetic predisposition. Irrespective of the correctness of this latter assumption, Bishop (1980) supplies examples of such studies, but points out a possible artefactual bias. If familial sinistrality includes siblings, the chance of an individual having a sinistral relative will increase with the number of siblings they have, thus confounding family size and sinistrality. In a further analysis of the issue, comparing predictions from Annett's right shift model (Annett, 1985) with those based on a prevalence of left handedness of 11.6% assuming no genetic relationships, Bishop (1990c) suggested that familial sinistrality was a very weak predictor of any possible genetic influence on handedness. The combined inventory used here (Appendix 2) asked respondents to indicate which hand (right, left or both equally) both their father and mother (i.e. excluding siblings and more distant relatives) used for writing to investigate possible effects of parental handedness in relation to PTSD as reported by Chemtob & Taylor (2003).

2.3 2D:4D

A link between *in utero* testosterone and left handedness has long been hypothesized (Geschwind & Galaburda, 1985). Direct study of *in utero* testosterone in humans is not easy as it is not amenable to experimental manipulation for ethical reasons. However, recent work has proposed that the relative lengths of the second and fourth digits reflect hormonal influences early in the gestational period: Homeobox, or Hox, genes control overall development in multicellular organisms and particular groups of these - the Hox a and Hox d - genes control the development of the testes and ovaries as well as the fingers and toes (Kondo et al., 1997). Manning (2002) argues that the length of the fourth digit (typically relatively longer in males) is determined by the level of testosterone, which is produced from week 8 of gestation and peaks at week 13. Similarly, the length of the second digit (typically longer in females) is determined by oestrogen, formed from testosterone by the action of the enzyme aromatase, found in the foetal ovaries and placenta of females. The ratio of the length of the second to fourth digit (2D:4D) is typically lower in males and higher in females (Manning et al., 1998); this study also found that in men, the 2D:4D of the right hand was significantly negatively correlated with circulating testosterone concentrations (from blood samples) and the negative correlation of testosterone with the left hand 2D:4D approached significance.

The evidence above, supporting Manning's (2002) position, while persuasive, is indirect. Lutchmaya et al (2004) examined direct associations between foetal testosterone and oestrogen and 2D:4D by analysing amniotic fluid obtained by amniocentesis and 2D:4D ratio in the subsequent children when aged 2 years. Directions of hypothesised associations with 2D:4D were as predicted but not significant for testosterone and oestrogen separately. However, in the right hand, the linear regression was significant for a calculated ratio of (foetal) testosterone to oestrogen: low 2D:4D values were associated with high foetal testosterone relative to foetal oestrogen levels and high 2D:4D associated with low foetal testosterone relative to high foetal oestrogen levels. This study provides a more direct form of evidence that levels of prenatal sex hormones influence the development of the digits, and that 2D:4D is a useful indicative measure of the *in utero* hormonal environment.

The 2D:4D is calculated from measurements made on the ventral surface of the hand from the basal crease to the tip of the digit. Measurements were made in all of the student and Glasgow Science Centre samples and the data pooled from all these sources; results are presented in Chapter 7. In the first sample in which PTSD and handedness was assessed, and in those first recruited to the experiment of Chapter 6, a scanner was used to capture an image of the ventral surface of both hands placed flat on the glass bed of the scanner. Measurements of digit length were then made using Autometric software (DeBruine, 2003). This method proved unsatisfactory for a variety of reasons and these, and other, methodological issues are presented in Appendix 18. For subsequent samples *in vivo* measurements were then made using a digital calliper. Chapter 7 presents these findings and provides further details of the methodology used.

2.4 A measure of perceived stress: The PSS10

The Perceived Stress Scale 10-item version (PSS10: Cohen & Williamson, 1988) was included as a measure of recent underlying stress (in the last month). The PSS10 is a validated instrument with norms from a large probability sample in the USA and internal reliability ($\alpha = .78$); items are designed to tap how unpredictable, uncontrollable and overloaded participants find their lives. This measure was included in all of the experimental studies included in this thesis, to check whether underlying stress, rather than manipulation of experimental variables, accounted for any possible relationships found.

2.5 The use of films

This section critically examines the appropriateness of laboratory stressors as analogues of fear and presents justifications for using movie excerpts.

There are ethical difficulties for any experimental study relevant to PTSD: no subject population can be subjected to trauma. Although predating the formulation of PTSD in the DSM, Lazarus (1964) considers the issue of laboratory analogues for conditions that give rise to what is now recognised as PTSD. He defines an analogue as manipulations in the laboratory experiment which are either parallel or similar to those processes postulated to occur in the natural situation, with an expectation that any findings may generalise to the real life situation. His view is that not all laboratory manipulations are good analogues to these postulated processes; manipulations may produce measurable biochemical (e.g. cortisol), ANS (e.g. HR, skin conductance) or behavioural (e.g. self report, cognitive disorganisation) reactions, but each of these can be outputs from a variety of processes which may not necessarily be those psychological processes of interest. For example, performing mental arithmetic, attacks to self-esteem by false feedback, plunging an arm in ice cold water, and watching a movie can all produce a "stress reaction", but Lazarus questions categorising these diverse procedures together as interchangeable "stressors".

Lazarus (1964) argues that a consideration of the physiological and psychological nature of the stimuli and the processes that occur between stimuli and response is vital to an understanding of why these stimuli produce a response - and that in this sense all "stressors" are not equivalent. For example, in the case of attacks on self-esteem, the underlying process is assumed to be the production of some form of psychological threat. Is therefore plunging an arm in ice cold water also a threat? Clearly not: a better alternative explanation is the homeostatic mechanisms in temperature regulation responding to physical demands on the tissues that activate the organism and which produce similar ANS changes. While the physiological end points may be similar, Lazarus suggests the key question is the *psychological mechanism* by which the effects are produced and that solely demonstrating that an experimental condition results in some form of stress reaction is not equivalent to producing an analogue of psychological stress.

As discussed in the first chapter, the experience of fear in response to threat underlies the development of PTSD and is required for its diagnosis. Lazarus (1964) suggests that the anticipation of potential harm is key to the concept of threat. It will be argued here that many experimental manipulations of "stress" lack this quality and hence are not analogue models of fear. For example, on this basis, it is apparent that psychosocial stressors, such as mental arithmetic or false feedback, and physical stressors, such as immersion in ice-cold water do not provide parallels to the experience of fear.

In some way then, the experience of fear needs to be experimentally manipulated. It is not intended here to review the mood induction literature; however, doubts have been raised about the effectiveness (for example, to generate intense emotions) and validity (are effects due to demand characteristics?) of standard laboratory mood induction procedures (Westermann et al., 1996). Their meta-analysis and a prior review (Gerrards-Hesse et al., 1994) concluded that film/story based mood induction procedures were not only the most effective of the procedures, but were also highly effective.

Different story-based methods have been used in attempts to simulate extreme emotional events in a laboratory. These have taken two main forms: a slide with narration sequence (e.g. Cahill & McGaugh, 1995) or where film media are used, of gruesome accidents (e.g. Holmes et al., 2004; Brewin & Saunders, 2001). It is suggested here that neither of these forms is appropriate in attempting an analogue study relevant to the real world experiences which may precipitate PTSD.

Cahill's (1995) slide with narrative procedure has been well used to probe memory for emotional events, but effects on arousal are not always replicated (O'Carroll et al., 1999b; O'Carroll et al., 1999a). The story follows a young boy's day; in the "emotional" version he is involved in a road traffic accident (not shown) and the differential interpretation of the target slide, of badly scarred legs positioned on an Operating Theatre green sheet, is that his severed feet have been successfully reattached. The neutral version describes the slide as an actor made up for a practice disaster drill taking place while the boy is visiting the hospital where his father works. Laney et al (2004) describe other similar slide narratives (of a young man bleeding from an eyeball after being shot; a woman whose throat has been cut), in all of which one target slide presents shocking, visual stimuli.

The use of such slide sequences appears problematic for several reasons. A slide sequence is not dynamic, and hence not veridical to real world experience. Detenber et al (1998) suggest that motion is a fundamental attribute of the physical world and that motion detection is an innate ability, present in neonates; they showed that picture motion, compared to still images, evoked increased self report and physiological (skin conductance and heart rate) measures of arousal particularly for those images which were already negatively (or positively) valenced. This finding supports the use of a film rather than a slide narrative. This may be particularly relevant in today's media aware world, with internet based video sites such as YouTube, and recreational computer gaming technology, which render slide narratives a thing of the past. The slide narrative method also fails to generate anticipation of threat, an important component of fear.

Indeed, film excerpts suddenly presenting shocking or gruesome visual material, will not necessarily generate a stress response. Nomikos et al (1968) used an industrial safety film depicting three wood-shop accidents and spliced the film to create two different versions of each of the first two accidents. In a surprise, or short anticipation, version (similar to the form of slide narrative sequences described above) most of the anticipatory scenes preceding the first two accidents were cut; these segments were spliced into the original film to extend the anticipatory period prior to the accident, producing a suspenseful or long anticipation version. Participants viewing the suspenseful version showed significantly higher levels of autonomic disturbance, particularly skin conductance. Most of the build up of the stress reaction occurred during the anticipation period just prior to each accident; viewing the actual event added little to the rise in autonomic activity. This is consistent with the role of temporal expectancies in producing suspense in film (de Wied, 1995) and if an analogue of fear is to be generated, argue against using a slide presentation where one target slide of a gruesome image is suddenly presented.

The starting point for a laboratory analogue of stress should be a conceptualisation of the processes underlying the phenomena (Lazarus, 1964). In fear, this is the anticipation of danger and threat. This cannot be for real, but may be experienced via the medium of a fearful film. On an objective level, in viewing a film we know that this is a staged and not a real event. However, film media, unlike other forms of narrative, exert powerful diegetic effects (diegetic refers to the internal world that the characters experience: the narrative "space" that includes all the parts of the story) which create an illusion, difficult to escape, of being in the characters spatial world and experiencing it as if a physical event (Tan, 1995). This is because movement within the scene simulates the same perceptual stimuli as in the real world generating true to life sensory experience, from which emotions occur: "…. [film viewers] appraisal of spatial proximity is based on an immediate and one-to-one perceptual equivalent that is missing in other forms of narration" p12 (Tan, 1995). In a film, space and time are controlled, as is the viewer's knowledge which unfolds through the narrative; the viewer takes the role of invisible, empathetic witness (Tan, 1995; Zillmann, 1995) moving around in a fictional world, assuming perspectives dictated by the film. The viewer, through their privileged views of all aspects of the fictional world may have knowledge beyond that of the characters, but is powerless to act; in suspense films this is deliberately manipulated to increase anticipation of danger and thus parallels the experience of traumatic events which may give rise to PTSD which are required to be experienced with helplessness. While everyone will respond to a film differently, it is suggested that responses to the extreme stress-inducing moments of a suspense film, approximate a global response, as if in general, people respond innately to the portrayal of a fearful situation, and thus can be intentionally manipulated by the filmmaker, who proceeds with accurate expectations of the response that will occur to a scene (Norden, 1980). This is consistent with the view of Delagdo et al (2006) summarising experimental evidence, that fear learning through observation of a con-specific's experience can be as pervasive as fear learning in one's own direct experience and subserved by neural systems which predate the emergence of language.

In media studies there is a central distinction between content and form (Detenber et al., 1998); while content clearly can and does affect cognitive and emotional responses, the structural attributes of film also affect psychological responses. A movie film director will be seeking to use techniques that both engage the viewer in the story and, in a suspense film, to use those techniques that are most likely to generate anticipation of danger and threat. Both content and form are discussed in more detail in Chapter 5 for the movie excerpt used as a laboratory analogue of fear in the experimental work of this thesis.

Some studies using film media have used real life examples with shocking and gruesome content: "horrific" real life footage from the aftermath of road traffic accidents (e.g. Holmes et al., 2004). While personal involvement in an RTA could be fearful and traumatic, simply being an onlooker on something not made personally meaningful and with no anticipation of danger is unlikely to approximate a similar emotional state. Disgust seems far more likely than fear to be generated by gruesome content. These studies have either not measured self-reported emotion (Brewin & Saunders, 2001) or where self-report measures have been used, have not included fear (Holmes et al., 2004). These studies cannot therefore determine whether the emotion of fear was subjectively experienced by participants. Other experimental studies measuring ANS responses to the industrial safety film of wood-shop accidents (Birnbaum, 1964; cited in Norden, 1980) found that in the flashback version (the second accident), where the viewer knows the outcome in advance of the flashback to the circumstances leading up to a traumatic amputation, ANS responses steadily increased throughout the operation of the tool concerned up to and including the point of the accident. The third film, of an impalement, provided anticipatory cues of the accident, and resulted in increasing ANS responses to the point of impalement; however, in the immediately following sequence of events where the victim graphically exsanguinates on the floor, ANS responses dropped, suggesting that stress responses occur in anticipation of danger, but not in confrontation with a gruesome scene. This provides another reason to suppose that gruesome films are not simulating fear.

Film generated emotion in healthy subjects has been found to activate brain structures relevant to the experience of emotion, including the amygdala and hippocampus which were not activated by a cognitive recall strategy based on autobiographical scripts (Reiman et al., 1997). This strengthens the case for using film stimuli for generation of emotions similar to those experienced directly. Indeed, reactions to film induced and a real threat (electric shock) were found to be similar (Alfert, 1964; cited in Norden, 1980), suggesting that these reactions are similar processes.

Excerpts from two movies are used as laboratory analogues of fear for the work of this thesis. Both had been previously found to evoke the target emotion of fear by self report measures (Gross & Levenson, 1995). The short excerpt used by Gross & Levenson (1995) from Silence of the Lambs (Saxon et al., 1991) was extended to an eight minute excerpt in order to build up the anticipation of threat and danger and to provide a coherent storyline independent of the whole film with sufficient material to investigate memory for the film. This film is also used as an experimental manipulation in the experimental study of Chapter 6. The first part of Chapter 5 investigates stress responses to both this longer episode and two short excerpts from The Shining (Kubrick, 1980); Chapter 5 also considers the specific mechanisms by which these films are likely to produce a laboratory analogue of fear.

The following chapters report the studies which form the experimental work of this thesis.

Chapter 3

Left handedness and Posttraumatic Stress Disorder in non-clinical populations

Background: Previous studies have found an increased prevalence of mixed/left handedness in male combat veterans and children with posttraumatic stress disorder (PTSD).

Methods: This study examined lateral preference and screened for possible PTSD using a self-completion instrument (PDS: Foa et al., 1997) in a general population sample (N =596).

Results: Fifty one individuals met all criteria for possible diagnosis of PTSD and significantly more left handers (15%) than right handers (8%) met diagnostic criteria. This effect was associated with strong left-handedness, rather than weak or mixed handedness. Left handers were found to have significantly higher symptom scores, particularly in arousal symptoms of PTSD.

Conclusions: This study extends previous findings to a civilian population and to women and suggests the association with left handedness is a robust finding in people with PTSD.

This chapter reports two studies using self-report measures of PTSD and lateral preference in ostensibly healthy general population samples. The first of these was a large sample of students and general public visitors to the Glasgow Science Centre (see publication by Choudhary & O'Carroll, 2007: Appendix 23). Individuals opted into the study by volunteering to complete the measures. In the second case, completion of the same self-report measures was included within the experimental studies reported in Chapter 5 and Chapter 6 and an experimental study not reported here; these students participated in order to gain course credit.

3.1 PTSD is related to left handedness in a general population sample

3.1.1 Introduction

While much of the focus of research on posttraumatic stress disorder (PTSD) has been with war veterans (particularly of Vietnam), PTSD is common in civilian populations. That lateralisation may be relevant to PTSD has been considered in Chapter 1; the neuropsychological, perceptual, neuroimaging and non-human primate evidence suggesting that the right hemisphere of the brain is differentially involved in the experience of emotion, particularly negative emotion such as fear, and in avoidance behaviour has been discussed there. In summary, in people with PTSD, evidence of relative left hemisphere hypoactivation and right hemisphere hyperactivation includes, for example, behavioural (Vasterling et al., 2000), electrophysiological (Metzger et al., 2004) and neuroimaging (e.g. Shin et al., 1997) studies.

The original two studies in male combat veterans (Spivak et al., 1998; Chemtob & Taylor, 2003) found increased mixed lateral preference in veterans with PTSD. Subsequently, Saltzman et al (2006) found increased mixed laterality in traumatized children with PTSD and a correlation between laterality scores and symptom severity, indicating a leftward bias with increasing symptomatology. In a study relating handedness to treatment outcome in male combat veterans with PTSD, left handers were excluded as there were insufficient numbers for analysis (Forbes et al., 2006); PTSD veterans with mixed handedness reported less treatment improvement than those with consistent right handedness. Since none of these study populations contained sufficient left handers, these findings could indicate that it is not lateralization to right or left *per se*, but possibly weak (a tendency to mixed) handedness in comparison to strong handedness (to either right or left) that may be important.

This study was designed to answer two research questions; first, to assess laterality and experience of trauma in a large, ostensibly healthy, sample, and second, to test the association between laterality and PTSD in this non-treatment seeking civilian population of mixed gender, since no previous studies had included adult women.

Hypothesis 1: Higher prevalence of PTSD will be associated with left rather than mixed handedness.

Hypothesis 2: Symptom scores will be higher in left compared to right handers.

3.1.2 Methods

3.1.2.1 Participants

The study population consisted of 596 volunteers recruited from two main sources: students (mainly psychology undergraduates) and some staff of the university (N=286) and a general population drawn from visitors to the Glasgow Science Centre (N=310).

Participants were asked if they would consider participating in the study by filling in a handedness inventory and a questionnaire about experience of certain life events.

3.1.2.2 Measures

Lateral preference was assessed by self-completion of an inventory consisting of the two measures discussed in Chapter 2 and used by Spivak et al. (1998). Responses on the Edinburgh Handedness Inventory (Oldfield, 1971) were scored using the summing method used by Spivak et al. (1998) rather than Oldfield's (1971) laterality quotient to give a handedness score (Oldfield10) and laterality score (Oldfield12) including foot and eye preference. Secondly, the behaviourally validated Coren inventory (Coren et al. 1979) measured hand, foot, ear, and eye preference, providing a laterality score when summed. On each measure, maximum negative scores indicate consistent left hand preference and maximum positive scores, consistent right hand preference. In addition, a question asked respondents to indicate which hand both parents used for writing.

The Posttraumatic Diagnostic Scale (PDS; Foa et al., 1997) is a self-report measure of exposure to trauma and consequent reactions. In the absence of a clinician interview, individuals were classified as having a possible diagnosis of current PTSD (assessed over the last month) if their answers to all sections of the PDS met the criteria stipulated in the DSM-IV (see Table 1.1). Symptom severity was measured for each symptom cluster (re-experiencing, avoidance and arousal) and summed for an overall score.

3.1.2.3 Ethics

The project was fully described in an information sheet preceding the questionnaire pack which included a consent form for those choosing to participate by opting into the study. Since completing the PDS may have caused distress to anyone reminded of their traumatic experiences, the front cover included a reminder that should this occur they may wish to seek help from their GP (or student support services for the student participants). This research study was approved by the Department of Psychology Ethics Committee (see Appendix 23).

3.1.3 Results

3.1.3.1 Sample Description

The university sample was significantly younger than the science centre sample (m=22.1, SD=5.67, years; range 17y0m – 52y2m compared to m=39.2, SD=10.60, years; range 15y6m – 72y11m, t(587)=24.08, p<.001). There were significantly more females than males: 76% in the university group, $\chi^2(1,N=286)=78.67$, p<.001, 64% in the science centre group, $\chi^2(1,N=310)=22.76$, p<.001, and 70% overall, $\chi^2(1,N=596)=91.87$, p<.001. The two groups did not differ on variables relating to handedness and experience of trauma, and were combined for further analysis.

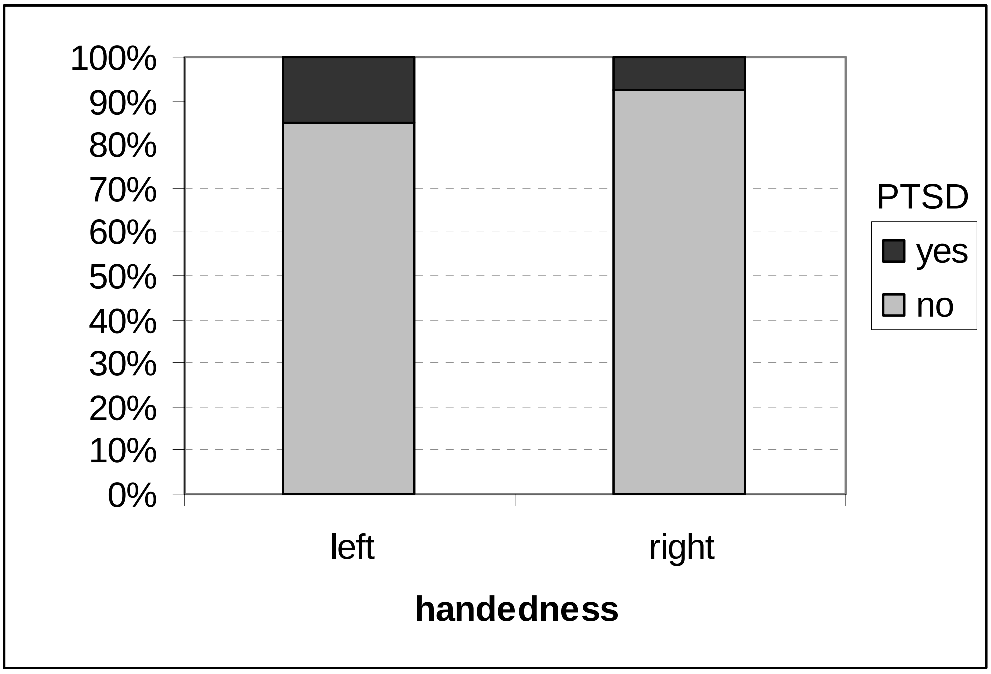
When classified by hand used for writing, 88% (N=524) were right handed, 11% were left handed (N=66) and 1% (N=6) reported using both hands equally; the latter two groups, as non-right handers, were combined for further analysis.

Over half of the participants (56%, N=333) reported experiencing a trauma; only 216 (36%) met Criterion A. Of these 216, approximately one in four (N=51: 8.6% of the total population – the PTSD group) met all DSM-IV diagnostic criteria for PTSD and have a possible diagnosis of PTSD, a figure consistent with estimated US prevalence rates (Kessler et al., 2005a; Kessler et al., 1995). Chi square tests revealed no significant differences in the distribution of those with PTSD between the two sample groups, or between males and females.

3.1.3.2 Relationships between Lateral Preference and PTSD

Identification of a PTSD group in this non-clinical sample allowed testing of the hypothesis that there would be relatively more leftward lateral preference in those with PTSD. Significantly more left handers (15%, N=11) than right handers (8%, N=40) met all criteria for a diagnosis of PTSD, $\chi^2(1,N=592)=4.62$, $p<.05$. This relationship is shown in Figure 3.1 below.

Figure 3.1 Prevalence of PTSD according to handedness



In order to investigate possible differences between (a) the PTSD group, (b) those that reported experiencing trauma on the PDS but did not meet diagnostic criteria for PTSD (the non-PTSD trauma group) and (c) those who did not report any experience of trauma (the control group), the various laterality scores each formed a dependent variable in a series of one-way ANOVAs. Significant effects were found for all handedness scores: for Oldfield 10, $F(2,566)=5.15$, $p<.01$; for Oldfield 12, $F(2,566)=4.27$, $p<.05$; for Coren, $F(2,561)=5.38$, $p<.01$, but not for other measures of laterality. Planned comparison t-tests showed that on the Oldfield10 measure the PTSD group (m=4.65, SD=7.2) had significantly lower scores (leftward bias) than the non-PTSD trauma group (m=7.2, SD=4.6), $t(58.1)=-2.44$, $p<.05$, and the control group (m=7.03, SD=5.5) , $t(62.4)=-2.24$, $p<.05$. On the Coren hand measure the PTSD group (m=2.0, SD=2.95) had significantly lower scores than the non-PTSD trauma group (m=3.1, SD=1.97), $t(57.5)=-2.52$, $p<.05$. These represent medium effect sizes of just over 0.4.

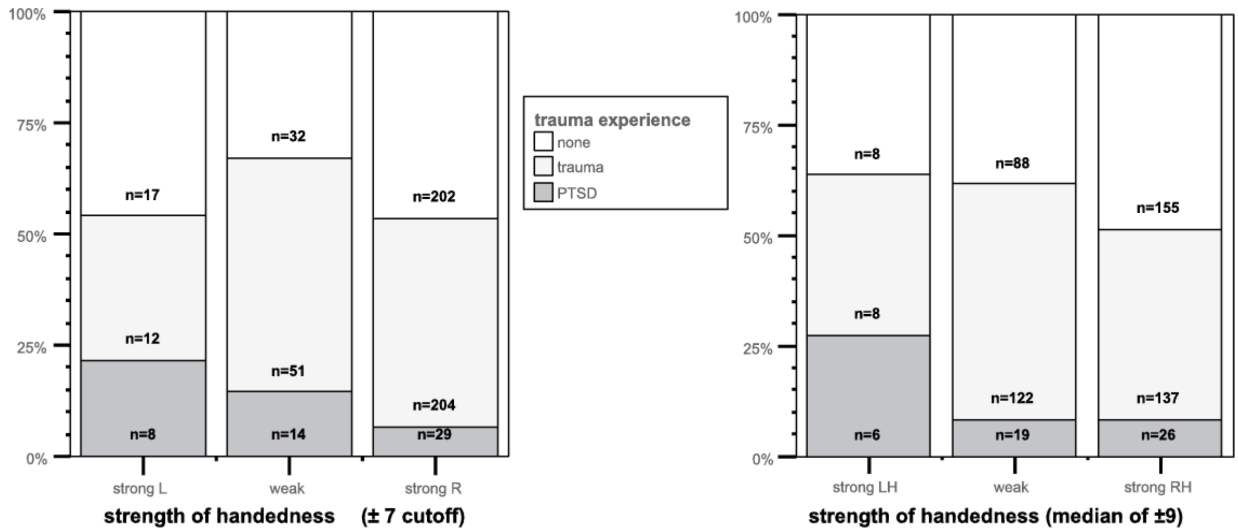
Table 3.1 Mean PTSD symptom scores by handedness

Variable	Handed	Whole sample *n*	m	SD	Science Centre sample *n*	m	SD
Re-experiencing score	left	34	2.94	3.219	18	3.28	3.511
	right	275	2.49	2.904	140	2.36	2.906
Avoidance score	left	33	4.06	5.488	18	5.33 *	6.212
	right	271	2.54	3.864	136	2.24	3.753
Arousal score	left	34	3.91 *	3.972	18	4.94 **	4.094
	right	276	2.41	3.232	141	2.51	3.418
Symptom severity score	left	33	10.94	11.025	18	13.56 **	11.888
	right	268	7.41	9.061	134	7.06	9.274
N traumas reported	left	36	2.14	1.150	20	2.10	1.165
	right	296	2.14	1.286	159	2.13	1.303

* p<.05. ** p<.01.

Symptom scores were compared for right and left handers (and separately for the Science Centre sample, since this may be more representative of the general population); results are shown in Table 3.1. Left handers had significantly higher scores for arousal (university sample: $t(38.6)=2.13$, $p<.05$; general population sample: $t(157)=2.78$, $p<.01$) and in the general population sample left handers had significantly higher scores for both the avoidance, $t(18.7)=2.06$, $p=.053$, and total symptom severity score, $t(150)=2.69$, $p<.01$. In order to further investigate this apparent relationship of symptom clusters with left handedness, the three symptom scores were entered in a stepwise logistic regression. Arousal score uniquely predicted variance in handedness; the regression equation [$\lambda=-2.5+0.116$ arousal] was significant ($p=.019$), the arousal contribution was significant ($p=.015$) and the proportion of variance explained was 2% (Cox & Snell).

Figure 3.2 Relationship between strength of handedness and experience of trauma: left: separation on a score of ± 7; right: separation on a median split score of ± 9 (Scores on Oldfield10 measure).



Two different cut-off points were used to consider strength of handedness: a median split (median = 0.90) and ±7 on the Oldfield10 measure (Christman & Propper, 2001). Both methods found highly significant differences between these groups in relation to PTSD, $\chi^2(4,N=569)=15.58$, $p<.01$, and $\chi^2(4,N=569)=18.01$, $p<.001$, respectively (Figure 3.2).

Relatively more of the strong left handers had PTSD, than either strong right handers or weak handers. Sample sizes for strong left handers are inevitably small, but show consistent differences from strong right handers (at ± 7cut-off: $\chi^2(2,N=340)=11.29$, $p<.01$; median split score of ±9: $\chi^2(2,N=340)=8.85$, $p<.05$). Using the median split score of ±9 all groups were significantly different from one another (right vs. weak: $\chi^2(2,N=547)=6.11$, $p<.05$; weak vs. left: $\chi^2(2,N=251)=8.39$, $p<.05$).

Of the 596 participants, 94% answered the question relating to parental handedness. The proportions of those with left handed parents were significantly different, $\chi^2(2,N=562)=11.50$, $p<.01$, and higher in the PTSD group (31%; N=15) than in the non-PTSD trauma group (19%; N=50) and control group (12%; N=31). Similarly, there was a significant additive effect on meeting diagnostic criteria for PTSD of having a left handed parent, $\chi^2(3,N=565)=14.62$, $p<.01$. Higher proportions of left handers with a left handed parent met diagnostic criteria for PTSD 32% (6 of 19) than right handers with a left handed parent (12%: 9 of 77); proportions of left and right handers without a left handed parent meeting criteria for PTSD were lower (8%: 4 of 49 and 7%: 30 of 417 respectively).

3.1.4 Discussion

This study extends previous work by considering a mixed gender civilian population experiencing a variety of trauma and, due to the large sample size, was able to examine prevalence of left handedness in those meeting diagnostic criteria for possible PTSD.

As predicted by hypothesis 1, this study found that relatively more left handers than right handers met diagnostic criteria for PTSD. An additive effect of parental left handedness was found, particularly in left handers, supporting Chemtob and Taylor's (2003) findings, although small sample sizes require cautious interpretation. Left handers were found to have higher symptom scores supporting hypothesis 2, particularly for the arousal symptom cluster, which uniquely contributed to a prediction of handedness in a logistic regression. This is interesting in the context of McFarlane's (1998) assertion that, while re-experiencing phenomena are common after any experience of trauma, it is disordered arousal that may best distinguish those with PTSD.

Relations between laterality and PTSD were confined to measures of handedness; relations with footedness found by Spivak et al. (1998) were not supported, and neither study found any relations of PTSD with ear and eye preference. Importantly, the number of traumas experienced by left and right handers does not differ (Table 3.1) suggesting that the increased risk of PTSD is not a consequence of increased risk of experiencing trauma as a left hander in a right hander's world.

With the caveats of small samples and that there are inherent confounds between strength of hand preference and inter-item consistency in handedness inventories (discussed in Chapter 2), as predicted by hypothesis 1 the current study finds that strong left handedness is associated with increased prevalence of PTSD compared to both weak and right handers. In contrast to Saltzman et al.'s (2006) conclusions, this suggests that it is not reduced lateralization, but rather leftward lateralization (in handedness) that is associated with PTSD prevalence and symptoms. This is consistent with a greater involvement of the right hemisphere, dominant for motor control in left handers, in experiencing negative emotion, but why left handers seem to be more vulnerable to PTSD is an important issue requiring explanation. It may be that left handers are responding to, or processing (or both), emotional events differently. Investigations into possible differences between right and left handers in these areas are presented in Chapter 5 and Chapter 6.

3.2 A replication using participants from the experimental studies: differences in reporting of types of trauma

3.2.1 Introduction

The sample described in section 3.1 above consisted of individuals from a general population who opted in to the study. This may be similar to the large scale community surveys (e.g. Kessler et al., 1994; Kessler et al., 2005a) that have reported on estimated prevalence rates. However, it has been suggested that some types of trauma, particularly sexual trauma, are under-reported (and PTSD prevalence consequently under-estimated) because participants are unwilling to disclose certain types of trauma and “skip out” of a questionnaire or interview at this point (e.g. Cusack et al., 2002). The experimental studies afforded the opportunity to administer the PDS to another large sample of participants in order to first, replicate the findings in the general population sample and second, to investigate reported trauma in a population that completed the PDS simply as part of another study and did not take the opportunity to opt out of this part of the study. The PDS was also included for participants in the experimental studies as a screen in order to ensure that the experimental variables of possible relevance in PTSD were not influenced by effects arising from participants who possibly had PTSD.

These individuals took part in an experimental study that at face value was not considering trauma and therefore had no expectation of being asked to fill in a trauma-related questionnaire (although any knowledge of the experimenter's research interest may have influenced their choice to participate in the experiments, so this may not be a completely naïve sample in respect of expectations about possible relevance of the experiments to trauma-related issues). This afforded the opportunity to consider issues related to possible handedness and sex differences in relation to PTSD in a different kind of sample to the population reported in the previous section.

3.2.2 Methods

3.2.2.1 Participants

The sample comprised participants from the experimental studies reported below in Chapter 5 and Chapter 6, and two other experimental studies not reported within this thesis, who had completed the PDS. They are not representative of a general population sample, as the Stroop study (Chapter 6) set out to recruit equal numbers of right and left handers. Although the Stroop study also set out to recruit equal numbers of males and females, this sample, and those of the other experimental studies, contained more females than males reflecting the sex mix of undergraduates studying Psychology, who were required to participate in experiments for course credit and formed the major source of participants.

Subjects who reported changing the hand they used for writing (on a permanent basis) were excluded from the sample as possibly atypical of natural left and right handers. The sample comprised 410 students (and staff) who completed the PDS but four of these did not complete the handedness inventory; 95 (of 406: 23.4%) were left handed, well above the general population prevalence of approximately 10%, and 275 (of 410: 67.1%) were female. Mean age was 22.6 years (range 17.3 – 67.8). This sample will be referred to as the "experimental sample" from hereon to contrast with the "general population" sample considered above.

3.2.2.2 Measures

All had completed the PDS as part of the experimental procedure of the study in which they participated. All but four participants completed the combined handedness inventory; other measures are reported elsewhere.

3.2.2.3 Ethics

Ethical approval for this part of the study was obtained within the application to the Department of Psychology Ethics Committee for each of the experimental studies reported in subsequent chapters (see Appendix 23); information to participants was included in an Information Sheet, which participants read before giving informed consent to participation. Since completing the PDS may have caused distress to anyone reminded of their traumatic experiences, the front cover included a reminder that should this occur, they may wish to seek help from their GP (or the university's student support services).

3.2.3 Results

3.2.3.1 Relationships between handedness and PTSD

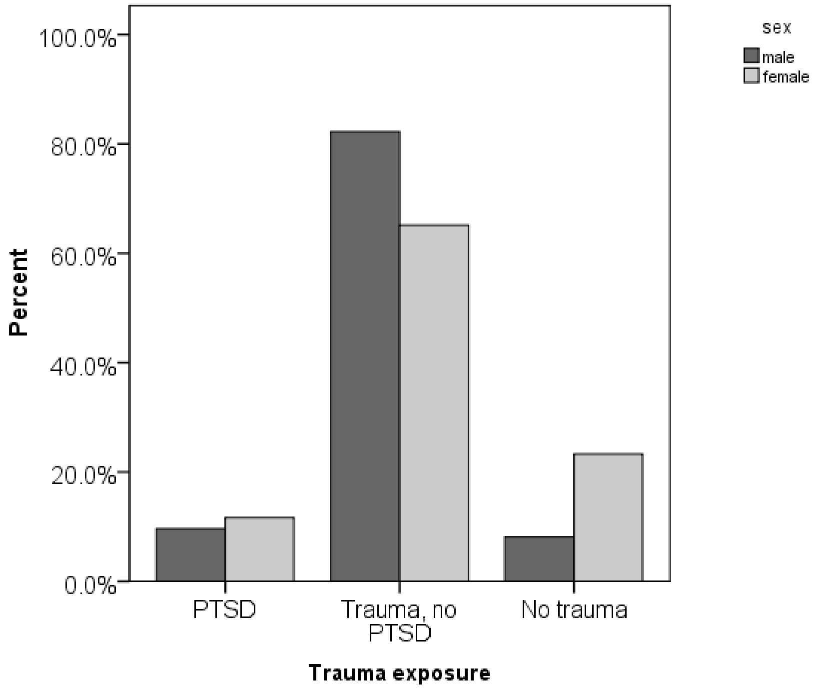
Out of the sample of 410, 43 (10.5%) met diagnostic criteria for PTSD on the PDS. The effect size (using GPower v 3.0; Faul et al., 2007) found in the general population sample for increased prevalence of PTSD found in left handers was small (Cohen's d = 0.1). The sample size of 406 in the experimental sample was therefore not large enough to detect such an effect size at a significance level of $p<.05$.

3.2.3.2 Sex differences in PTSD

In the general population sample, no sex differences in prevalence of PTSD were found, contrary to expected findings. The experimental sample, however, did reveal significant sex differences.

Chi-square analysis, investigating possible sex differences between (a) the PTSD group, (b) those who reported experiencing a traumatic event, but did not meet diagnostic criteria for PTSD (the non-PTSD trauma group) and (c) those who did not report any experience of trauma (the no trauma group) revealed a significant effect $\chi^2(2,N=410)=15.413$, $p<.001$. Figure 3.3 shows the proportions of males and females in each trauma category. Relatively more females (n=32; 11.6%) than males (n=13; 9.6%) have PTSD, but relatively more of the males than the females report experiencing trauma, such that only 8.1% (n=11) of the males but 23.3% (n=64) of the females are in the no trauma group. Proportions of those exposed to trauma who met criteria for PTSD were 10.5% for males and 15.2% for females.

Figure 3.3 Graph to show proportions of males and females in each category of trauma exposure: relatively more males experience trauma, but relatively fewer have PTSD



Independent sample t-tests revealed that females report significantly higher scores on symptoms: all symptom scores, except arousal (which just escape significance) are significantly different, but not the number of traumas reported. Table 3.2 shows these differences.

Table 3.2 Sex differences in PTSD symptom scores, but not in number of traumas reported

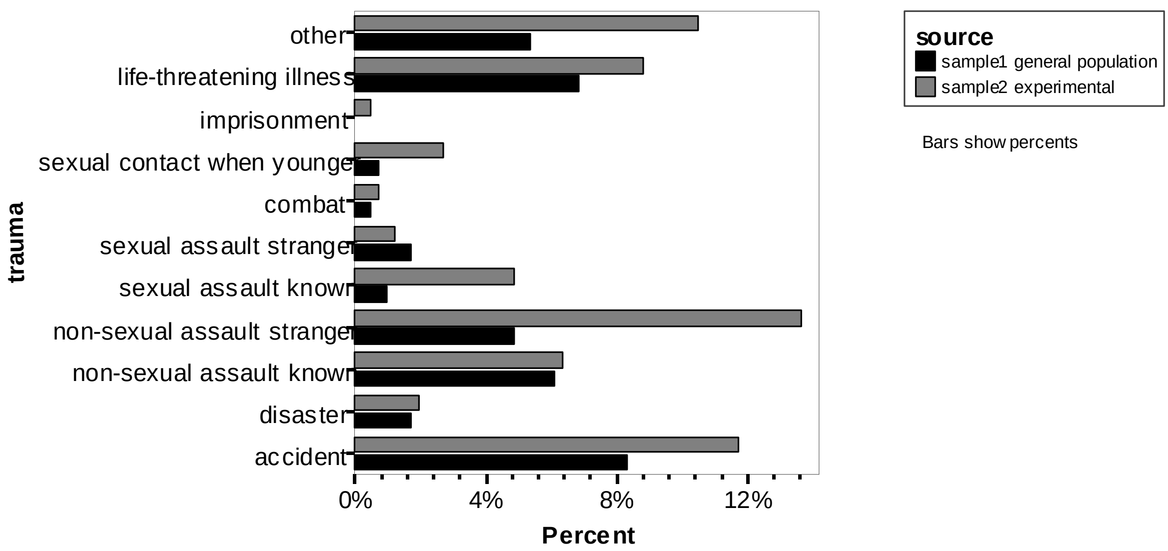
	sex	*N*	*Mean*	*Std. Dev*	*p*
re-experiencing symptoms score	male	95	1.47	2.004	< .001 ***
	female	163	3.10	4.776	
avoidance symptoms score	male	95	1.91	2.768	.001 ***
	female	163	3.42	4.168	
arousal symptoms score	male	95	2.14	2.923	.056
	female	163	2.92	3.289	
symptom severity score	male	95	5.52	6.732	< .001 ***
	female	163	9.45	9.751	
n traumas reported	male	98	1.87	1.052	.791
	female	163	1.91	1.280	

*** sig at p < .001

3.2.3.3 Differences in types of trauma reported

There seemed to be particularly low levels of reporting of sexual assault and sexual contact under the age of 18 in the general population sample considered above. A comparison was therefore made between the types of trauma reported in the experimental and general population samples. Chi square analysis revealed the distribution of types of trauma reported by the two groups was significantly different $\chi^2(10,N=410)=18.947$, $p = .041$. Figure 3.4 shows these distributions. More of those participants in the experimental study reported sexual assault and sexual contact when younger, categories that were perhaps surprisingly missing in the general population opt-in study, as well as more trauma in some other categories, notably non-sexual assault.

Figure 3.4 Bar chart comparing types of trauma reported in two samples: those that opted in to a study on PTSD and handedness (general population sample) and those completing the PDS as part of an experimental study (experimental sample)



3.2.4 Discussion

This sample was not large enough to find associations between handedness and PTSD. However, there were sex differences in prevalence of PTSD in this experimental sample not found in the general population sample. Relatively more men (91.9%) than women (76.7%) had experienced trauma; but of these 10.5% of the men met criteria for PTSD on the PDS, whereas 15.2% of the women met criteria for PTSD. This pattern is consistent with the epidemiological literature on PTSD (e.g. Kessler et al., 1994; Kessler et al., 2005a) but sex differences in prevalence here were not as great as the 2:1 rate of PTSD in women than men normally reported. Total symptom scores on the PDS were significantly higher in females than males as were re-experiencing and avoidance scores, while arousal scores showed a trend towards significance. This is consistent with other evidence that suggests that women show greater chronicity of symptoms than men (Norris et al., 2002).

There were also differences found between samples in reports of the type of trauma experienced, with particularly sexual trauma appearing underrepresented in the general population sample. Taken together with the fact that sex differences in prevalence were not apparent in the general population sample, these findings suggest that when a study is in an opt-in basis, those who experience sexual trauma (and this will include more women) will tend not to opt-in, consistent with concerns in the literature that this form of trauma may be under-reported for these reasons (e.g. Cusack et al., 2002). This may be important, since general community surveys are the instruments used to estimate prevalence rates, and sexual trauma one of the more potent stressors for developing PTSD. If sexual trauma is underestimated by general population surveys this will consequently possibly under-estimate PTSD prevalence rates.

Chapter 4

Left handedness and Posttraumatic Stress Disorder in clinical populations

Background: Previous studies have found an increased prevalence of mixed/left handedness in male combat veterans and children with posttraumatic stress disorder (PTSD). In a large general population sample which for the first time included left handers, leftward bias and not mixed handedness was found to be associated with PTSD and severity of symptoms. However, PTSD was by self-report and not clinically assessed.

Methods: This study pooled clinical samples (N=382) in whom diagnosis was known (trauma exposed +/- PTSD and a control group with other anxiety disorders: GAD and panic disorder) and handedness was assessed by questionnaire.

Results: Prevalence of PTSD was significantly higher in left handers (81%) than right handers (64%), confirming previous findings. In addition the prevalence of left handedness was significantly higher in the PTSD group (13.2%) compared to those with other anxiety disorders, where prevalence of left handedness was only 5.1%.

Conclusions: This study extends findings of increased prevalence of PTSD associated with left handedness. The unexpectedly low prevalence of left handedness in the other anxiety disorders remains to be explained, but supports the view that PTSD is fundamentally different to other anxiety disorders.

4.1 Introduction

The studies presented in Chapter 3 used the PDS as a self-report instrument for large scale studies in ostensibly healthy populations. The prevalence rates of PTSD in these samples were consistent with known population prevalence rates. Nevertheless, these samples had not been assessed by a clinician to confirm PTSD. The study reported in this chapter was an international collaboration, in which handedness data was collected from several clinical samples and pooled to achieve a larger sample size with the likelihood of sufficient left handers to allow analyses not possible with individual clinical populations to date.

There were four sources of data: a specialist trauma clinic (Aberdeen), an evaluation of a screen and treat programme for victims of the 2005 London bombings (London), the complete data set for Australian combat veterans with PTSD (Forbes et al., 2006; Melbourne) and a database of anxiety disorder patients taking part in several treatment studies across Central Scotland (Durham et al., 2005) held by the Clinical Psychology department at the University of Dundee. Although all individuals had been seen and diagnosed by a clinician, each sample differs in terms of type of trauma exposure. Not all patients had been assessed for PTSD using the same instruments and symptom severity data was not available to test for associations with left handedness as previously reported (Choudhary & O'Carroll, 2007).

This study was designed to investigate two research questions; first, to test whether the association of left handedness with PTSD in non-clinical populations was found in clinically assessed populations of mixed gender, since no previous studies had included adult women, and second, to test whether any association with left handedness was specific to PTSD or to anxiety disorders in general. There were two hypotheses.

Hypothesis 1: Prevalence of PTSD will be higher in left handers compared to right handers.

Hypothesis 2: The prevalence of left handedness will be higher in PTSD than in other psychiatric disorders.

4.2 Methods

4.2.1 Samples and procedure

The four samples (total N=382) comprising this study population are described separately below.

4.2.1.1 Aberdeen

The Aberdeen sample consisted of general PTSD cases previously seen by the Aberdeen Trauma Clinic under the direction of Professor Alexander. All records currently available in the Medical Records store were examined and strict criteria applied to whether trauma met Criterion A for inclusion in the sample. All diagnoses (ICD-10) were reviewed and confirmed by the Consultant Clinical Psychologist (PTSD, other psychiatric disorders, or none as appropriate). The nature of the trauma and diagnosis was recorded for 231 patients. Co-morbid disorders were not considered.

Patients' GP's were contacted to check that the patient was not known to be deceased (to avoid causing upset to surviving relatives) and that the address held was current. Sixty one patients were not traceable (26.4% of the original sample). Of the remaining

170, on reviewing the list of patients, 21 were not contacted either because (1) the Consultant felt that a reminder of their traumatic experience was not appropriate or (2) sending a lateral preference questionnaire to those suffering limb amputations were considered insensitive. However, handedness for writing was noted in the case notes and therefore known for four of the latter.

Chi square analysis showed that the proportions of those with, compared to without, a PTSD diagnosis were not significantly different between those who (1) were excluded, n=21; (2) were untraceable, n=65; (3) did not reply, n=65 and (4) did reply, n=80: $\chi^2(3, N=231)=.094$, $p=.993$. However, it is possible that the exclusion criteria favoured exclusion of some of the most severe cases. The evidence from Chapter 3 suggests left handers had higher PTSD symptom scores than right handers; although a decision about inclusion was made blind to handedness, excluding the most serious cases may also have excluded relatively more left handers thus diluting the hypothesised effect. Postal questionnaire packs were sent out to 149 patients; 80 replies were received (54% response rate). For handedness for writing the sample size was therefore 84.

4.2.1.2 London

The 7/7 London bombings (on 7th July 2005) were a co-ordinated series of bomb blasts instigated by terrorist suicide bombers and which occurred during the morning rush hour at four locations, three on London Underground trains and one on a bus. In all, 52 commuters were killed and approximately 700 injured. Two weeks later, on 21st July, there were four attempted bomb attacks, again on the Underground and a bus; only the detonators of the bombs went off and a fifth failed to detonate. Only one minor injury was reported.

An NHS Screening Team used the Trauma Screening Questionnaire (Brewin et al., 2002) as a brief screening instrument for PTSD and offered follow up to anyone with a total score >5 (out of 10 symptoms listed). A team evaluating, retrospectively, the effectiveness of the screen and treat programme (for both incidents), collected handedness data using a sample from these referrals and some participants from the Metropolitan Police witness list. Only the participants who had been seen by a clinician and given a diagnosis (PTSD, other psychiatric or none: ICD-10 or DSM-IV) and completed the handedness questionnaire were included in this study (n=23). 57% of these (n=13) had a diagnosis of PTSD.

4.2.1.3 Melbourne

A treatment study (Forbes et al., 2006) of 150 male combat veterans with severe PTSD (confirmed by the Clinician Administered PTSD Scale, CAPS: Blake et al., 1995) had excluded seven consistent left handers, since numbers were too small to allow meaningful statistical analyses and 12 others with incomplete treatment data. Data for the whole sample (N=169) were supplied for the current study since handedness for writing was known for all in the sample and the EHI (an 8-item version) had been used for assessment of handedness. However, the EHI data was scored differently for the present study as described in section 4.2.2 below.

4.2.1.4 Dundee

The Dundee database included patients with a variety of anxiety disorders, diagnosed by clinicians (all according to DSM-IIIR or DSM-IV criteria), who had taken part in one of eight separate treatment trials, over the preceding ten years (Durham et al., 2005). Only one of these trials was of patients with PTSD; the others consisted of patients with Generalised Anxiety Disorder (GAD) or panic disorder and were included in the present study as patients with other psychiatric diagnoses to compare with patients with a PTSD diagnosis.

The database for the eight treatment studies (n=881) was extensive but dated, since some of the earlier treatment trials had taken place more than ten years previously. Patients' GP's were contacted to check that the patient was not known to be deceased and that the address held was current. Only 582 (66%) of these patients were traceable and mailed questionnaire packs; of these 20 were undelivered, or participants refused or were too ill to participate. Of the remaining 562, 116 (21%) replied and 446 (79%) did not. Chi square analysis showed no significant differences in the proportions of those with diagnoses of PTSD, GAD and panic disorder who (1) were untraceable (2) did not reply and (3) did reply [$\chi^2(4,N=881)=2.405$, $p=.662$]. Of these 116, 16 (14 %) had PTSD, 37 (32 %) had GAD and 63 (54%) had panic disorder diagnoses.

4.2.2 Measures

For the Aberdeen, London and Dundee samples the combined lateral preference inventory used in the other studies of this thesis and described in Chapter 2 was used. However, Forbes et al (2006) used an abbreviated 8-item EHI. An 8-item score (Oldfield8) was therefore separately calculated using the scoring method described in Chapter 2 above for all samples in order to include this sample's data. In addition, their treatment study used a 100% response criterion to determine consistent left and right hand preference. This method is not recommended as it results in a rate of consistent handedness inversely proportional to the length of the assessment questionnaire. A categorical variable based on handedness for writing was determined for all samples;

cut offs for determinations of mixed handedness are discussed in the Results section which follows.

Not all participants completed all items on the inventories. Several older participants did not respond to the questions asking about which ear they would use to listen to a conversation behind a closed door, or which eye to look through a keyhole, annotated the questionnaire to indicate they would never do these things. Laterality scores could not therefore be computed for these individuals, although handedness for writing was established. Participants who indicated they had (permanently) changed the hand they used for writing (n=10) were excluded from further analysis, as they may not be typical of either innate left or right handers. A total sample of 382 remained.

4.2.3 Ethics

For two of the samples (London and Melbourne) ethical approval was obtained by the collaborators. For access to the clinical records of the Aberdeen sample and use of the database held by Dundee, approval was sought from the relevant COREC. Letters of approval are included at Appendix 23. Although the study required only the completion of a handedness questionnaire, since reference was made in the covering letter to trauma, which may have prompted reminders of participants' experiences, the letter contained advice to make use of sources of help such as their General Practitioner if they became distressed or troubled by reminders of their own trauma.

4.3 Results

4.3.1 Sample Description

When combined, the whole sample comprised 68% males and 32% females. These relative proportions are influenced by the combat sample (Melbourne) which was the largest component sample and contained only one female. Overall, the sample contained 41 left handers (for writing; 10.7%) which appears consistent with prevalence in the general population. Table 4.1 summarises the distribution of sex, left handedness and diagnoses in the four component samples.

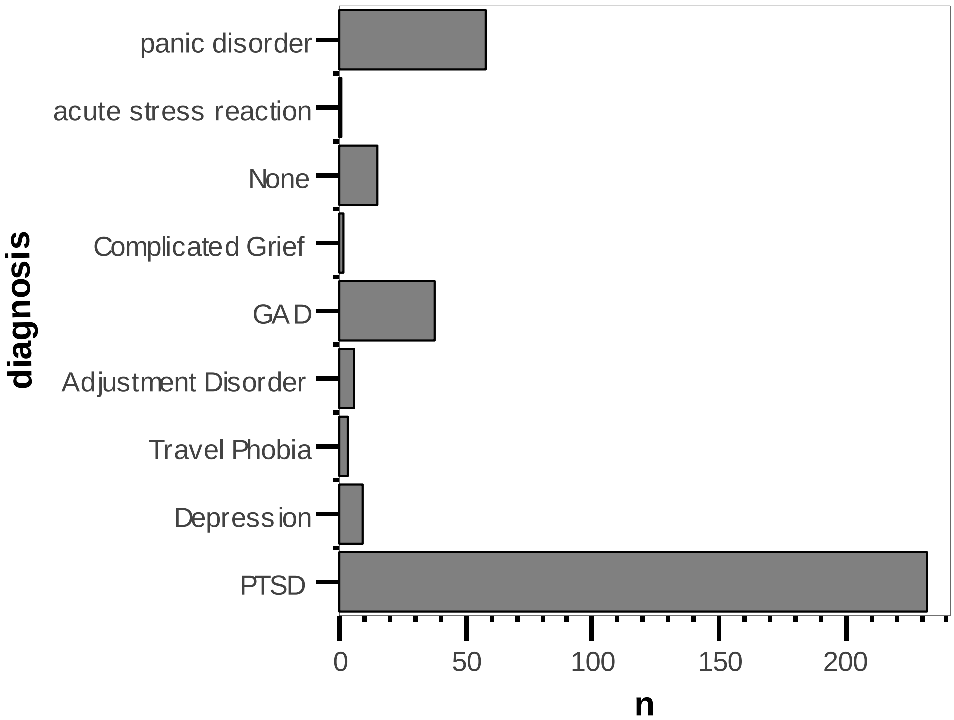
Table 4.1 Summary of gender, handedness and diagnostic distributions in the four component samples (after exclusions for change in hand use)

	male	*female*	*LH*	*LH*		*Diagnosis(n)*		**Total**
	n	*n*	*n*	*%*	*PTSD*	*other psych*	*none*	**n**
London	8	15	2	8.7	13	3	7	23
Aberdeen	41	38	10	12.7	52	19	8	79
Melbourne‡	167	1	22	13.0	169	-	-	169
Dundee	42	69	7	6.3	16	95	-	111
Total	258‡	123‡	41	10.7	250	117	15	382

‡ 1 case missing sex

Figure 4.1 shows the distributions of individuals across diagnostic categories. Due to small numbers, all non PTSD positive diagnoses were combined for further analysis.

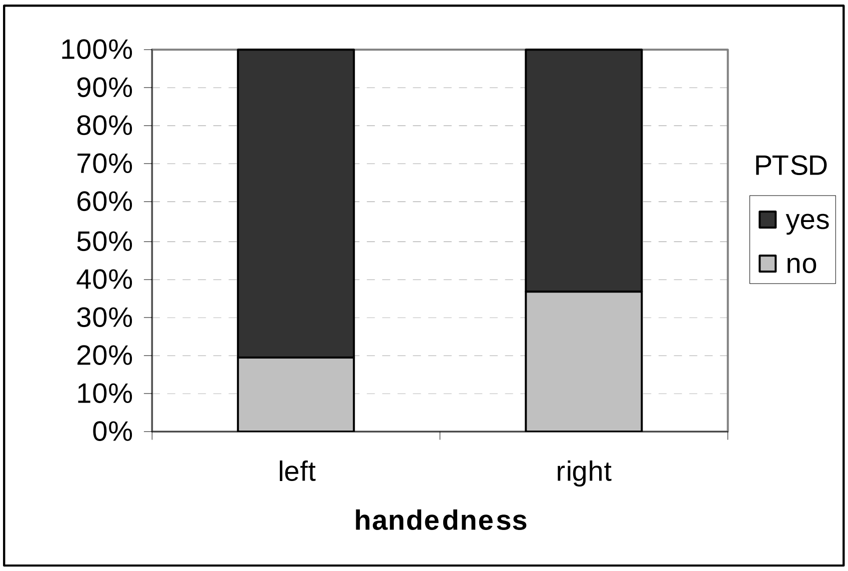
Figure 4.1 Clinical diagnoses in the whole sample



4.3.2 Relationships between Lateral Preference and PTSD

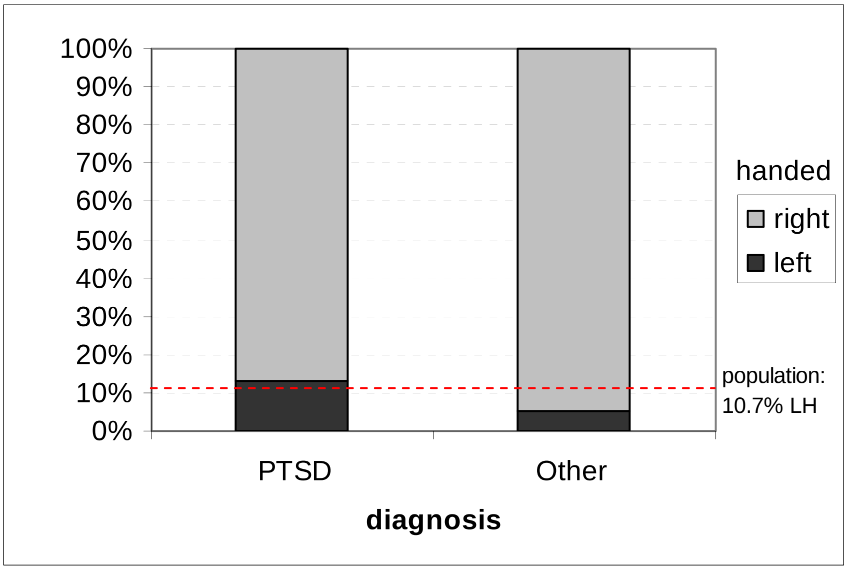
A chi-square analysis revealed a significant difference in the proportions of left handers in those with and without PTSD, $\chi^2(1,N=382)=4.596$, p=.032; prevalence of PTSD was higher in left handers (80.5%, n=33) than in right handers (63.6%, n=217). This supports the first hypothesis and is shown in Figure 4.2.

Figure 4.2 Significantly more left than right handers have a diagnosis of PTSD



The whole sample contained only 15 individuals who had received a nil diagnosis; this number was too small to allow further analysis and the rest of the sample was grouped into two categories: PTSD and other psychiatric diagnoses. A chi-square analysis revealed a significant difference in the proportions of left handers in those with PTSD and those with other psychiatric disorders, $\chi^2(1,N=367)= 5.468$, p= .019. The proportion of left handers in the PTSD sample was 13.2% (N=33 of 250), significantly higher than the proportion of left handers (5.1%, N=6 of 117) in other psychiatric diagnostic categories. Since the PTSD sample was considerably larger than the other anxiety disorders sample, the small numbers of left handers in the latter group require cautious interpretation, but it seems that these diagnostic groups have effects in opposite directions, and neither are similar to the whole sample prevalence of 10.4% left handedness (see Figure 4.3).

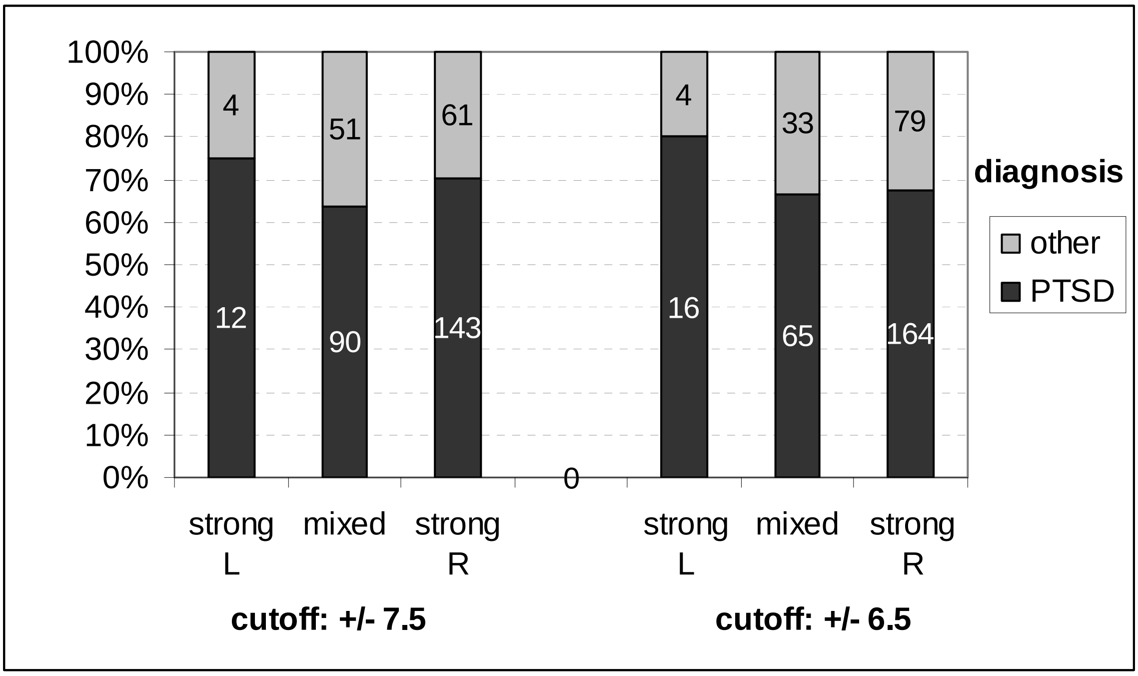
Figure 4.3 Prevalence of left handedness is significantly higher in PTSD than in other psychiatric disorders



The Melbourne sample completed only an 8-item version of the EHI, thus the calculated Oldfield8 laterality score was used (for the whole sample) to further examine possible differences between diagnostic groups and with strength of handedness in relation to diagnostic category. An independent t-test showed that the mean Oldfield8 laterality score was significantly lower (and thus more leftward) in PTSD (M=5.7, SD=4.7) compared to other psychiatric diagnoses (M=6.4, SD=3.2): $t(312.945)=-2.006$, $p=.046$.

In order to investigate strength of handedness, the Oldfield8 score was used with two different cut-off points. A conservative split, using only +/-8 as an indication of strong handedness and a second split using -6 through +6 as a mixed handed group were both used to compare strength of handedness distributions in groups with PTSD and other psychiatric diagnoses. Figure 4.4 shows these relationships as the proportions of individuals with each diagnosis in the strong right and left and mixed handedness groups. While there are higher proportions with PTSD in the strong left handers (by either criterion) relative to mixed or strong right handers, chi-square tests failed to reach significance (both p>.05). Power calculations (using GPower v 3.0; Faul et al., 2007) indicate that for this sample size an effect size of w=.20 (between a small and medium effect) was detectable.

Figure 4.4 Relationship between strength of handedness and diagnosis. Left using cutoff of +/- 7 (conservative split) and right, cutoff of +/- 6.5



The combined lateral preference inventory included a question about parental handedness which was not included in the Melbourne sample; 194 participants answered this question but 24 of these were excluded as the handedness of at least one parent was not known. The proportion of people with a left handed parent was higher in the PTSD group (n=17, 25%) than in the other diagnoses group (n=15, 15%), but these differences failed to reach significance, $\chi^2(1,N=170)=2.569$, p=.109; Fisher's exact test (1-tailed) showed a trend to significance, p=.081. Power calculations indicate that for this sample size only an effect size of w=.278 (approaching a medium effect) was detectable.

4.4 Discussion

The main finding of this study confirmed that prevalence of PTSD was significantly higher in left compared to right handers extending findings to a sample in which diagnosis has been made by a clinician. Thus both clinical assessment and the PDS self-report measure for PTSD are finding these same associations, suggesting they are robust and not due to diagnostic method. In addition the prevalence of left handedness was significantly greater in those with PTSD compared to other anxiety disorders. The Oldfield8 measure also showed a significant difference between these two groups. However, despite pooling four clinical samples, at approximately 10% of the population, the absolute number of left handers is small, a common problem in handedness research.

Using clinical data from a variety of sources meant that clinical assessments differed and no analyses were possible to test potential relationships of laterality scores with symptom severity scores, as each source sample was too small for individual analysis. Effects of parental handedness were not found, but because of the high proportion of the total sample provided by the Melbourne study which did not ask this question, the sample size was greatly reduced; for this sample to 170, and was sufficient to detect only a medium (or greater) effect. The effect size found previously was small: .16 and .17 for the two analyses reported in Chapter 3. Similarly, the proportion of people with PTSD appeared higher in the strong left handers, compared to mixed handers, as found previously (using GPower v 3.0; Faul et al., 2007). However, the effect size in the sample of 600 is .18; this is a smaller effect size than the current sample of 364 completing the handedness inventory has the power to detect. Even though four different clinical samples were pooled, since the effect is a small one, the sample of 600 in the non-clinical sample (reported in Chapter 3) was large enough to detect these effects, but the current sample of almost 400 is not sufficient. This demonstrates the difficulties in investigating a condition such as PTSD, which has a prevalence of somewhere around 8-10%, in left handers who comprise only 10% of the population. This is a common problem in handedness research when attempting to investigate relationships of left handedness with other variables of interest which do not occur at high rates in a population.

Several studies have now linked either left handedness with PTSD (Choudhary & O'Carroll, 2007) or in the absence of a left handed sample, mixed, or non-consistent right, handedness with PTSD (Spivak et al., 1998; Chemtob & Taylor, 2003; Saltzman et al., 2006) and with poorer treatment outcome (Forbes et al., 2006). Other studies have not generally found higher prevalence of non-right handedness in other anxiety disorders.

Merckelbach et al (1989) investigated student and clinical populations; in the student population there was no support for relationships of non-right handedness with phobia or OCD scores; indeed the only significant finding was that phobia scores were higher in right, not left, handers and particularly so for the social phobia subscale. No associations were found in the clinical sample. (Giotakos, 2001) found an excess of non-mixed handedness associated with panic disorder in males with a narrow, but not a broad, definition of handedness (using Annett's (1985) hand preference questionnaire). Chemtob et al (2002) investigated personal and familial handedness in phobia in student and clinical samples. In relation to personal handedness no differences were found in the student sample, but an increased prevalence of left handedness was found in the relatively small (n=52) clinical sample, for other, but not simple, phobias. This finding is opposite to the previous two studies. Familial handedness also showed an excess among those with a phobia diagnosis, but this included first degree relatives, not just parental handedness and may be liable to confounds. On balance, it seems there is more evidence that anxiety disorders other than PTSD are associated with increased *right* handedness rather than left handedness. In addition to the findings reported here, this suggests that in relation to lateral preference measures, PTSD is not similar to the other anxiety disorders. Further research into lateralisation in psychiatric disorders would seem to be a promising area for future research.

Chapter 5

Physiological responses to, and memory for, events of fearful films

> "The Shining may be the first movie that ever made its audience jump with a title that simply says 'Tuesday'." (Maslin, 1980)

Background: Laboratory investigations have not generally targeted the manipulation of specific emotions, despite growing evidence that underlying physiological and psychological mechanisms may differ, at least between the basic emotions. Part 1 determines theoretically that movie excerpts are targeted to fear and practically generate self-report and skin conductance (autonomic nervous system) responses indicative of fear. Part 2 investigates possible differences between left and right handers in memory for events of one of the above films. In the context of findings in PTSD it is hypothesised that a fear response may enhance (right hemisphere) sensory memory and reduce (left hemisphere) memory for verbal material in left handers, due to their existing shift towards right hemisphere dominance. In the context of clinician reports of fragmented memory in PTSD, fragmentation is defined as errors of temporal sequencing, predicted to be more frequent in left handers.

Methods: Viewing a fearful film was used as a laboratory analogue of fear in the Stroop paradigm study reported in Chapter 6. This was followed one week later by surprise tests of recall and recognition memory for events in the film and the AVLT, a standard test of verbal memory (for neutral material).

Results: Consistent with hypotheses, any significant differences between left and right handers in recall and recognition memory showed a consistent pattern towards enhanced memory for visual items and reduced memory for verbal material in left handers, who also performed significantly less well in immediate recall on the AVLT. Left handers made significantly more errors of sequencing, and associated repetitions, than right handers. Unexpectedly, females showed significantly poorer recall and recognition memory for film events than males but superior performance on the AVLT as expected.

Conclusions: After watching a fearful film, memory in left compared to right handers exhibits features observed in PTSD trauma narratives. Females also show unexpected deficits in memory for events in the film compared to males. All of these findings are shown to be amenable to explanation by relative hypoactivation of left hemisphere language areas in response to fear as observed in people with PTSD. These findings also suggest that effects in response to fear on variables such as memory which are affected in PTSD may be different to other laboratory studies of "emotional" material not specific to fear.

This chapter has two components. Firstly, physiological responses to fearful film excerpts are examined in order to establish that they are capable of generating a measurable autonomic nervous system response, (Skin Conductance Response: SCR). Secondly, an experiment probing memory for events in the longest of these film excerpts is reported. In this context, and extending the justification for the use of films made in Chapter 2, the mechanisms operating in a fearful film as a laboratory analogue of fear are explored conceptually and related to this longer excerpt.

5.1 Skin conductance as a measure of arousal in response to fearful films

The main purpose of this experiment was to establish that fearful film excerpts are capable of generating a response known to be a part of the ANS stress response. This section reports a two part experiment using (1) two short film excerpts from The Shining (Kubrick, 1980) and (2) the eight minute excerpt from Silence of the Lambs (Saxon et al., 1991) used as a fearful stimulus in the experiment reported in Chapter 6. In both experiments the target film excerpts are compared with a dynamic, neutral stimulus.

5.1.1 Introduction

Chapter 2 introduced the arguments supportive of using a fearful film to generate a realistic laboratory analogue of fear in an ethically acceptable manner. The two movies used here have both been used for the target emotion of fear (Gross & Levenson, 1995). The first excerpt from The Shining (clip1) is that used by Gross & Levenson (1995); both this and clip2 were rated as the most fearful scenes in an edited version of the film (compressing the first hour to a 45 minute film) by participants in an experiment not reported here. The 3’29” excerpt from Silence of the Lambs used by Gross & Levenson (1995) is included within an extended 8 minute excerpt used previously (Choudhary, 2004) and which is discussed further in the second part of this chapter.

The ability of the skin to conduct electricity is effected by the sweat glands; the eccrine sweat glands, one of two forms of sweat glands and which are widespread throughout the body, are involved in thermoregulatory control (at temperatures above 30°) and in the response to emotional stimuli (Venables & Christie, 1980). The skin conductance response (SCR) is a measure of the transient changes in skin conductance that are associated with particular experiences (Pinel, 2003). The SCR therefore provides a dynamic measure of an individual's response to an emotional stimulus.

While the target emotion is that provided by the experimental stimulus (the fearful film clips), ethical considerations require that participants are informed of the procedure in order to give consent. In order not to prejudice responses, participants were informed that they would be asked to view excerpts from a movie rated 18, which were not pornographic or violent in nature, but were not explicitly told that these were from horror movies. Nevertheless, however this is framed, the knowledge that they will encounter an unknown but likely unpleasant stimulus in itself generates uncertainty and apprehension similar to suspense, the key ingredient in generating fear. This anticipatory anxiety may well confound any experimental manipulation of physiological variables and a simple resting baseline period prior to an event may compound this by providing a period of time with no activity to divert attention from the impending, unknown, event. This makes investigation of stress physiology problematic. Rather than using a resting baseline, in the following experiments, a neutral dynamic stimulus was used for a comparison to the fearful film clips. This was achieved by capturing a segment of the "pipes" screensaver in Windows, which was run for just over two minutes to provide a dynamic, coloured stimulus, similar to a film, but with meaningless content. It was hoped this would avoid a baseline condition likely to compound the problem of anticipatory anxiety.

The main purpose of these experiments was to establish that watching the events in fearful film excerpts generate a SCR. Since there are inter-individual differences in baseline physiological variables, simple comparisons of mean values (of SCR in this case) may not necessarily exhibit differences (Lazarus et al., 1963); variability in response over a time period may thus be a better indicator of a physiological response. It was therefore hypothesised that:

Hypothesis 1: Measures of SCR (mean; standard deviation; maximum & minimum values; range and average slope) will be significantly greater, and/or reflect greater variability, in response to fearful film stimuli compared to a neutral stimulus.

The experiments in Chapter 6 and the second part of the present chapter use the eight minute segment of Silence of the Lambs, but do not measure a physiological response. They do, however, include a self rating of specific emotions experienced during the film. It was therefore considered desirable to establish that the SCR and subjective rating of emotion were associated.

Hypothesis 2: Self ratings of the target emotions (fear and a measure of overall tense arousal) will be greater in response to watching fearful films than the neutral stimulus.

Hypothesis 3: SCR measures and subjective ratings of fear and arousal will be associated.

Finally, these are both highly rated films and many participants will have seen them prior to participating in these experiments. If they are to be used reliably to elicit the target emotion of fear in experimental studies, then it is important to know whether having seen a fearful film before diminishes the physiological (and subjective) responses.

Hypothesis 4: SCR measures and subjective responses will be lower in participants who have previously seen the movies.

5.1.2 Methods

5.1.2.1 Participants

Participants were undergraduate students from the Department of Psychology's subject pool who took part in order to gain course credit. Twenty three students watched the short excerpts from The Shining and 19 students watched the longer excerpt from Silence of the Lambs. Due to technical difficulties SCR data were lost for three of the first sample (leaving n=20) and two of the second sample (n=17 remaining). The first sample included only three male students (85% female) and the second sample was exclusively female. Sex differences were therefore not examined. There were three left handers in each sample and handedness differences were not considered.

5.1.2.2 Apparatus

Skin Conductance Response was measured using an ADInstruments ML116 GSR Amp front-end unit with bipolar finger electrodes with Velcro™ attachment suitable for adults, attached to an ADInstruments ML780 Powerlab/8S 8 channel recording unit. Data was captured using Chart for Windows 95 v3.4.2 running on a Dell PC with a Pentium® II processor, running Windows 98. The film excerpts were played from video tape using a Sony SLV-SE210 VHS Video Cassette Recorder to a Sony Trinitron colour TV with a 12 inch screen; participants listened to the audio soundtrack through Digital stereo headphones. A Sealey digital caliper, measuring to 0.01 mm, was used for measurements of digit length for calculation of the 2D:4D (for the study reported in Chapter 7).

5.1.2.3 Materials

An information/consent sheet and a debriefing sheet were prepared for this study. All participants completed the PDS (Appendix 1), PSS10 (Appendix 3) and the combined handedness inventory (Appendix 2) used in all studies of this thesis. A self report emotion rating form was devised to record subjective emotion for each film clip viewed (Appendix 13).

The film excerpt from Silence of the Lambs was prepared by playing the commercial video on a Sony SLV SC820 four head video machine and copying the excerpt using a Sony RDR GX7 DVD recorder onto a TDK DVD-R. The film excerpts from The Shining were prepared by playing the commercial DVD on a Sony SACD/DVD DVP-N5900V player and recording on to a VCR using a Sony SLV-E210 video cassette recorder. Editing instructions for the films are included at Appendix 14 (The Shining) and Appendix 15 (Silence of the Lambs). SPSS v16.0.1 was used for subsequent data analysis.

5.1.2.4 Procedure

Participants first read the information sheet about the study and gave informed consent. The SCR recording was by metal plates attached to finger cuffs, kept in place by Velcro™; the plates were placed on the palmar aspect of the medial and distal phalanxes of the index (second) and middle (third) fingers of the non-dominant hand. Participants then completed the PSS10 and handedness inventory before viewing the film clips. They were asked to wear headphones attached to the TV and then to place the hand attached to the recording equipment face down on the table and to keep it still during the viewing. They were then asked to sit quietly and watch the blank (blue) screen of the TV while the researcher set up Chart recording and checked the SCR trace on the PC monitor; if the recording trace had not settled around the zero mark after a minute, "subject zero" was implemented on the Chart recording.

The "pipes" screensaver clip was then started and run for two minutes, with start and end times marked on the Chart recording. Participants then completed the first section of the Film Rating Form and remained sitting quietly watching the blank screen of the TV while the SCR recording settled to a stable level (although this may not have been a return to zero). The first film excerpt was then played, and start and end times marked on the Chart recording; participants then completed the second part of the Film Rating Form. For participants viewing the shorter excerpts from The Shining, this procedure was repeated for the second scene from the film. At the conclusion of viewing, finger plates and headphones were removed and the PDS completed (to avoid any effect of reminders of any adverse events on responses to the fearful film(s)). Finally *in vivo* measures of second and fourth digits were made using callipers to include participants in the sample reported in Chapter 7. Participants read a debriefing sheet and had the opportunity to ask questions of the researcher.

5.1.2.5 Data capture and analysis

Recordings in Chart were set at a screen ratio of 50:1 and by selecting the chart record between start/end markers for each event (corresponding to the clips viewed) mean, standard deviation, maximum, minimum and range values and the average slope over the time period recorded were obtained using Chart Datapad. These data were then transferred to an Excel file and saved for subsequent transfer to SPSS for analysis. Paired t-tests were used to compare SCR dependent variables recorded during the neutral (pipes) and film clips (hypothesis 1) and self-reported ratings of fear and arousal (hypothesis 2). Correlations between SCR and self-report measures were performed to test hypothesis 3, and independent sample t-tests were used to compare these dependent variables according to whether participants had previously viewed the movie used (hypothesis 4). Analyses were performed separately for the two parts of the experiment, based on the two movies used.

5.1.2.6 Ethics

Ethical approval for this study was obtained from the Department of Psychology Ethics Committee (see Appendix 23). Participants read an information sheet describing the study before signing a consent form; this advised that the film excerpts were from films rated 18, but that these were not violent or pornographic in nature and reminded participants that they could withdraw from the study at any time. No participant chose to withdraw.

5.1.3 Results

The main purpose of these experiments was to establish whether watching a fearful film could both generate a greater SCR and produce higher self ratings of fear and arousal compared to a neutral, dynamic stimulus. Results of paired t-tests for the film clips from The Shining are presented in Table 5.1 and for the longer excerpt from Silence of the Lambs in Table 5.2.

Table 5.1 Paired t-tests between pipes and two short film clips from The Shining for SCR and self report of emotion variables

				film clip1				film clip2			
	DV	*clip*	*n*	*mean*	*std dev*	*t*	*p*	*mean*	*std dev*	*t*	*p*
Pair 1	mean	pipes	20	-1.55	2.13	-6.550	<.001***	-1.55	2.13	-3.798	.001 **
		film	20	.97	3.06			.94	3.83433		
Pair 2	std dev	pipes	20	1.11	.668	-.826	.419	1.11	.668	.154	.879
		film	20	1.03	.630			1.13	.70984		
Pair 3	max	pipes	20	1.53	2.69	4.788	<.001***	1.53	2.69	3.035	.007 **
		film	20	3.60	3.37			3.82	4.05391		
Pair 4	min	pipes	20	-3.16	2.37	-6.124	<.001***	-3.16	2.37	-4.391	<.001***
		film	20	-.71	3.13			-.81	3.62844		
Pair 5	range	pipes	20	4.68	2.59	-.951	.353	4.68	2.59	-.104	.918
		film	20	4.30	2.20			4.63	2.71831		
Pair 6	av slope	pipes	20	-.02	.019	-.625	.539	-.0216	.019	-1.923	.070
		film	20	-.02	.029			-.0092	.029		
Pair 1	fear	pipes	21	.05	.218	-5.316	<.001***	.05 †	.229	-5.316	<.001***
		film	21	1.67	1.390			2.53†	1.896		
Pair 2	arousal	pipes	21	.57	.926	-4.958	<.001***	.58†	.961	-4.958	<.001***
		film	21	2.05	1.244			2.89†	1.912		

† n=19
*** sig at p < .001; ** sig at p < .01;

Both film clips from The Shining (Table 5.1 above) show a similar pattern of results; mean SCR and maximum and minimum values of SCR are all significantly greater in clips 1 & 2 compared to the pipes stimulus. All are highly significant and survive Bonferroni correction at p=.008. Variability measures (standard deviation and range) did not show significant differences. In all clips the average slope was negative, reflecting the subsiding effects of anticipatory anxiety during these short clips. A visual inspection of the Chart recordings (included at Appendix 16) shows that between clips SCR increased due to anticipatory anxiety. Self reported fear and arousal were significantly greater in response to the film clips than the pipes stimulus at a high level of significance.

In response to the longer excerpt from Silence of the Lambs (Table 5.2 below) mean differences in SCR were not significantly different from the pipes clip. However, mean values of variability measures (standard deviation, maximum and range) were all significantly different: standard deviation and range values were significantly higher, and the maximum greater, in the film than pipes clip. The average slope was significantly more negative in response to the pipes clip than the film, again generally reflecting subsiding anticipatory anxiety in the former (see Chart recordings at Appendix 17).

Table 5.2 Paired t-tests for pipes and excerpt from Silence of the Lambs for SCR and self-report of emotion variables

	DV	*clip*	*mean*	*n*	*std dev*	*t*	*p*
Pair 1	mean	pipes	.7803	17	2.73512	-1.184	.254
		film	1.8105	17	3.99683		
Pair 2	std dev	pipes	1.3390	17	.82859	2.801	.013 *
		film	2.0208	17	1.20130		
Pair 3	max	pipes	4.0568	17	2.79490	2.817	.012 *
		film	6.4047	17	3.72227		
Pair 4	min	pipes	-1.4092	17	2.89724	.343	.736
		film	-1.7260	17	4.18526		
Pair 5	range	pipes	5.4660	17	3.31890	2.881	.011 *
		film	8.1308	17	4.69370		
Pair 6	av slope	pipes	-.0177	17	.02445	-2.159	.046 *
		film	-.0015	17	.01206		
Pair 1	fear	pipes	.21	19	.713	6.647	<.001 ***
		film	4.00	19	2.539		
Pair 2	arousal	pipes	1.00	19	1.333	-7.349	<.001 ***
		film	4.53	19	2.220		

*** sig at $p < .001$; * sig at $p < .05$

Self reported fear and arousal were significantly greater in response to the film than the pipes stimulus at a high level of significance. All of these results demonstrate that fearful film excerpts generate a significant SCR compared to a neutral stimulus supporting hypotheses 1 and 2.

Hypothesis 3 suggested that SCR variables and self report measures of fear and arousal would be associated. Pearson correlations were performed to test this hypothesis, but although in the hypothesised direction (positive) none were significant. Examples of observed relationships and results of correlations are shown below in Figure 5.1 for film clip2 from The Shining in relation to self rating of arousal and the average slope of the SCR response and in Figure 5.2 below for self reported fear ratings in relation to the range of SCR for the longer excerpt from Silence of the Lambs.

Hypothesis 4 suggested that SCR and self report ratings of fear and arousal may be diminished if participants had previously viewed the movie from which the excerpts were taken. 47% had previously viewed Silence of the Lambs and 53% The Shining. A series of independent t-tests were performed for each movie used, on SCR variables and ratings of fear and arousal with two groups: those who had and those who had not viewed the movie concerned. None of these t-tests produced a significant result (all $p>.01$), thus hypothesis 4 was not supported.

Figure 5.1 Scatter plot to show relationship between average slope of SCR during film clip2 from The Shining and self rating of arousal: r = .304, p=.206, N=19 (ns)

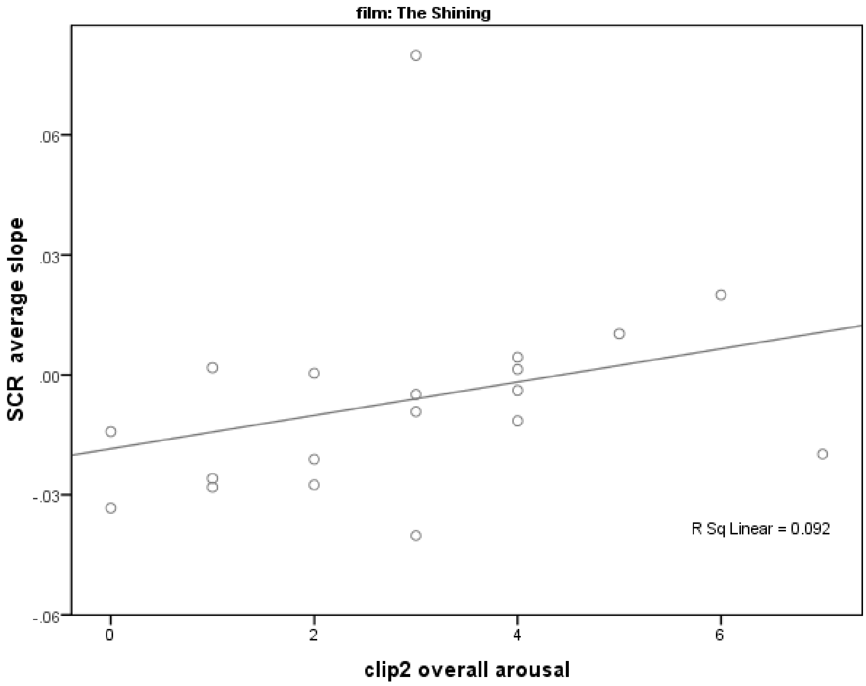
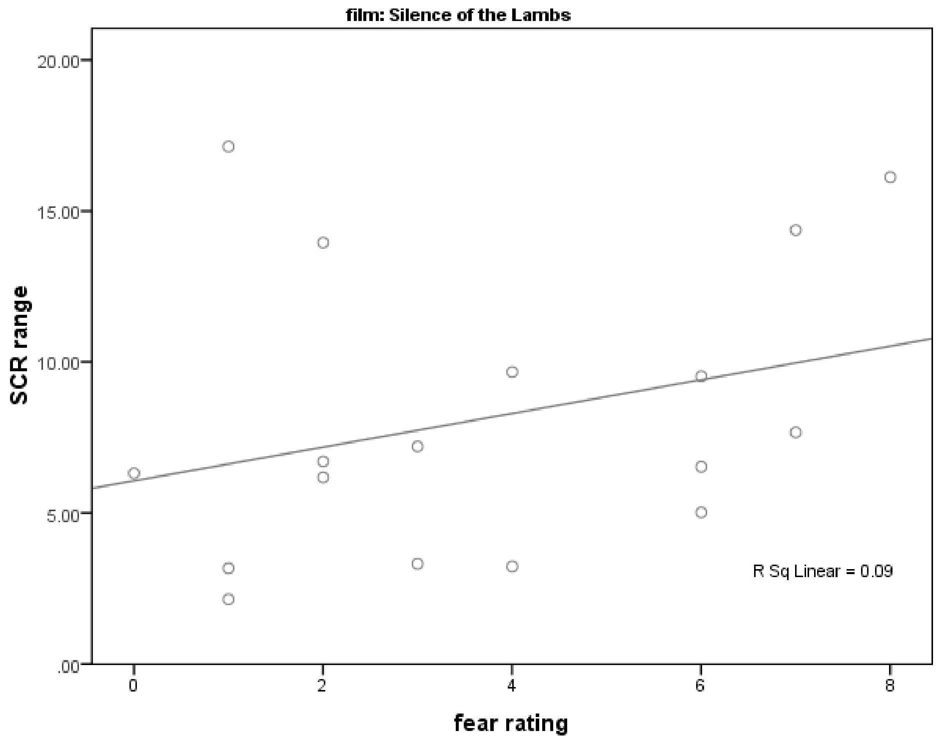


Figure 5.2 Scatter plot to show relationship between SCR mean range value and self reported fear rating: r = .299, p=.243, N=17 (ns)



5.1.4 Discussion

Results from these experiments, using both short excerpts of individual scenes and a longer storyline, suggest that increases in values of the SCR themselves and/or indications of increased variability in response, occur while viewing fearful films compared to a neutral stimulus and are accompanied by reports of greater experienced fear and arousal. Although the direction appeared as predicted, significant correlations were not established between SCR and self reported fear and arousal, but the sample sizes were small, and this direct association could benefit from re-testing in a larger experimental sample.

These experiments were not intended to examine in detail the timing of SCR peaks (or troughs) in relation to events occurring during the storylines contained in the film clips used. Nevertheless, a qualitative impression of the greater variability in SCR in response to a fearful film in the majority of subjects can be gained from inspecting the Chart traces included in Appendix 16 and Appendix 17; an impression of the levels of anticipatory anxiety prior to viewing each clip can also be gained from these recordings. Watching the neutral stimulus was effective, in the majority of participants, in reducing anticipatory anxiety and this offers promise for use as a true baseline condition preferable to the "resting" baseline of looking at the blank screen, when anticipation of an unknown stimulus to come typically generated waves of SCR activity. All film excerpts were preceded by high levels of anticipatory anxiety, which subsided during viewing, accounting for negative average slopes in all cases, but values were least negative in response to the Silence of the Lambs excerpt.

Hypothesis 4 set out to test whether these SCR responses would be diminished by familiarity with the movie content. None of the variables, physiological or self-report, showed any significant differences between those who had and those had not previously seen either of the movies used. This suggests that these fearful movies remain so even when the content is familiar and that physiological responses are not compromised in these circumstances. This finding provides further support for the utility of fearful films as a useful laboratory analogue of fear.

5.2 Memory for events in a fearful film: do left and right handers remember things differently?

The eight minute excerpt from Silence of the Lambs considered above was used as a fearful stimulus for the experimental work using the Stroop paradigm which follows in Chapter 6. Since the protocols of the latter involved participants returning for a second part experiment after one week, this afforded the opportunity to investigate possible differences between left and right handers in memory for the events of the film one week after the viewing. This part of the chapter examines aspects of the film relevant to the experience of fear and to tests of memory, in the context of deficits in memory, particularly verbal memory, found in people with PTSD.

5.2.1 Introduction

Fear occurs as a response to threat or danger with inherent uncertainty of outcome. Experiencing an event as uncontrollable (induced helplessness) is part of the subjective criterion A2 (see Table 1.1) which qualifies an event as likely to lead to PTSD. This is exploited in suspense films. de Wied (1995) suggests that questions of what happens next are what make any experience interesting, but not all interesting experiences are suspenseful. In discussing the literature on theory and psychological research on suspense, she identifies the following as important.

A film comprises both an event structure (the underlying events) and a discourse structure (the presentation of the events in the discourse); the latter may be manipulated, particularly temporally, thus creating suspense through anticipation. In a film, suspense is prompted by an initiating event in the discourse structure and terminated only at resolution – when the outcome is known. Arousal increases as the resolution becomes subjectively nearer as demonstrated by Nomikos (1968). If this temporal expectancy is then violated by extending the period slightly, then uncertainty increases and may add to suspense. The initiating event may signal *what* may occur by generating expectancies of possible outcomes, but questions of *how* and/or *why* are only answered over time. Preoccupation with a feared or dreadful outcome, particularly a physical, rather than abstract threat, is more suspenseful; reactions to film-induced and real threats have been found to be similar (Alfert, 1964; cited in Norden, 1980). de Wied (1995) suggests other events may be inserted along this timeline-to-resolution to reinforce suspense. The intensity of suspense is increased when the following conditions apply: when the character in danger is perceived positively, with increased degree of uncertainty concerning outcome and with longer duration of the anticipatory, uncertain, period. All of these factors serve to increase suspense.

It has long been recognised that we are able to experience vicariously the experiences of others. In considering how we feel when witnessing the horror (as a form of extreme terror and fear) of someone else, Darwin (1872) notes:

> "…. there is no danger to ourselves; but from the power of the imagination and of sympathy we put ourselves in the position of the sufferer and feel something akin to fear." p 305

We all know that drama, in its various narrative art forms, can move us to feel emotions, yet at the same time we know that the drama is not real, and only fictional, but we continue to act as if the protagonists are our real friends or enemies. In answer to why this is, Zillman (1995) argues against the common view that this occurs through identification with a character, a concept with its origins in Freud's Oedipal theory. Zillman (1995) points out that on the subject of drama, Freud considers that the playwright and actors are agents who make it possible for the spectator, in whose life nothing much of interest happens, for a short time to *become* that hero that he aspires to be and attain fulfilment of his wishes through identification with a hero. Zillman (1995) considers these mechanisms inadequate and unsupported by evidence which suggests instead that we remain as third party observers. He gives the example, relevant to all suspense films, of the wild-west hero walking coolly into an ambush: the audience feels the fear from the situation, not the calmness of the hero.

Instead, Zillman (1995) argues that it is empathy which explains our emotional reactivity to the plight of others. Respondents to drama bring with them a set of empathetic dispositions, which arise from a number of mechanisms. These may be innate (motor mimicry), learned via conditioning mechanisms, either through a large number of learning trials and/or by a few critical emotional experiences and partly as a result of perspective taking cognitive efforts.

The use of these various mechanisms can be related to the Silence of the Lambs excerpt.

Silence of the Lambs (Saxon et al., 1991) is a highly rated film scoring 84/100 in an internet based meta-critic review (Doyle, 2008). The excerpt used in this experiment includes a two minute segment, previously found to evoke the target emotion of fear (Gross & Levenson, 1995). That this excerpt can succeed in generating fear is likely due to the way it has been constructed by the filmmaker, incorporating many of the points mentioned by de Wied (1995) above and using long and extended anticipation times (Nomikos et al., 1968). An outline of the excerpt is provided next, identifying these mechanisms and with indications of some of the aspects probed by the memory tests. A transcript of all events, identifying the storyline and associated details in the excerpt is included at Appendix 11.

The excerpt begins with a shot which pans from an old caravan on a grassy area across a railway line to show a car parked outside a house. This is an effective establishing shot, giving the context for what follows without requiring the prior film. This shot will be referred to again later, as it was one of the target scenes identified for probing visual memory of the film. Next, the scene cuts to a woman who is inferred to have entered the house as she gradually moves from the front door down a hall (and is wearing a coat). Her dialogue is with a man, standing further inside the house at the other end of a room from the hall. As he asks if "they are close to catching anyone" and mentions the FBI and she questions him about the previous owner, the role of the woman as detective is established and an uncertainty about the man generated. This is reinforced as the scene cuts to various items around the room (again probed in a memory test), consistent with the woman's viewpoint. Someone who has seen the film before may understand completely the significance of the items, such as the moths fluttering on a box of threads, which potentially link the man to the underlying whole film structure of the search for a serial killer, but this is inferred even without this specific prior knowledge. The woman is young and attractive and played by Jodie Foster, all attributes likely to generate positive feelings towards the character. She is clearly in a vulnerable position, leading to expectancies of danger.

These are increased, during the conversation, by a shot of her hand pushing aside her coat and unbuttoning the gun holster worn on her belt, which immediately cuts to a shot of another gun (the man's) resting on a cooker in another room. Both the ring worn on the woman's hand and the cooker are probed in the memory test as weapon focus theories might predict better memory for such items (Loftus et al., 1987). There is then a further build up of underlying tension simultaneous with the ongoing factual dialogue where one senses the man is clearly realising now that the woman suspects him, before the perhaps now predictable, though sudden, command of the woman for the man to "Freeze!" and spread his legs, put his hands behind him. Though the viewer may now expect this outcome, its anticipation has been over an extended, time period. This should be resolution.

However, the man turns and darts away into the next room, where the viewer assumes (through prior knowledge) he has picked up his gun. The event structure is now one of an armed chase, with home advantage to the man. Again this generates a general expectancy: they have to find one another for resolution, but the how is protracted and the actual outcome uncertain (unless viewed before). The first part of the chase follows the woman's progress downstairs to the basement, acted fearfully (and accurately) and into dark, dingy corridors. Again memory for the visual elements she sees around her are probed. The suspense of the chase is interrupted by the woman finding another woman, who the first woman can identify by name, trapped down a well. The terror of the second woman is also communicated to the viewer, particularly when she is left down the well, as the first woman resumes the chase. As this and the initial man-woman dialogue is the only dialogue in the film, both conversations are probed in the memory test for their verbal content.

The chase is resumed: the underlying event structure continues as expected. However, temporal expectancies are violated when, after a very short time, and as the woman glimpses a decomposing body in a bathtub (probed), the lights go out. This again is a sudden, unexpected event, felt directly by the viewer: the screen is black momentarily, drawing directly on innate fears of darkness. The moment of total darkness is replaced with a green, night vision goggle shaped view of the woman feeling for her surroundings. We see the man in complete control, watching her struggle. This has introduced a completely unexpected twist and increased the degree of threat to, and disadvantage of, the woman character. The interplay of sound is also used to effect, her loud breathing replaced by music as the scene continues and we endure more uncertain expectancies as we see the man reaching out to touch her, then withdrawing his hand - another unexpected resolution - and then we see his other hand raising the gun. The final seconds contain the outcome and resolution: the woman's desperate response to the sound of the gun being cocked, turning and firing her gun to camera before we cut to her view of the man. In sudden light, from a window behind him (broken by the shots) we see him hit twice in the chest and falling to the ground. In this climax there is not just the final resolution but also a sensory change: a visual contrast in the sudden onset of daylight from the previous black darkness with superimposed goggle shaped, green scenes. The excerpt ends at this point; this last shot is so short, that it is possible to miss seeing the impact of the shots if one blinks.

The excerpt contains several points at which the degree of uncertainty is raised to a still higher level. Twice, significant items are presented briefly and visually before a major shift in the sequence of events: first, tailors dummies bearing patches of skin at the climax of the first chase before the main character finds the second woman, second, the decomposing body in the bathtub just prior to the lights going out as well as the very brief final scene of the man's gunshot wounds. According to Ehlers (2004) view of memory for events precipitating PTSD, these are the sort of events that may be remembered as sensory fragments, occurring just before things get worse for the main character. These three scenes and the initial panning shot, a visual event separate from the storyline as such, were probed by memory tests and identified specifically as four target items, visual in nature, within free recall accounts.

Neuroimaging studies in PTSD show extensive right hemisphere activation of the amygdala and sensory areas and hypoactivation in Broca's area, in the left vmPFC, when the traumatic memory is being re-experienced (Shin et al., 1997; Rauch et al., 1996). It may be hypothesised that during a fearful experience, these patterns of activation will be similarly evident. In left handers, at least for motor control, the right side of the brain is dominant, and in response to a fearful stimulus, the shift towards hyperactivation of the right and hypoactivation of the left hemisphere (especially frontal cortex) may therefore be more exaggerated. If so, then they may exhibit some of the features seen in people with PTSD. While watching the film, it is possible the viewer will become alert to threat resulting in increased sensory awareness of the sights and sounds (other than dialogue) that may be signs of danger in the film. Since the right hemisphere is associated with sensory experience, left handers may preferentially process sensory rather than verbal material, since in the majority, language is retained in the left hemisphere, but the latter is less dominant in use than in right handers. In people with PTSD memory is also reputedly more fragmentary in relation to trauma as described by Ehlers (2004) above. If this is related to a relative shift towards sensory and away from verbal material consequent on a fearful stimulus, then this may also occur to some extent in left handers.

There are, however, issues with the way "fragmentation" has been operationalised. While clinicians consistently report fragmentation of trauma narratives in people with PTSD (e.g. van der Kolk & Fisler, 1996; Ehlers et al., 2004), experimental studies have claimed not to have demonstrated such an effect. This may not be indicative of the absence of an effect, but rather the way fragmentation has been measured. For example, Gray & Lombardo (2001) considered a measure of reading difficulty as an operationalisation of fragmentation, but this seems less than satisfactory, and does not correspond with what clinicians are reporting. There is no reason to suppose that an educated person with PTSD will revert to a narrative style with a lower reading difficulty as a consequence of having PTSD. There is however support for the idea that fragmentation may be due to temporal disruption in the sequence of events remembered.

Hypoactivation of Broca's area has been demonstrated in response to reliving of a traumatic event. Not surprisingly, since language depends particularly on temporal sequence, this part of the left PFC is also involved in temporal sequencing (Levitin & Menon, 2003). Thus hypoactivation of left PFC in response to a fearful stimulus may also interfere with sequencing. Fragmentation may therefore be better considered as disruption to the temporal sequence of events and measured by the number of sequencing errors within a free recall narrative. Repetition of material within free recall may be another direct measure of fragmentation and loss of sequence. There is support for this proposed operationalisation of fragmentation. Trauma survivors seen by Ehlers' research team (Ehlers et al., 2004) were unclear about the exact temporal order of events, whereas in a student study (Porter & Birt, 2001) there was no difference in coherence in recall for "traumatic" compared to positive memories. Indeed Ehlers et al (2004) comment specifically about the inadequacy of fragmentation indices used in studies of this phenomenon and suggest that it is disjointedness which is crucial in true traumatic memories.

On the other hand, these could simply be considered as errors, along with errors of commission (adding in spurious events to the recall narrative) and by explicit admission of uncertainty about whether recalled material was accurate or not. During information recording from the taped free recall narrative, all these types of errors were noted on the recall recording sheet (Appendix 12). An increased propensity for errors in general would be reflected in an increase in all types of errors in left handers; a specific problem with fragmentation would be supported by an increase only in errors of sequence and possibly repetition.

Since this experiment was probing memory for events in the fearful stimulus, it was also thought desirable to include a standard test of verbal memory to demonstrate specificity of any differences to the film excerpt; the AVLT (auditory verbal learning task) (Rey, 1958; Lezak et al., 2004) was included for this purpose, with the expectation that there would be no basis for expecting differences between left and right handers on this task. However, it is clear from the PTSD literature that this task (Vasterling et al., 1998; Vasterling et al., 2002; Uddo et al., 1993), and a similar variant, the California Verbal Learning Test (Veltmeyer et al., 2005; Jenkins et al., 1998), is one which shows deficits in verbal memory in people with PTSD. So, the same arguments apply to this task: left handers, like people with PTSD, may show deficits on the measures of verbal recall arising from the AVLT.

There is strong evidence for sex differences in declarative memory (Maitland et al., 2004); females perform better than males on tests of both recall and recognition memory, suggesting that this is due to differences in encoding rather than retrieval processes (since retrieval is supported in recognition, but not recall, memory) and in verbal fluency. Other evidence also suggests that women encode events in greater detail than men in accounting for consistently better performance of women in recall of life events (Seidlitz & Diener, 1998). Females also show increased performance on immediate acquisition and recall in the AVLT, but not in delayed recall (Ragland et al., 2000), although performance was near ceiling on the fifth recall attempt and the small sample may have precluded detection of differences in the delayed recall condition. Females also show better recognition memory for emotional pictures (Canli et al., 2002).

The main aim of this experiment was therefore to explore possible differences in memory for events in a fearful film in left and right handers, with hypotheses that left handers may behave similarly to people with PTSD, based on lateralisation effects. Both recall and recollection memory was probed. Based on previous findings in the literature, sex differences were expected on memory tasks. Sex differences in subjective ratings of fear after watching the movie were also predicted. Specifically, the following hypotheses were proposed.

Hypothesis 1: left handers will perform better than right handers on memory for sensory (visual and sound) elements, or details, within the film and less well than right handers on memory for verbal material (in the film and on the AVLT).

Hypothesis 2: left handers will show greater fragmentation of recall memory than right handers, operationalised as susceptibility specifically to fragmentation errors (errors of sequencing) rather than to errors in general.

Hypothesis 3: females will perform better than males on measures of recall and recognition memory and on the AVLT in line with previous findings.

Hypothesis 4: females will report higher subjective ratings than males of fear and overall tense arousal.

5.2.2 Methods

5.2.2.1 Participants

Participants were those taking part in the study reported in Chapter 6 (N=156: participants in the standard and reversed protocols who viewed the film); they were primarily recruited from within the psychology department subject panel. However, since the majority of psychology undergraduates are female and only 10% of the population is left handed, recruitment of males and left handers was augmented by appeals through posters and the University's portal log-in page to the whole university population.

5.2.2.2 Apparatus

The film excerpt, recorded on a DVD, was presented on a HP Compaq nx9010 Pentium 4 laptop, running Windows XP, using Windows Media Player (Version 9 series) and fitted with digital stereo headphones. A Sony cassette recorder (TCM-939) was used to record participants' free recall of the film.

5.2.2.3 Materials

The film excerpt from Silence of the Lambs (Saxon et al., 1991) was prepared by playing the commercial video on a Sony SLV SC820 four head video machine and copying the excerpt using a Sony RDR GX7 DVD recorder onto a TDK DVD-R.

Editing instructions are included at Appendix 15. The associated Emotion Rating form (Appendix 4) was completed after watching the film. Subjective ratings were made indicating how strongly each of the negative emotions (anger, fear, disgust and sadness) and an overall measure of tense emotional arousal were experienced during the film, using 10 point Likert rating scales.

Recognition memory was tested with a series of four-alternative multiple choice questions (MCQ) constructed around events and details in the film (see Appendix 8); false answers were intended to be plausible alternatives. Questions were presented in the order as seen in the film.

The AVLT considers learning and retention of a 15 item word list – List A (see Appendix 9). The AVLT was modified as follows. Three repetitions of the test of immediate recall of the word list were performed instead of five; the intervening interference List B was omitted as participants completed a Stroop task before the delayed recall test instead, and the practice and neutral words used in the Stroop task (see Appendix 5) were used as distracters in the recognition part of the test in place of List B words. The layout of words was maintained from the standard test list with new distracter words inserted and the new list (second page Appendix 9) was read from top to bottom in each of the columns from left to right. None of the words in word list A had salience to the film (with the possible exception of house).

5.2.2.4 Procedure

The full procedure for the experiment based on the Stroop paradigm, of which this investigation forms a part, is included in Chapter 6. For the purposes of the current chapter, that procedure is briefly outlined here as it relates to the viewing of the film and the tests of memory.

Participants viewed the film after completing two brief questionnaires (handedness inventory/PSS10) at week one. Participants signed a consent form that informed them specifically that they would view a film rated 18 as this was considered ethically necessary, and were told this was not violent or pornographic in nature; the exact nature of the film was not explicitly stated in order to avoid particular expectations in advance of the viewing. The experiment was conducted in a windowless cubicle; the lights were switched off while participants viewed the film and headphones worn, to make the experience essentially a private one, and unaffected by any extraneous noise. The experimenter remained at the back of the room for the duration of the excerpt and switched on the lights as the film concluded. Participants then completed the emotion rating form.

Seven days later, they returned for part two of the experiment. They were immediately asked to remember the film they had watched the previous week and to relate aloud to the experimenter as much as they could remember about the storyline and any details in the film; it is important to note that this was a surprise memory test, as the purpose of the session had been described as a return to perform another Stroop task. The tape recorder was switched on and the participant allowed to recall freely and uninterrupted until they indicated they had recalled everything they could. The MCQ was next presented and participants asked to make a "best guess" if they did not know an answer so that a forced choice response was made to each question.

Next the first part of the AVLT was completed; the experimenter read through Word List A at an even pace with no intonation and at the end of each of three readings through the list, participants were asked to recall as many of the words as possible. During this time the experimenter looked only at the list of words, not at the participant, and no clues were given about whether the list was complete; the experimenter waited until the participant indicated they had finished each attempt before continuing. After the three immediate recall tests, the Stroop task was performed. Following this, participants were asked to remember back to the list of words they had been read earlier and to recall as many as possible (the delayed recall test). Finally the recognition test was conducted: the AVLT recognition checklist was read out one word at a time and participants responded yes or no according to whether they recognised the word as belonging to List A. Participants were then debriefed as to the purposes of the study, and given the opportunity to ask any questions of the experimenter. Participants in the standard and reversed protocols of the Stroop paradigm (*qv*, Chapter 6) completed the memory tests for the film and the AVLT; participants in the control protocol, who did not view the film, completed the AVLT.

5.2.2.5 Analysis

Analysis of participants' free recall narrative was carried out as follows. A transcript of all events in the film was prepared, split by storyline and details, and agreed by two independent judges who watched the film while following the transcript; minor changes were made so that all content was included and agreed (Appendix 11); a division into six sections (introductory; chase1; woman in pit; chase2; climax; resolution) was similarly agreed. These were not of equivalent duration, but reflected the event structure of the excerpt. The transcript was then condensed to reflect the main events, at a narrative level used by participants in the recall exercise, and a recording sheet prepared for use by the experimenter while listening to each participant's taped recall

(Appendix 12). This sheet also included tick box columns for recording locations, speech, sounds and visual details; details likely to be mentioned were included in the template and anything else that was mentioned in the recall narrative was entered in the relevant column. Reference to an emotion being portrayed by any of the characters was also recorded. Four types of error were also identified after a sheet was completed: reversals of sequence (by numbering the events captured on the recording sheet in order of recall: an error was recorded when, having mentioned an event, the time sequence was broken by returning to mention an earlier event); errors of fact (where erroneous statements were made); repetitions (where an event or detail was mentioned separately on more than one occasion); uncertainties (where something was mentioned but the subject stated that they were unsure about this recollection). Anything about the film that a subject could only know from having watched the film before, and which was not actually viewed in the excerpt, was ignored and not recorded on the sheet. The number of items mentioned within each part of the film's storyline and each category of detail, and errors, were then summed. The duration of the taped free recall was also recorded. Variables of interest were then analysed by independent t-tests, comparing right and left handers and also, separately, by sex.

The MCQ responses were recorded and scored for correctness. The AVLT produces three immediate recall attempts and a summed learning total over these three attempts, one delayed recall attempt (recall attempts ceiling score =15), and a recognition test (scored out of 15) with incorrect intrusions from the distracter words also scored. Errors on the recall attempts were scored as repetitions (of target words) or intrusions (of non-target words).

5.2.2.6 Ethics

Ethical approval for this study was obtained from the Department of Psychology Ethics Committee as part of the Stroop study reported in Chapter 6 (see Appendix 23); ethical issues are discussed in relation to the procedure used (see section 6.2.4 below)

5.2.3 Results

5.2.3.1 The sample

The mean age of the total sample was 22.93 years (SD ±7.15) and ranged from 17 years 4 months to 62 years 0 months. There was no significant difference in age between males and females, but an independent samples t-test (with unequal variances) showed that the left handed sample was significantly older and had a higher standard deviation from the mean (24.4 years ± 8.9) than the right handed sample (21.9 years ± 5.3) [$t_{(129.462)}$=2.276, p=.024]. This reflects the wider sourcing of left handed participants than from psychology undergraduates. The sample consisted of 45.5% males (n=71) and 54.5% females (n=85); 47.5% (n=74) were left handers and 52.5% (n=82) were right handers.

The PSS10 was included as a measure of underlying state stress before participation in the experiment; the mean value for the whole sample was 14.41 (± 6.501) with no significant differences between right and left handers, or between males (13.77 ± 6.097) and females (14.85 ± 6.758), $t_{(207)}$= -1.190, p=.235.

When mean ratings for all negative emotions on the film rating form were compared using independent t-tests, there were no significant differences in reported emotion between left and right handers, or between the two experimental protocols which viewed the film (standard and reversed protocols).

There were no significant differences between proportions of both right and left handers, or males and females, who had previously seen the film used in this study (both p>.05). Overall, 60% of subjects had previously seen the film. These distributions are shown in Table 5.3 for both handedness and sex. There was a trend for relatively more subjects (36.5%) in the standard protocol to have previously seen the film, compared to the reversed protocol, in which 23% of participants had seen the film [$\chi^2_{(1,N=156)}$=2.846, p=.092].

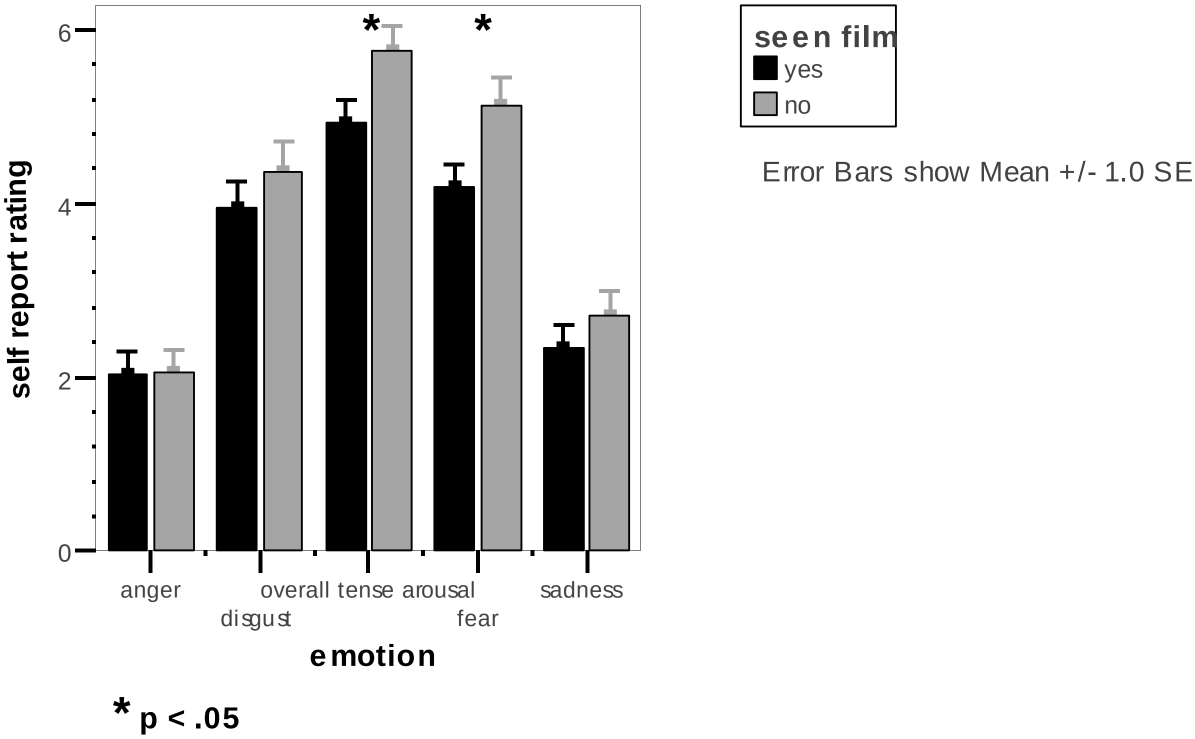
Table 5.3 Proportions of subjects who had seen the film previously, by handedness and by sex

	Handed						*Sex*			
Seen film	left		right		**total**		male		female	
before:	n	%	n	%	**n**	**%**	n	%	n	%
Yes	46	*29.5*	47	*30*	**93**	***60***	47	*30*	46	*29.5*
No	28	*18*	35	*22.5*	**63**	***40***	24	*15.5*	39	*25*
Total	74	*47.5*	82	*52.5*	**156**		71	*45.5*	85	*54.5*

However, having seen the film previously attenuated the self report levels of both fear and overall tense arousal, but not ratings of the other emotions (fear: [$t_{(156)}$= -2.237, p=.027]; overall tense arousal: [$t_{(156)}$= -2.071, p=.040]). These differences are shown in Figure 5.3.

Perhaps unsurprisingly, having viewed the movie prior to the experiment resulted in more items being recalled in the free recall task, for both storyline (mean: seen before 12.06 items; not 9.12 items) [$t_{(143)}$=4.444, p<.001] and details (mean: seen before 9.31 items; not 6.97 items) [$t_{(142.912)}$=2.695, p=.008]. There were also more errors of sequence reversal (mean: seen before 1.118 occasions; not .820 occasions) [$t_{(143)}$=1.995, p=.048], but not other types of error. Participants who had seen the movie previously were also more likely to recall visual events (mean: seen before 3.13 items; not 1.82 items) [$t_{(140.233)}$=3.384, p=.001], and the four key visual items (mean: seen before .82; not .45) [$t_{(142.589)}$=2.742, p=.007], particularly the skin suit on the tailor's dummy (mean: seen before .27; not .02) [$t_{(102.986)}$=4.954, p<.001].

Figure 5.3 Attenuation in self ratings of fear and overall tense arousal in those participants who have previously seen the film



In respect of the MCQ testing recognition memory, similar results were obtained (Table 5.4). Those who had viewed the movie previously had significantly higher scores overall and for all parts of the film except for the central two segments: the discovery of the woman in the pit and the resumption of the chase following this.

Table 5.4 Effects on recognition memory (MCQ) according to whether movie had been viewed prior to participation in this experiment

	difference	*t*	*df*	**p**
total score	seen > not	4.220	140	< .001***
1- introductory	seen > not	3.940	142	< .001***
2- chase1	seen > not	2.140	141	.034 *
3- woman in pit	seen < not	-.664	143	.508
4- chase2	seen > not	.462	143	.645
5- climax	seen > not	1.983	143	.049 *
6- resolution	seen > not	2.419	117.439	.017 *

*** sig at p < .001; * sig at p < .05

5.2.3.2 Differences between left and right handers in memory

Hypothesis 1 predicted that left handers will perform better than right handers on memory for sensory (visual and sound) elements, or details, within the film and less well than right handers on memory for verbal material (in the film and on the AVLT). Results from the free recall narrative are presented first followed by results from the 21 item MCQ test and finally the AVLT.

Overall, duration of recall was positively correlated with total scores of storyline events [r=.634, p<.001, N=145], number of details recalled [r=.712, p<.001, N=145] and total number of errors [r=.521, p<.001, N=145] indicating that the longer the recall, the more was included, but that there was also increased susceptibility to errors.

There were no differences between left and right handers in duration of recall or in recall of storyline events either in total, or when separated into the component sections of the storyline. There was a trend for left handers to recall significantly more details overall than right handers (mean number recalled L: 9.16 items; R: 7.61 items) [$t_{(143)}$=1.681, p=.095].

There were no significant differences in recall of speech [$t_{(143}$= -.420, p=.675] items, there was a trend towards left handers recalling more sounds [$t_{(143)}$=1.676, p=.096] than right handers (mean: L: .79 items; R: .56 items) and left handers did recall significantly more visual items in the excerpt, $t_{(143)}$=1.973, p=.050] (mean: L: 3.03 items; R: 2.19 items). For the four targeted visual scenes (opening establishing shot, tailors dummies, body in bathtub and gunshot wounds) there was a trend for left handers to mention more of these items than right handers (mean: L: .81; R: .55) [$t_{(143)}$=1.842, p=.068]. Furthermore, recall of the establishing shot was highly significantly different, with more left than right handers mentioning this scene (mean score: L: .25; R: .08 for this item): [$t_{(108.953)}$=2.812, p=.006]. There was also a trend for left handers to make more mentions of specific emotions portrayed in the film (mean L: .71 items; R: .43 items) [$t_{(114.889)}$=1.864, p=.065].

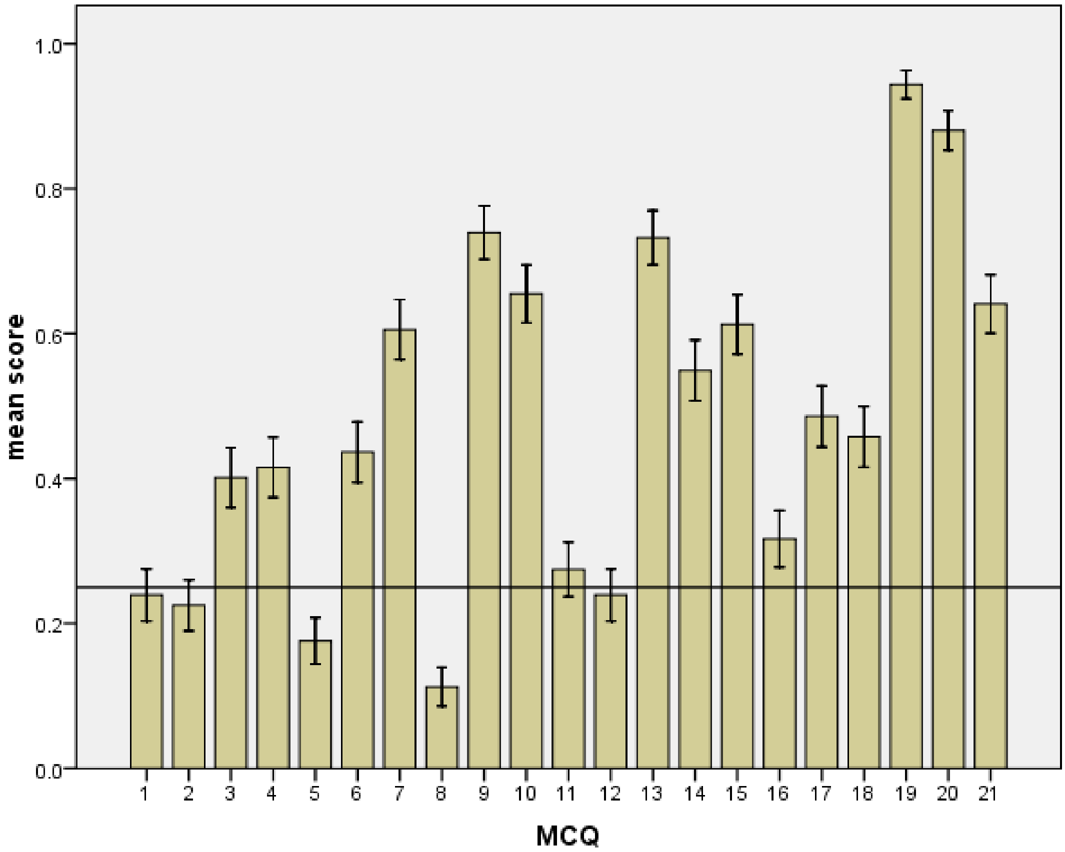
In summary for recall of the film, there were mixed findings in relation to hypothesis 1: there was support for left handers better performance on recall of visual items, less strong support for better performance in recall of sounds and poorer performance in recall of spoken items was not supported.

Hypothesis 2 predicted greater fragmentation of recall memory via fragmentation errors (errors of sequencing) in left compared to right handers. All errors made during recall were recorded. Overall, left handers made more errors than right handers (mean L: 2.85; R: 2.01), and this difference just escaped significance [$t_{(143)}$=1.929, p=.056]. However, this was accounted for by two specific types of error in which left and right handers were significantly different. Left handers made significantly more errors of reversals of sequence than did right handers (mean L: 1.04; R .68) [$t_{(143)}$=2.210, p=.029] and made significantly more repetitions (mean L: .57; R: .18) [$t_{(86.209)}$=2.416, p=.018]. These two types of errors are probably related in that when events are described out of sequence, if the participant then backtracks to an earlier event, they may well re-describe the subsequent event that has already been mentioned. There were highly significant positive correlations between these two types of error in left handers [r=.607, p<.001, N=68]; in right handers these were also positively correlated, but not as strongly, and at a lower level of significance [r=.227, p=.047, N=77], suggesting that in right handers repetition errors were also occurring independently of reversals. These findings support hypothesis 2, which suggested left handers would show more fragmentation of narrative operationalised as sequencing errors; these were specifically the errors showing significant differences between left and right handers.

To return to hypothesis 1, before considering possible differences between left and right handers on the MCQ (recognition memory) task, overall scores are presented in Figure 5.4 below.

Two questions, Q5 and Q8, are answered at worse than chance levels. Both of these questions combined two pieces of information, about what the characters were wearing (as did Q12 - answered at chance); which had to be in the correct combination to answer and were therefore more difficult to get correct. Of the other items answered at chance levels, Q1 asked about the colour of the car seen parked outside the house in the initial establishing shot, Q2 asked about the colour of the woman's coat, Q11 asked about details in the first part of the chase – the colour of the doors (green, but later doors are brown; brown was the modal answer, n=75: 36% of participants) and item 16 about what was the last statement in speech from the FBI agent to the woman trapped in the pit.

Figure 5.4 Overall mean scores on MCQ with horizontal line showing chance level at .25. X axis values refer to question number on MCQ - see Appendix 8.

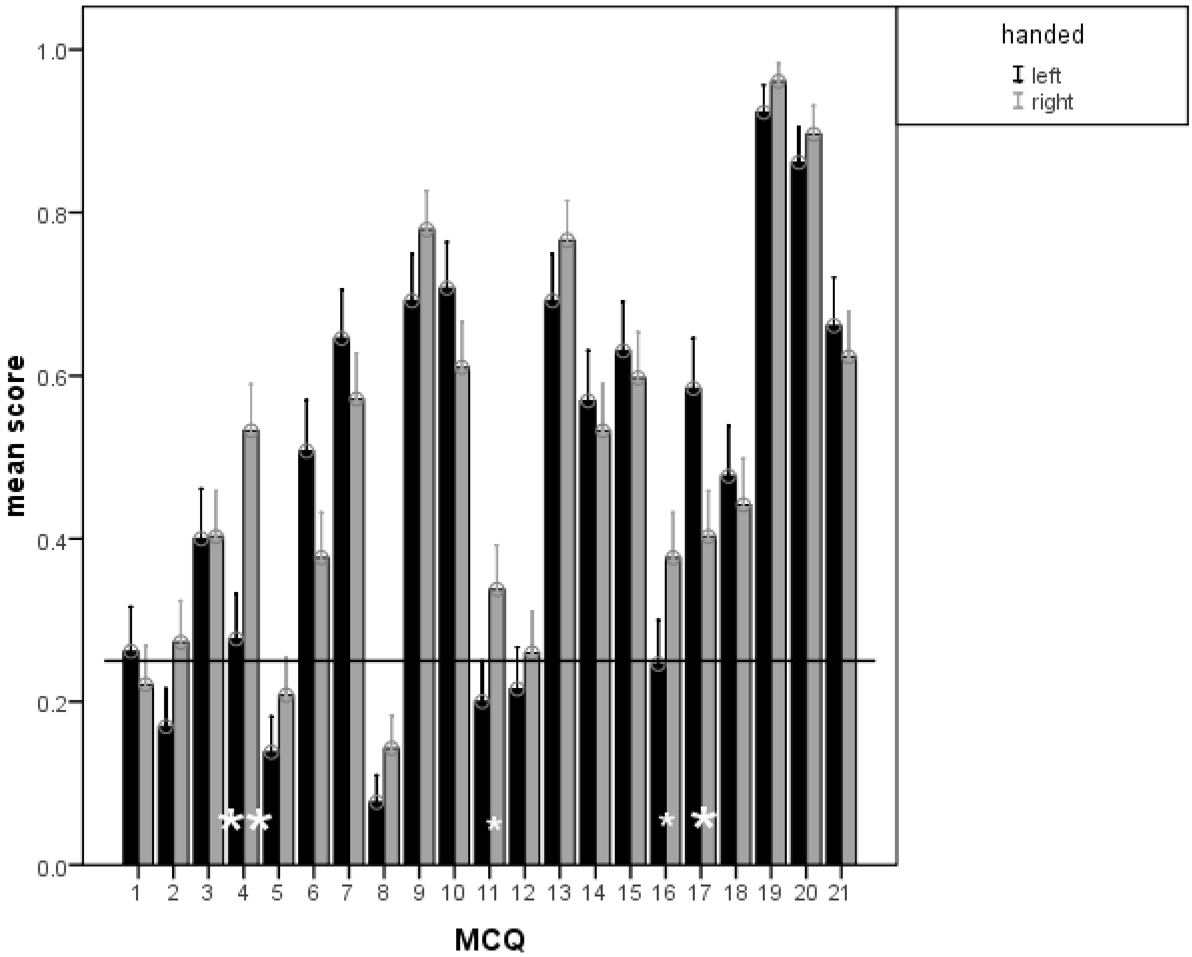


NOTE: Q1, Q2, Q11, Q12 and Q16 are answered at chance.

Q5 asked about jewellery (ring and necklace) worn by the FBI agent: she was wearing both. The necklace is evident particularly in the first part of the film when the woman is looking around, noticing clues; the ring is evident when the woman unbuckles her gun holster and might be expected to be remembered according to weapon focus theories. When the answers to this question are examined further, only n=38, 26% of participants, equivalent to chance level, noticed the ring (combined answers to “ring” and “both”). The man’s gun was seen resting on a cooker (Q9); this, in contrast, was correctly answered by n=109, 74% of participants. This provides mixed support for weapon focus theories of memory.

When MCQ scores are compared for left and right handers there were no differences in total correct (mean total score: R 10.31; L 9.94) with both groups approaching 50% correct [$t_{(143)}$= -.921, p=.359]. Mean scores for individual items are shown in Figure 5.5 below; there were significant differences on two items and a trend towards significance for two other items. The latter were Q11 (colour of first doors in the chase) [$t_{(142.867)}$= -1.796, p=.075] and Q16 (speech to woman in pit) [$t_{(142.993)}$= -1.860, p=.065] discussed

Figure 5.5 Distribution of MCQ answers for left and right handers (error bars shown mean +/- 1.0 SE) X axis values refer to question number on MCQ - see Appendix 8.



**** p<.01; * p<.05; * .05 < p < .10**

above as being answered at chance overall; in both instances the mean score of the left handers was lower than the right handers. Further analysis revealed that for item 16, relating to speech content, only the left handers answered at chance: the right handers mean score was significantly different, and better, than chance [$t_{(77)}$=2.278, p=.026]. There were two questions in which mean scores for left and right handers were significantly different. Q4 refers to the question the woman (FBI agent) asks of the man “Did [the previous owner] leave behind any *records, any business records*…” At this point in the film, the man is looking through a handful of business cards. As can be seen from Figure 5.5 above, the mean score for left handers was significantly lower than the right handers [$t_{(142.943)}$= -3.193, p=.002].

When the actual answers are considered, (Table 5.5) the modal answer for left handers (35% of left handers) was “business cards” and not “business records” suggesting that the left handers were remembering the visual rather than the verbal content of this scene; the modal answer for right handers is the spoken “business records”. The distribution of answers shown in Table 5.5 is also significantly different for left and right handers when analysed by a chi square test [$\chi^2_{(3,N=145)}$=10.375, p=.016].

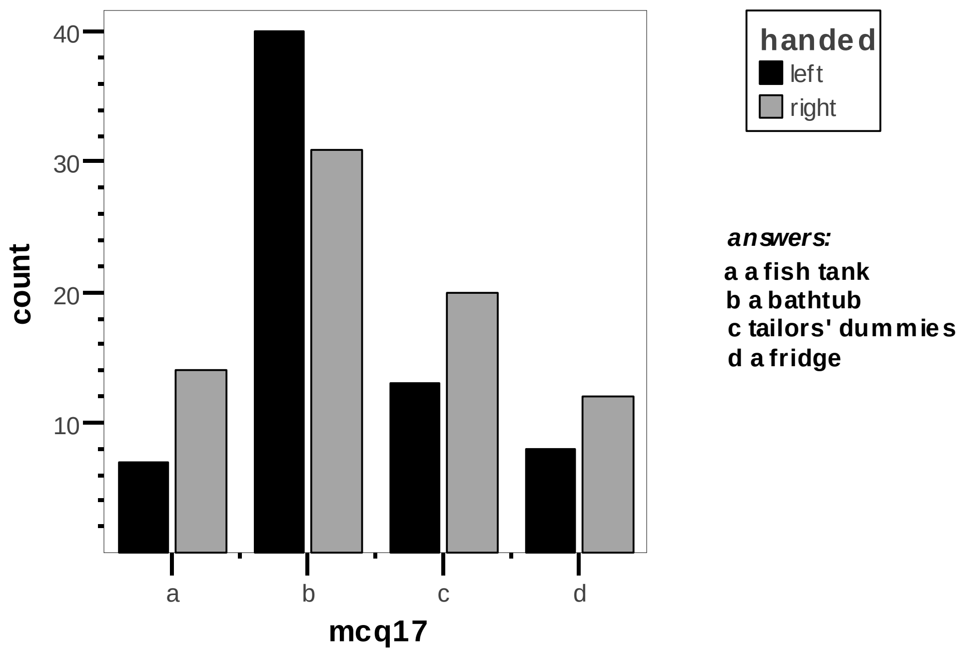
Table 5.5 Answers to MCQ 4

	handed		
answer:	left	right	**Total**
a business records	19	41	**60**
b business cards	24	14	**38**
c phone bills	15	13	**28**
d accounts	10	9	**19**
Total	**68**	**77**	**145**

Q17 was the remaining question in Figure 5.5 for which answers were significantly different for left and right handers; left handers scored significantly higher in response to what was visible when the lights go out [$t_{(140.636)}$=2.255, p=.026]. Figure 5.6 below shows the distribution of answers: bathtub is correct. All of the items mentioned in this question have been visible in this part of the film.

There were three questions (Q3, Q4, and Q16) which asked about information conveyed in dialogue. When the scores for these three items were combined, left handers scored significantly lower than right handers (mean scores: R 1.31 (44% correct); L .93 (31% correct)) [$t_{(142.461)}$= -3.109, p=.002].

Figure 5.6 Answers to MCQ17 by handedness

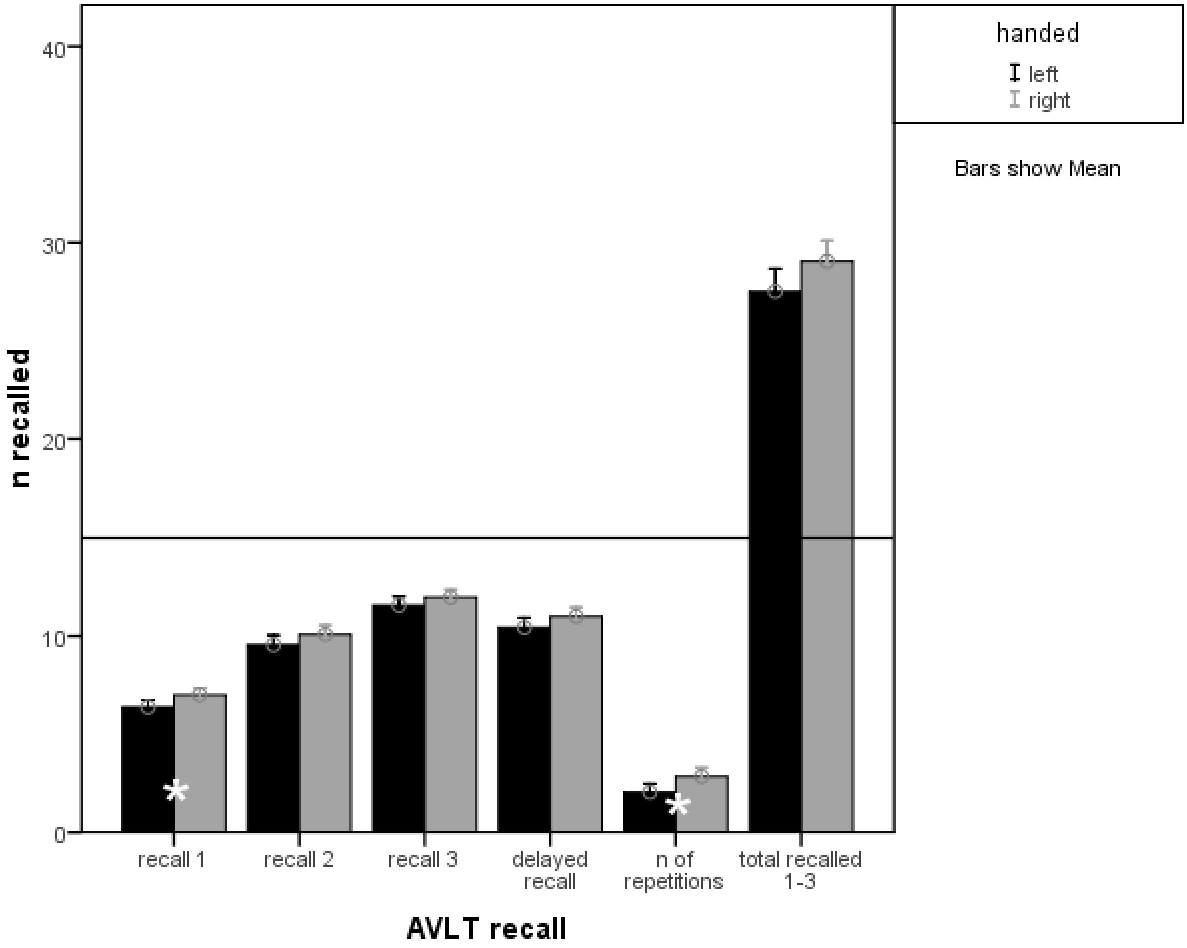


In summary, on the recognition memory MCQ, while there were no overall differences in memory, there was some support for hypothesis 1. There were two questions with significant differences between left and right handers. On Q17 about a briefly glimpsed scene before the lights went out, left handers scored significantly better than right handers, although this would not have survived correction for multiple t-tests. In respect of Q4 there was a highly significant difference with left handers more likely to be incorrect on the question but apparently remembering what they were seeing and right handers remembering what was said in dialogue and more likely to answer correctly. Left handers also showed significantly poorer performance when questions about dialogue were combined.

Results for the AVLT were considered only for participants in the standard and reversed, but not control, protocols of the Stroop paradigm, for reasons discussed in Chapter 6.

Overall, after three attempts, left handers did not differ from right handers in their ability to recall the 15 item word list; however, they seemed to have more difficulty with immediate recall on the first attempt, scoring significantly lower than right handers (L: 6.38 ± 1.84; R: 7.00 ± 1.90) [$t_{(143)}$= -1.985, p=.049]. Left handers were also found to commit less repetition errors during recall attempts than were right handers [$t_{(143)}$= -2.065, p=.041]. Distributions of recall attempts and repetition errors are shown in Figure 5.7. Neither group performed close to ceiling level at the third recall attempt: one-sample t-tests against the ceiling value of 15 were both p<.001.

Figure 5.7 Differences between left and right handers in AVLT; horizontal line at value 15 shows ceiling for recall attempts (error bars show mean +/- SE)

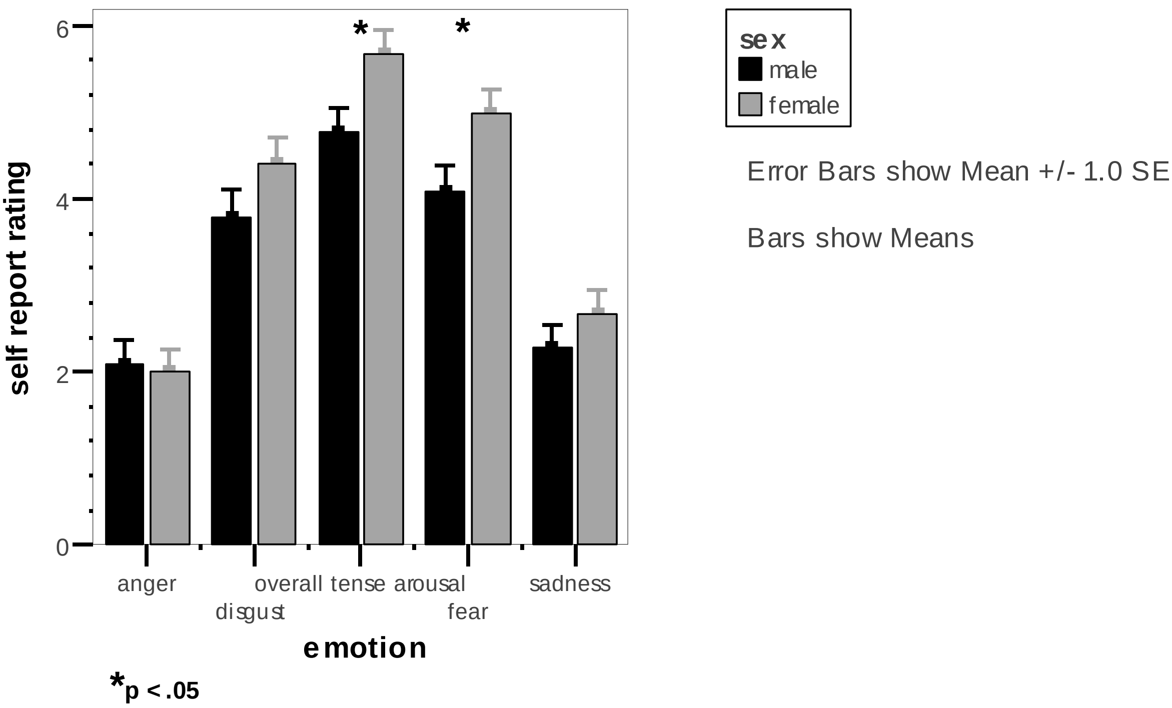


*** p<.05**

5.2.3.3 Sex differences in emotion and memory

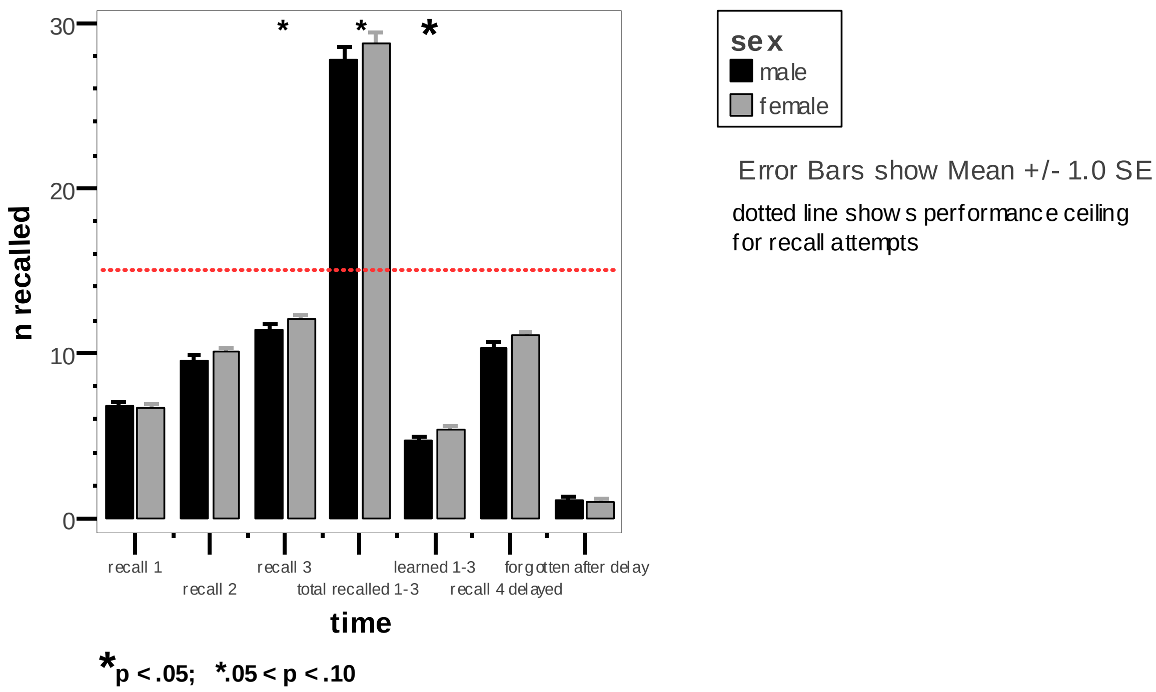
Hypothesis 4 predicted females would report higher subjective ratings than males of fear and overall tense arousal. Independent sample t-tests showed sex differences in ratings of subjective emotions experienced while watching the film. Females ratings of fear [$t_{(156)}$= -2.167, p=.032] and an overall measure of tense arousal [$t_{(156)}$= -2.359, p=.020] were significantly higher than males' ratings, with no differences in ratings of anger, disgust and sadness; these results are shown in Figure 5.8 and support this hypothesis.

Figure 5.8 Sex differences for experienced emotions of fear and an overall measure of tense arousal in response to watching a fearful film



Hypothesis 3 predicted that females would perform better than males on measures of recall and recognition memory and on the AVLT. On the AVLT there was some evidence for superiority of females in verbal memory in support of hypothesis 3; performance is shown in Figure 5.9.

Figure 5.9 Sex differences in AVLT variables



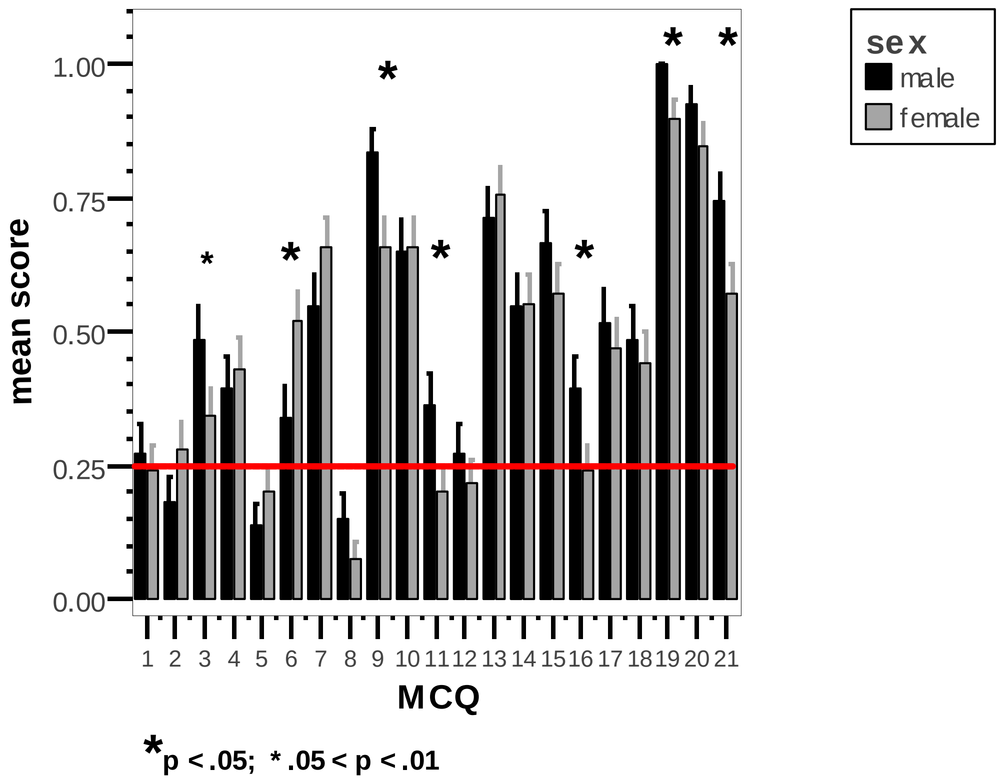
There was a trend towards significance for females recalling more items than males on the third attempt [$t_{(143)}$= -1.772, p=.079] and at the fourth, delayed recall, attempt [$t_{(125.722)}$= -1.752, p=.082]. While these variables produced only trends towards significance, when the amount of learning was considered (that is, improvements in recall scores at the third attempt over baseline - attempt 1), females were found to have learned significantly more items than males [$t_{(143)}$= -2.307, p=.022]. However, these differences would not have survived correction for multiple t-tests.

While results on the AVLT were in the expected direction, results for recall and recognition memory in relation to the film were not. The recall task revealed sex differences in several areas. The duration of free recall was significantly longer in males (mean time: males 118.8 secs; females 92.06 secs) [$t_{(143)}$=2.682, p=.008]. Males recalled significantly more items than females in the storyline overall (mean: males

12.02 items; females 9.86 items) [$t_{(143)}$=3.92, p=.002], and for several of the component sections of the film: introductory (trend towards significance: p=.072); chase 1: p=.037,; climax: p<.001; and resolution: p=.011. Only for two of the middle sections of the film excerpt, pit and chase 2, did they not score significantly differently than females. There was also a trend towards significance for males to remember more details than females (mean: males 9.26 items; females 7.57 items) [$t_{(143)}$=1.828, p=.070]. When types of details recalled were considered, males scored significantly higher in two areas – for recall of location details (mean: males 3.08 items; females 2.39 items) [$t_{(143)}$=2.577, p=.011] and in recall of the establishing shot (mean: males .26; females .08) [$t_{(102.823)}$=2.930, p=.004].

On the MCQ, males' scores were higher than females at a level just at significance (mean total score: males 10.57; females 9.78) [$t_{(140)}$=1.970, p=.051]. Figure 5.10 below shows the distribution of scores by sex for each of the questions; with the exception of Q6 (in which females did better on memory for a roll of cling film on top of the fireplace - the male modal answer was aluminium foil), where there were significant difference in scores between the sexes, males performed better than females. In order to test whether the differences between males and females in memory for items on the MCQ could be related to the differential self-reporting of fear and overall tense arousal, reported above, correlations were performed on these self-report ratings and the total score on the MCQ test; no significant correlations were found between these variables either for the whole sample or when males and females were considered separately.

Figure 5.10 Distribution of scores on MCQ by sex; horizontal line at .25 indicates chance performance



In summary, on tests of memory for events in the film, differences were counter to hypothesis 3; where there were significant differences in performance, and these were on multiple measures, males performed significantly better than females.

5.2.4 Discussion

With respect to memory for events in the film, those who had previously seen the movie remembered significantly more on measures of both recall and recognition memory. This was true for both storyline and details overall and for the four key visual clues that were generally rarely mentioned - that would make more sense to someone who had seen the film before, and perhaps, therefore, be noticed and recalled. This is unsurprising, and since there were no significant differences between either left and right handers or males and females who had seen the movie, this should not have affected results comparing these groups. That more errors of sequencing were made may be explained by recalling additional information outside of the excerpt viewed and hence interrupting the narrative with this.

Hypothesis 1 proposed specific differences between left and right handers. In free recall there were trends in the expected direction of left handers showing better recall for sounds and also for emotional states of the characters. However, the difference in respect of recall for visual items just reached significance, and would not have survived correction for multiple t-tests. The strongest finding was that left handers were significantly more likely to mention the establishing shot with which the excerpt opened; this could be interpreted as representing a heightened awareness of visual context. This perhaps further supports the hypothesis that left handers are more likely to remember the purely visual scenes occurring within the film than are right handers. While left handers did not perform differently from right handers in recall of spoken items, they did perform less well on the MCQ relating to spoken items, as hypothesised. There were two questions of the MCQ in which left and right handers were significantly different; one was in relation to a glimpsed scene (of a decomposing body in a bathtub) just prior to the lights going out, one of the target visual scenes, and the only one which featured in the MCQ. Left handers performed better than right handers at a high level of significance.

The highly significant finding in respect of the other, Q4, was particularly interesting with respect to hypothesised differences. This question related to spoken dialogue about *business records*, but one of the answers related to what the man was seen to be doing: handling *business cards*. Not only did the scoring reflect poorer performance of left handers on the question, supporting the hypothesis of poorer performance with verbal material, but the pattern of answers, significantly different by a chi square analysis, showed that left handers were responding to the visual material rather than the spoken material. Where there were differences on the AVLT, left handers showed significantly poorer performance on immediate recall of verbal material on the first trial, again providing support for hypothesis 1.

Hypothesis 2 was also supported: significantly higher error rates in left handers recall narratives were accounted for by errors in reversals of sequence, accompanied by repetitions of previously mentioned material. If this is a measure of fragmentation approximating clinician reports of fragmentation of trauma narratives in people with PTSD, then left handers are exhibiting similar effects. This operationalisation of fragmentation also seems to have some merit over other attempts to measure it in the literature, in that it is capturing disorganisation in narrative accounts. Though errors of sequence were relatively easy to measure here in response to a standardised “event” portrayed by the film, this is more akin to autobiographical memory for real events than other laboratory memory tests involving lists of words, and may be a useful technique in assessing fragmentation in real world trauma narratives.

Taken together, these findings are inherently consistent: compared to right handers, left handers are showing better memory for visual items, poorer memory for verbal material and they narrate events in a more fragmented manner with errors of temporal sequence. While some of the individual results are less strong than others, nevertheless this pattern is evident in both recall and recognition memory tasks. This suggests that these may arise from differences in encoding rather than retrieval since otherwise the support afforded to retrieval processes in recognition memory tasks should improve recognition relative to recall memory. The HERA model (Tulving et al., 1994; Cabeza & Nyberg, 2000) mentioned in section 1.3.9 above, suggests that encoding of information into episodic memory, at least as far as verbal material is concerned, is lateralised to the left PFC which is also involved in retrieval of information in semantic memory to an extent that the right PFC is not. The deficits that left handers are showing relative to right handers are in relation to verbal material in spoken dialogue and in the immediate recall of the AVLT. This is evident in recall and recognition tasks, though retrieval is supported in recognition relative to recall and suggests encoding, rather than retrieval, is affected. The errors in sequencing in left handers are also consistent with left PFC involvement. That this is not a general memory deficit in left handers is suggested by their superior performance on memory relating to visual material. If encoding is responsible, then this suggests that in left handers visual material is encoded to an extent that verbal material is not.

These observations are also consistent with the hypothesis that left handers, in response to a fearful stimulus (the film), are behaving in a similar way to people with PTSD who show hypoactivation of Broca's area and hyperactivation of sensory, particularly visual, cortex in response to their trauma narrative.

If left handers (as a group, since it cannot be demonstrated exactly which left handers retain language in the left hemisphere) are considered from the point of view of having at least some form of brain organisation which is right hemisphere dominant, it is interesting that they should demonstrate, in subtle ways, phenomena reminiscent of those found in people with PTSD. Although all significant differences observed were consistent with this pattern, some were not highly significant differences in themselves, and replication of these specific effects would seem to be required to substantiate these conclusions.

In relation to sex differences, the predictions that females would show higher subjective ratings of fear and arousal (hypothesis 4) were supported. Women are typically considered more emotional than men (LaFrance & Banaji, 2000), but these authors point out that emotion is a multidimensional construct measurable in different ways: phenomenological experience of emotion as measured by self report; physiological reactions to emotional situations and non-verbal expressivity as measured by facial expression of emotion. Reviewing evidence for each of these areas suggests that findings of sex differences may depend on both which emotion is considered and how it is assessed. Relevant to this chapter, sex differences in physiological responses do not consistently appear. This could not be tested in the experiment reported in the first part of this chapter, as there were insufficient male participants to make meaningful comparisons. In terms of self report measures, women appear more emotional than men on measures that ask directly about emotions experienced - as assessed after watching the film; on self reports of private experience females have been found to score higher than men on fear (and sadness). According to LaFrance & Banaji (2000) while some self-reporting may be influenced by gender stereotyping, self-reports as used here, asking about responses to particular situations, are more likely to be determined by the situational factors giving rise to the emotion rather than by gender stereotypes. The current findings are also consistent with greater fear reactions in females' written narratives about the most memorable slasher [‡] film viewed (Nolan &

[‡] According to Nolan & Ryan (2000) p40, the slasher movie is defined as "the immensely generative story of a psychokiller who slashes to death a string of mostly female victims, one by one until he is subdued or killed, usually by the one girl who has survived" (Clover, 1992) p21.

Ryan, 2000) and in self report ratings after viewing a scary movie in a date setting (Harris et al., 2000).

That females are more susceptible to fear makes sense from an evolutionary point of view. In accounting for reduced aggression in females compared to males, Campbell (1999), argues that the mother's presence, as principal carer and protector, is more critical to her offspring's survival and hence her own reproductive success. In order for her children to survive, she must survive and women therefore have greater concern than men with staying alive; Campbell suggests we should therefore expect some psychology in females that weights the costs of aggression higher than for males. She suggests this mechanism is fear, and that faced with an equal degree of objective risk, females will experience greater fear than males. The findings from this study support this hypothesis. Campbell also suggests that, in human and other primates, there is a substantial threat to the infant from other males; females are highly sensitised to this and display high levels of vigilance for this threat. Indeed, threat by an infanticidal male is the one occasion in which typical low level aggression may alter dramatically in females. The excerpt from Silence of the Lambs contained a female lead character placed in a fearful situation, and another female, trapped in a pit, who is the next intended victim of the male serial killer. It may therefore also be the case that female participants in this study feel greater empathy with these female characters and greater threat from the male character than do male participants.

In terms of sex differences in memory, the standard test of verbal memory, the AVLT, produced results consistent with hypothesis 3 which proposed that females would show better performance on verbal memory tasks than males. However, results on recall and recognition tasks relating to events in the fearful film consistently showed better performance by males which was counter to the direction hypothesised and to general findings in the memory literature, and in relation to emotional memory e.g. recognition memory of unpleasant pictures (Canli et al., 2002). The superiority of females over males on sex differences in the AVLT argues against generally poorer memory performance of the particular females included in this study.

There are several possible explanations for this. Harris et al (2000) investigating differences in autobiographical memories of watching a fearful film on a date, found that gender stereotypes were reinforced. The young men reported more positive experiences and wanted to be viewed as less fearful, while the women reported more negative experiences, particularly fear reactions to the film, and were more likely to want their dates to think they were scared. Interestingly, however, it was biological sex, rather than assessed gender-role behaviours, which predicted measures of negative reactions to the scary movie, suggesting that these responses are biologically hardwired and serve an evolutionary purpose, consistent with Campbell's views. In their textual analysis of written accounts of memorable slasher films, Nolan & Ryan (2000) found that men were more verbose, but not significantly so, in their accounts.

Taken together, these findings may be relevant to the experimental setting of the current study. The sex of the experimenter may have created demand characteristics: the (predominantly) young men may have felt they wanted to impress the (female) experimenter with their knowledge of this scary film and to demonstrate that they had not been scared by it. Many embellished their recall with extra details to demonstrate they had seen the film before, which may have contributed to the significantly longer duration of their recall efforts, but this does not explain the significant increase in storyline events, and location details recalled, as all extraneous information not a part of the excerpt used was ignored when recall recordings were scored. Using a male experimenter may alter the male participants' behaviour, if this factor is relevant, but then may be also likely to alter females responses towards fearfulness and protective need in line with Harris et al's (2000) findings, thus potentially perpetuating differences. However, this factor would also not explain the differences observed on the recognition, MCQ, test.

Another explanation is possible. In finding better recognition memory in females for emotional pictures (Canli et al., 2002) sex differences in lateralisation of amygdala encoding were apparent: females showed increased activity in left amygdala, which has been shown to respond to verbal representations of threat: (Phelps et al., 2001). Canli et al (2002) suggest that women, but not men, may use a left-lateralised, language based encoding strategy while men may have used visual-spatial encoding strategies. This is consistent with sex differences in rCBF (regional cerebral blood flow) in cognitive tasks which show greater left lateralised frontal activity in women than men (Esposito et al., 1996), and in left temporal regions related to superior performance over men in story recall, episodic memory tasks (Ragland et al., 2000).

The advantage of females generally found for memory appears, then, to be linked to activity in the left hemisphere. In the context of the fearful film, to which females at least subjectively respond to a greater extent than males, consistent with what is known about effects of the fear response in people with PTSD, experience of fear may lead to relative hypoactivation of this area. If this is the case, then the basis of the advantage normally enjoyed by females disappears, and may be replaced by a relative disadvantage relative to males who may be first, less affected by fear and second, whose encoding strategy may be right hemisphere based.

In contrast to the present study, Canli et al (2002) found superior recognition memory in females, but their experimental tasks likely did not target fear, using only static pictures rated as "emotionally intense" and hence different to the dynamic film used here to specifically target the emotion of fear. It is likely that responses to fear are different than to other emotions and require to be separated in any investigation of "emotional" memory. Further research investigating whether the sex differences observed here in recall and recognition memory occur for a non-fearful film, would be useful in this context.

This is potentially an important finding, requiring replication, as it suggests that functioning in females may be more compromised by a fear response than in males. This could help to explain why females are at greater risk for PTSD following trauma.

With the caveat of limitations in multiple t-testing, the main findings can be summarised as follows.

Left handers, relative to right handers, showed: (1) greater memory for visual events in the film; (2) poorer memory for verbal material in spoken items probed in the MCQ and (3) in immediate recall on the AVLT; (4) greater fragmentation of their free recall narrative account of the film.

In relation to sex differences, females compared to males showed: (1) greater fear responses to the film; (2) better verbal memory on the AVLT but, unexpectedly, (3) poorer performance in recall and recognition memory for the film.

All these findings are amenable to explanation consistent with effects in people with PTSD exposed to their trauma narrative, invoking fear responses, who show relative hyperactivation of right hemisphere and visual cortex areas involved in sensory experience and relative hypoactivation of left hemisphere language areas.

Chapter 6

The Stroop paradigm: differences in left and right handers

Background: The emotional Stroop paradigm produces interference effects in colour naming trauma-related words in people with PTSD, to a considerably greater extent than do other condition-specific words in other anxiety disorders and depression, and not in healthy populations. A review of the literature suggests the Stroop effect occurs in left hemisphere language processing areas at a late, response output stage.

Methods: The Stroop paradigm is adapted here with the target condition related to a fearful film viewed either immediately after the film or one week later after memory tasks described in Chapter 5. A novel, non-verbal form of Stroop task was designed to examine the extent to which interference may be related to the verbal nature of stimuli.

Results: Immediately after the film, but not one week later, left handers showed an overall significant increase in response latency and significant interference effects to "general threat" and film-related words. Absolute values of response latency in left handers approached values within the literature for people with PTSD. There were no significant effects in relation to the non-word Stroop task and overall response latency was significantly reduced to these stimuli compared to words, supporting hypotheses that the Stroop effect is related to language processing. Correct and false recognition memory showed no effects of handedness. An intended control group who did not view the film appeared to recruit students different to those in the other protocols and constitutes a limitation of the study.

Conclusions: Absence of handedness effects in recognition memory for the task words suggest that encoding is not differentially affected in left and right handers or by viewing the film. Effects observed immediately after viewing the film therefore appear to operate adversely on left handers in relation to verbal processing in ways similar to people with PTSD when exposed to their trauma narrative.

The previous literature on lateral preference in PTSD, which set the context for this thesis, has been introduced in Chapter 1, extended in the work presented in Chapter 3 to civilian populations, including women, and found links with left handedness in PTSD prevalence and symptoms. These findings were replicated in clinical populations in the work presented in Chapter 4. Although as yet unexplained, these findings suggest there may be some vulnerability to PTSD in those without a strong right lateral preference and the work on memory for a fearful film presented in Chapter 5 suggested that left handers are exhibiting some similarities to people with PTSD. The main aim of this chapter is to use a Stroop paradigm that has a robust effect in PTSD, but not other mental disorders, to examine possible differences between left and right handers (in a student population). This uses a fearful film, demonstrated in Chapter 5 to generate a physiological effect, as a laboratory analogue of fear, to substitute for real life experience of trauma prior to the Stroop task, since clearly it is not ethical to subject participants to traumatic experiences in the laboratory.

As people with PTSD appear to have deficits in processing verbal material, a non-verbal version of the Stroop task was also devised to compare with the standard word Stroop task; in order to examine the effects of different variables, three different versions or protocols of the experimental procedure were used. The rationale underlying the experimental work of this chapter is presented after an introduction to Stroop paradigms in healthy and PTSD samples.

6.1 Introduction

This section first introduces the Stroop phenomenon and the modified emotional Stroop used in clinical conditions and which is associated with a relatively huge effect in PTSD. Early theoretical models of the interference effect as “attention to threat” are critiqued, as is an alternative task, the dot probe; more recent neuroimaging and ERP evidence instead suggests that interference is due to language processing conflicts at the response output stage. This has consequences in terms of lateralisation effects observed in PTSD and which may pertain to left handers and forms the theoretical basis for the experimental work of this chapter.

6.1.1 The Stroop phenomenon

Although the first accounts of colour-naming phenomena can be attributed to Cattell (1886), the Stroop effect is credited to the publication of Stroop’s (1935) article on attention and interference. This paper described the phenomenon where naming aloud the colour of ink in which a word is printed takes longer when the word is the name of a colour different, or incongruent, to the ink (for example the word “green” in red ink) compared to congruent conditions (the word “red” in red ink). This increase in response latency to incongruent conditions turns out to be an extremely robust effect. In a major review of the Stroop literature MacLeod (1991) concludes that this effect generalises to other analogues of the procedure such as, blocked/individual stimulus presentation (although the effect is stronger with blocked presentations), variants of stimulus other than colour (e.g. pictures, geometric shapes) and on the nature of the response required (although the effect is stronger with a verbalised response than a manual key press).

Neuroimaging and ERP methods are potentially useful tools in understanding the neurocircuitry and temporal sequencing respectively underlying the Stroop effect, but neither procedure can use verbal responses since they are sensitive to movement associated with vocalisation. Since the phenomenon relates to incongruence in the stimuli rather than perception of colour *per se* a counting Stroop has been developed which uses number rather than colour incongruence and a button press response: for example, the word "three" written twice is an incongruent, while "three" written three times is a congruent condition. This task produces comparable effects to the colour Stroop (Bush et al., 1998). Substituting emotional words for the numbers constitutes an equivalent emotional Stroop task (Whalen et al., 2006; Whalen et al., 1998).

The Stroop effect has been used to investigate cognitive accounts of "attention-bias" in anxiety disorders. Mathews & MacLeod (1985) described a modified Stroop task where target words were related to physical or social threat. Anxious subjects were slower overall in colour naming words, and showed greater interference to threat words than neutral words, particularly where threat words related to the concerns of a particular individual. This effect is not normally produced in healthy controls but can arise where the words used in the task relate to some personally relevant current concern in clinical anxiety (Williams et al., 1996; Mathews & Klug, 1993). On some occasions, patients with anxiety have shown interference for positive words, leading to an emotionality hypothesis for emotional Stroop effects, but findings in PTSD patients do not support this view (e.g. McNally et al., 1990 *qv*) and it is thought this effect arises due to apparently "positive" words having negative associations, for example "success" may be associated with lack of success and failure (Martin et al., 1991).

6.1.2 The emotional Stroop in PTSD

In the last twenty years there have been many other studies using modified 'emotional Stroop' tasks. Of particular interest here are those in people with PTSD. The results of early studies will be described along with the theoretical accounts of the phenomena that were considered at the time; these accounts will be further reviewed below.

In line with early accounts of PTSD which emphasised the intrusive elements of the disorder, Mc Nally et al (1987) considered that fear/trauma-related memory networks were more readily activated (through a priming effect) in response to fear cues and that this mechanism was responsible for intrusive symptoms. Due to their subjective nature, re-experiencing phenomena are not amenable to objective measurement and introspective reports are open to sources of bias, such as interviewer demand, culturally relevant ideas or commonsense theories held by individuals (Mathews & MacLeod, 1985) while McNally et al (1993) suggest responses may also be biased by malingering.

Interference effects on a Stroop paradigm were proposed as a quantitative measure of intrusive phenomena. McNally et al (1990) presented four classes of words and a control (OOOOO) condition to male Vietnam combat veterans, with and without PTSD. Words were presented using the standard card presentation: for each condition, five words are presented in five different colours and each is repeated four times on the card which therefore contains 100 words, in a quasi-random order so that words and colours do not repeat adjacently. The four classes of words were, PTSD words (related to combat in Vietnam), neutral words (matched in number of syllables and frequency of usage to the PTSD words), positive words and OCD words. In a pilot study, participants complained that following the PTSD word card, they were unable to stop thinking about these words while trying to continue; for this reason, and so that any possible practice effects ran in the opposite direction to hypothesised interference effects, the cards were presented in a fixed order: control, neutral, positive, OCD, PTSD. These principles have been applied to the current study for the same reasons. Interference effects are calculated by subtracting the time to complete the colour naming of words on the control card from time taken on each target card. Veterans with PTSD took significantly longer to colour-name PTSD related words relative to other word classes and this effect was specific to those with PTSD, rather than to combat exposure. This study was replicated by McNally, English & Lipke (1993) with similar findings. In addition, test-retest reliability (one week later) was found to be high ($r_{(22)}=0.80$, $p<.001$).

Cassiday et al (1992) used a computerised Stroop paradigm with rape victims (+/- PTSD) and non-traumatised controls. Using this method, words are presented individually on a computer monitor; this gives rise to a measure of response latency which is averaged across words of each class (and for comparison with blocked presentations of 100 words the average response latency can be multiplied x100). Rape victims with PTSD showed increased response latency for high-threat words over moderate-threat and neutral words and for moderate-threat over neutral words. Response latency correlated positively with scores on the intrusion subscale of the Impact of Event Scale (Horowitz et al., 1979), but not the avoidance subscale. While this appears to support a priming model, McLeod's (1991) review of the Stroop literature suggests priming effects are not responsible for the Stroop effect. Williams et al (1996) also review possible artefactual explanations but conclude that effects are not due to inter-item priming or repetition of items in the task. They also discount word frequency of usage or inter-category association due to practice or expertise as explanations of the Stroop phenomenon in emotional disorders.

Foa et al (1991) used an emotional Stroop paradigm with female rape victims (+/- PTSD) and a control group not exposed to trauma. Word classes used were: non-words, neutral, general threat (related to physical harm and death) and specific threat (related to rape). Only the women with PTSD showed increased response latency and this was to rape-related words. Interestingly, one of the neutral words presented was GRAPE; the response latency for this word in the PTSD group was equivalent to the word RAPE. These findings again suggest that the effect is associated specifically with PTSD rather than experience of trauma. In relation to the priming account (already considered above), Foa et al (1991) suggests two additional explanations. First, that threat words may elicit defensive avoidance reactions which then make demands on cognitive resources which compete for capacity required for colour naming. Second, that people with anxiety disorders have an attentional bias towards threat stimuli, based on findings from the dot-probe task (MacLeod et al., 1986): this is considered further below. This bias is presumed to result in selective allocation of cognitive resources to the threat word hence neglecting the colour naming task. However, Mogg et al (1991) failed to replicate evidence supporting the view that anxiety-related biases depend on competition for processing resources.

Vrana, Roodman & Beckham (1995) still assuming a priming account of interference, suggest that an alternative to selective attention to threat as the basis for the phenomenon could be avoidance of anxiety relevant words, hence either diverting cognitive resource away from the colour-naming task or because sensory processing of the stimulus is also avoided. They also included tests of recall and recognition memory for the three categories of Vietnam–related words used in their study. Veterans with PTSD showed greater interference to these words compared to control words and to a greater extent than veterans without PTSD. Importantly, the tests of memory showed recall and recognition advantages for the emotion words, suggesting attention, rather than avoidance, was responsible for the interference effect.

However, Kaspi et al (1995) suggested that it was still unclear whether interference was attributable to intrusiveness or simply to greater emotionality of trauma related words. They had combat veterans taking part in their Stroop study rate words for personal emotional significance. While typical interference effects were found for combat words in PTSD patients, even when positive and negative words were rated equal in magnitude on a seven-point personal emotional significance scale, positive words produced no more interference than neutral words. A control group of medical students exposed to a salient but non-traumatic stressor (they were about to take Part I of the National Medical Board Examination) did not exhibit Stroop interference.

In a review of Stroop studies in patients with anxiety and depressive disorders, Williams et al (1996) note that the size of the effect is consistently much larger in PTSD than in any other disorder; this difference is considerable, interference effects being typically an order of magnitude greater in PTSD. McNeil et al (1999) using outpatients with OCD, major depressive disorder and PTSD performing general anxiety, depression and colour Stroop tasks found that only the PTSD patients showed significantly increased latency of response – to the emotional words in the anxiety and depression tasks - even though these did not use specific trauma-related words (traumas experienced were of heterogeneous nature). These differences are apparent irrespective of presentation or response modes and Williams et al (1996) suggest that different or additional mechanisms may operate in PTSD. Indeed, Moradi et al (1999) found that children of adults with PTSD, who did not themselves suffer from PTSD, showed a significant increase in response latency to threat words relative to neutral, happy and depressed word types whereas a control group did not, but were not able to suggest a definitive explanation for this.

To summarise, response latency is increased to specific trauma-related words (but not generally emotionally valenced words) in people with PTSD but not in trauma exposed people without PTSD or in healthy controls. The effect is also resistant to malingering: professional actors could fake general slowing of response latency, but were unable to modulate their responses according to stimulus content (Buckley et al., 2003). Although these are robust findings, an understanding of the basis of this effect was incomplete and accounts were couched as "attention to threat"; the appropriateness of this is discussed further in the next section.

6.1.2.1 The dot probe paradigm: slow disengagement from threat

An alternative, apparently simpler approach, the dot probe task, had been used to investigate attention (MacLeod et al., 1986). In this paradigm, two stimuli, for example a threat word and a neutral word, appear in different locations (usually above and below the central fixation point) on a monitor screen. After offset of the stimuli, a probe (in the form of a dot) appears at one of these two locations; typically, the response time (for a button press indicating location of the probe) is faster when the probe appears in the same location, or congruent with, the threat word than when the probe appears in the location of the neutral word. Despite appearing to be a more direct assessment of attention to threat, and amenable to alternative stimuli, such as pictures, as is the Stroop paradigm, the dot probe has not succeeded in producing robust findings according to its theoretical predictions, for example, in non-clinical anxiety (Mogg et al., 2000), in children with anxiety disorders (Waters et al., 2004b), in phobia (Waters et al., 2004a), in PTSD (Bryant & Harvey, 1997) and for other forms of putatively relevant words to other disorders (e.g. eating disorders: Johansson et al., 2004). When the Stroop and dot probe tasks have been compared directly, one study (Egloff & Hock, 2003) found no effects of threat stimuli over neutral in a student population but did find moderate agreement between the two tasks, while other studies have failed to find relationships between the tasks (Mogg et al., 2000; Johansson et al., 2004). In addition, in reporting their own study and reviewing previous other studies, Johansson (2004) note that there appears to be a bias (consistently shorter response latencies) for a certain probe position, especially the upper (compared to lower) probe position. This remains unexplained.

Furthermore Koster et al (2004) point out a flaw in the procedure, which may fundamentally alter the interpretation of results from the dot probe task (and associated theories which claim cognitive bias and attention to threat e.g. Mathews et al (1997)). No version of the dot probe task previous to their experiment (with undergraduate students) had assessed the effect of having two neutral stimuli appear prior to the probe and assessing reaction times relative to those for probes congruent and incongruent to threat stimuli. If response latency is reduced by *attention to threat*, then there should be shorter response latency to a congruent threat stimulus than to an N-N (two neutral) presentation. On the other hand, if the effect is due to difficulties with *disengagement from threat*, then response latency to a location incongruent to the threat stimulus should be increased relative to the N-N presentation. In fact not only was the latter observed, but this effect was exaggerated in a high threat, compared to mild threat condition, a finding that runs counter to the previously asserted effect: that the response to a probe congruent with a threat stimulus is facilitated by attention to threat. This finding, inexplicable according to the basis of the dot probe paradigm, perhaps appears to be more reminiscent of increased Stroop interference to specifically relevant threat.

It seems therefore that the dot probe (and also Stroop: see the meta-analysis by Phaf & Kan, 2007) is about slow disengagement from threat rather than facilitated attention (cognitive biases) to threat. This is supported by a study using fMRI and ERP's to study the dot probe task which suggested that spatial attention was held more strongly to threat stimuli than to neutral or positive stimuli (Pourtois & Vuilleumier, 2006). Since the Stroop paradigm is robust and free of methodological issues, and since trauma related words in the emotional Stroop show such a differentially large response in people with PTSD, it is the paradigm used here to investigate possible differences in left and right handers to fearful stimuli after watching a fearful film.

Neuroimaging techniques have been applied in attempting to understand the neural circuitry underlying the Stroop paradigm; a full consideration of these findings is beyond the scope of this thesis, particularly as they remain inconclusive. Briefly, activation of frontal networks and anterior cingulate cortex (ACC) occurs in the Stroop task (Harrison et al., 2005) and is considered to be related to cognitive attention functions. There is functional coupling to wider networks (e.g. Peterson et al., 1999), within which not all roles are clear. While the ACC is considered to have some role in conflict situations, whether this is error monitoring, error detection, mediation of response selection (e.g. Mitchell, 2006) or allocation of attentional resources (e.g. Bush et al., 1998) remain unresolved. Different parts of the ACC appear to be involved in colour and emotional Stroop paradigms (Whalen et al., 1998; Bush et al., 1998; Davis et al., 2005; Swick & Jovanovic, 2002; Bush et al., 2000). In PTSD, the ACC shows abnormalities in structure (Abe et al., 2006) and function (Seedat et al., 2005) and appears to be dysregulated, although the implications of this remain unclear (Hopper et al., 2007). Studies using the emotional Stroop paradigm in PTSD have found decreased activation of the ACC in those with compared to those without PTSD (e.g. Lanius et al., 2003) and in women with abuse-related PTSD (Bremner et al., 2004b). Further research will be required before these relationships are fully understood.

6.1.3 Evidence for interference effects as late stage, language processing conflicts in response output

Despite this lack of clarity of the roles of cortical areas involved, some explanatory models of the Stroop effect are more successful than others in matching empirical facts derived from the Stroop paradigm. It is still common to find accounts or models which ignore incompatible empirical evidence, for example those which view the effect as due to the relative automaticity of reading (words) compared to naming colours, hence the need to inhibit a well practiced response in order to respond by colour naming the words instead (e.g. Kaplan et al., 2007). This is despite empirical evidence that this is not the case. According to this view, Stroop interference should increase as children become better at reading, and more practised. In fact, interference decreases with increasing reading skill: the youngest children and the oldest adults show greatest interference (MacLeod, 1991).

Other early views not supported by evidence are those emphasising early processing which suggest that perceptual coding of the ink colour is affected by incompatible information from the colour word and those proposing general response competition in relative speed of processing of the two potential responses from word reading and colour naming processes (MacLeod, 1991).

In contrast to these sequential models of processing, MacLeod (1991) suggests that a PDP (parallel distributed processing) model (Cohen et al., 1990) shows greater promise in accounting for the colour Stroop interference effect; in PDP accounts attention is accorded a role but not privileged status. Adjustments of weights in the network between attention, colour-identification and word reading modules can replicate Stroop effects with interference emerging from interactions between modules representing different forms of information. Any model which attempts to explain the Stroop paradigm should be capable of explaining both the interference effects in the colour Stroop (and its variants) and the particular effects seen in the emotional Stroop paradigm in PTSD. Williams et al (1996) consider how well the PDP model may apply to emotional Stroop phenomena in clinical disorders, but this approach is still based on the idea of attention to threat and the model is still found to be incomplete. For example, the PDP model still relies in large part on automaticity in reading through practise; Williams et al (1996) point out that subsequent to therapy, which may involve extensive practise with relevant stimuli, interference effects can be reduced, rather than increased as the model would suggest.

Roelofs & Hagoort (2002) using the colour Stroop paradigm as prototype task of willed control of language use, compare two connectionist models of control in naming and reading which assume different roles for the ACC and relate them to empirical findings in the Stroop literature and to emerging neuroimaging findings in relation to ACC. They make the same point about assumptions of automaticity in respect of one model, GRAIN, (which assumes automaticity in reading compared to naming and a conflict monitoring role for the ACC). The other model, WEAVER++, is based on processing intentions among representations within language production architecture, which involves a hierarchy of stages: perception of colour, conceptual identification and lemma retrieval, actual word form encoding and articulation and overt speech. The model suggests that the perception of the word (separately from its colour) also engages lemma retrieval and word form encoding and that it is at this stage that conflicts (and interference effects) occur and are resolved by either input control (suppressing inputs from perceptual channels with respect to the word – possibly ACC function) or goal control (ensuring that the correct response is made for the task demanded – possibly dlPFC function). Differences in interference in children and older people (as mentioned above) are accounted for by strengthening and weakening of these control structures over the lifespan.

While neuroimaging evidence remains incompletely understood in relation to Stroop paradigms, evidence from ERP studies has been helpful in assessing such models. ERP's (event related potentials to a stimulus) are waveforms of neuronal activity recorded at scalp locations; latency of positive (P) and negative (N) waveforms indicates the time course of stages of neuronal processing, while an increase in amplitude of the waveform is thought to indicate the intensity of engagement of processing (Springer & Deutsch, 1981; Luck et al., 2000). While they lack the spatial resolution of neuroimaging techniques, ERP's provide temporal specificity. In response to Stroop tasks, early components (P1-N1-P2-N2) are thought to be indicative of early sensory processing and later components, including marked positive slow wave, thought to be indicative of language processing (Pérez-Edgar & Fox, 2003).

Consistent with the dominant role of the left hemisphere in language processing, ERP studies of the Stroop effect observe greater activity related to interference in the left than the right hemisphere (Roelofs & Hagoort, 2002). When hemifield presentations of emotional Stroop stimuli are considered, LVF presentations (to the contralateral right hemisphere) result in increased interference effects, particularly to negative words, suggesting that interference effects in the emotional Stroop *arise* in the right hemisphere (van Strien & Valstar, 2004; Borkenau & Mauer, 2006).

On an emotional Stroop task in children, ERP's differentiated effects of negative words in the absence of a behavioural, reaction time, interference effect. In the early response complex, negative words showed shorter latencies in the right hemisphere; for the positive slow wave, negative words had the largest mean amplitude (reflecting the amount of processing resources allocated to the task) and this was greater in the left hemisphere (Pérez-Edgar & Fox, 2003). Other ERP studies have found increased amplitude of early components in the right hemisphere to aversive stimuli (Simon-Thomas et al., 2005) and there was also evidence of attenuated transfer of visual information across the corpus callosum from aversive stimuli presented to the left hemisphere. (Interhemispheric interactions will be considered further below in section 6.1.5 considering possible differences between left and right handers.) A study of ERP's to trauma-related Stroop stimuli in PTSD concluded that interference does not occur during the early stages of processing (Metzger et al., 1997). Roelofs & Hagoort's (2002) assessment of the WEAVER++ model suggests that the Stroop conflict arises in planning the target word in left perisylvian cortex which includes Wernicke's and Broca's areas. Indeed Stroop (1935) postulated that interference occurred due to word meaning accessed during the response stage of processing. This is consistent with other evidence.

Thomas et al (2007) found that interference in an emotional Stroop was associated with late ERP's which could be indicative of the verbal response stage in the Stroop task; Atkinson et al (2003) came to a similar conclusion in respect of the colour Stroop. In addition, Jiacheng et al (2007) found that interference in a Chinese Stroop, where the right hemisphere is predominant for Chinese logographs, found that the upper right cortex was associated with Stroop interference. Together this evidence is consistent with preferential and early right hemisphere activation in response to fear, not related to reaction time responses, and suggests that left hemisphere language processing stages are where the Stroop interference happens. If this is the case, this may make sense of the extraordinarily large interference effect in people with PTSD, where a fear response is known to selectively activate the right hemisphere and deleteriously affect language processing (e.g. Rauch et al., 1996); in the emotional Stroop, this may further compromise language processing in the output stage and thus delay the response still further in comparison to people without PTSD who are not fear conditioned to the threat words, or at least not to the same extent.

6.1.4 A rationale for Stroop effects relevant to PTSD

While early models (of the emotional Stroop and dot probe) discussed above suggested that selective attention to threat was a feature of high and clinically anxious individuals, it is apparent that attending to threat is of evolutionary importance in ensuring survival in everyone. As early as 1993, Fox (1993) using a modification of the Stroop task reported results inconsistent with the attention to threat hypothesis; she found that threatening stimuli outside the focus of attention produced interference.

Selective attention, in the cognitive sense, assigned to higher cortex, is suggested to allocate resources to attend to task relevant stimuli (at the expense of any competing stimuli) in pursuing goal directed behaviour. However, Armony & LeDoux (2000) point out that if this is unconditional, selective attention is deleterious in threat or danger situations: the organism needs to (and does) respond to potential sources of danger that lie *outside of* attention. There needs to be some form of *attention independent* channel to detect sources of danger, and Armony & LeDoux (2000) suggest that the direct thalamo-amygdala pathway is the mechanism by which threat is detected by the amygdala outside of attention. Since the amygdala has back projections to early sensory processing areas, it can then control the sensory inputs it receives and the processing occurring in these areas via arousal mechanisms and thus has the capacity to affect ongoing cognitive responses.

Armony & LeDoux (2000) extended the connectionist model of Cohen et al (1990) and the resulting network was capable of simulating Stroop interference in response to threat stimuli. Parallel processing streams representing different aspects of the environment (in this case, colour naming and word reading) were set up to compete for processing resources; selective attention units were set to bias one over the other according to where attention is allocated, but with the thalamo-amygdala pathway not subject to attentional bias. The outputs from the network derived from competition between the cognitive responses, but could be interrupted by the amygdala response, reflecting observations that when a stimulus has acquired strong negative value through fear conditioning (memory for which is stored in the amygdala) the consequent fear reaction can disrupt the ongoing (cognitive) behaviour. This is consistent with findings that linguistic representations of threat are sufficient to activate the amygdala (Isenberg et al., 1999) and that a manipulation of spatial attention to fearful/neutral faces, capable of altering activation of the fusiform gyrus (areas involved in face processing) did not affect amygdala activation to the fearful faces (Vuilleumier et al., 2001).

This also suggests that even though participants in the Stroop paradigm are instructed to ignore the words and focus only on the colours (which they are to name) they are unable to do so, resulting in memory advantages for the emotional words of the task (Vrana et al., 1995). To test that this is the case, and whether there are differences between left and right handers, a memory (recognition) test was included within the experiments presented here and findings are presented after those from the Stroop paradigm itself. Such a test also checks whether participants have simply blurred their vision in order to only see the colours rather than the words in order to perform the task quickly.

In summary then, the best current models, consistent with empirical evidence in the colour and emotional Stroop literature, emerging neuroimaging findings and results of ERP studies, suggest that threat stimuli are detected outside of (cognitive) attention by the amygdala with consequent early right hemisphere activation which is not in itself related to behavioural responses; interference effects appear to be related to later activity in regions associated with language processing (in the left hemisphere for western languages). These latter effects occur for both colour and emotional Stroop but are augmented by threat stimuli.

The emotional Stroop task thus seems appropriate in investigating possible differences in left and right handers.

6.1.5 Studies of the Stroop effect in left handers

It is not apparent that studies mentioned in MacLeod's (1991) review have considered handedness in relation to the Stroop effect. An experiment using the colour Stroop paradigm with left and right handers (Christman, 2001) showed that left handers showed increased Stroop interference compared to right handers to centrally presented stimuli (but not to RVF/LVF presentations). This procedure used congruent and incongruent stimuli as normal, but also used neutral stimuli which "consisted of a series of X's" (p108). Interference effects were calculated by subtracting neutral from incongruent trials rather than the normal procedure of incongruent minus congruent. Any implications of this change to the normal procedure are unclear. In a same-different task, using only the congruent and incongruent stimuli (where participants were required to make a judgement of same/different to pairs of words) there was a main effect of decision (same faster than different) but no main effect of handedness. The two tasks are therefore not actually comparable due to using neutral stimuli in calculating interference effects.

The thrust of Christman's (2001) hypotheses and explanatory account is around interhemispheric interaction in processing of bidimensional stimuli. He makes several assumptions which warrant further consideration. One of his fundamental assumptions in using the colour Stroop task is that while the left hemisphere has control over reading (and speech as in naming of colours) colour perception is lateralised to the right hemisphere: the experimental procedure uses a manual key press response in an attempt to ensure right hemisphere processing of the colour dimension. However, Grimshaw (1998) challenges the assumption of right hemisphere specialisation for colour perception. Indeed, the Stroop effect generalises to other analogues not involving colour (MacLeod, 1991) such as numerosity (Whalen et al., 2006) and it seems unlikely that all of these features are lateralised to the right hemisphere. In addition, models of language processing in Stroop paradigms (such as WEAVER++ considered above) suggest that perception of colour also engages the relevant lemma for colour, that is, perception cannot be isolated from associated lemma generation as Christman (2001) suggests.

Christman (2001) suggests that interhemispheric processing may differ in left and right handers. This is based on findings of a larger corpus callosum in left handers (Witelson, 1985; Witelson, 1989) and lesser degrees of hemispheric asymmetry in left handers. As a group, left handers are a more heterogeneous group than right handers at least in respect of language lateralisation. However, assumptions that an increase in corpus callosum size is indicative of more nerve fibres is not justified (Banich, 1995): there is an absence of correlation between size and number of fibres at least in the rat and rhesus monkey. Banich (1995) also points out that relationships between size of the callosum and function are not clear: in different populations, size is hypothesised to have opposite effects on function.

Banich (1995) suggests there are cases where interpretations of size of callosum is less ambiguous, such as in multiple sclerosis patients, where demyelination may be reliably associated with decreased density of the corpus callosum, at least longitudinally. Myelination of the corpus callosum occurs progressively from early childhood through to early teens (Banich, 1998) so that interhemispheric interaction may increase with age as a result. Stroop interference effects in children, mentioned above, are greatest in the youngest children (with least interhemispheric interaction). This appears consistent with Christman's (2001) hypotheses, but on the other hand, in split brain patients, with no interhemispheric transfer via the corpus callosum, and patients with corpus callosum agenesis, the Stroop interference effect is reduced or absent (Banich, 1998). These findings suggest any relations between the corpus callosum and interhemispheric interactions are likely to be complex, as described by Banich (1995).

Grimshaw (1998) similarly questions Christman's (2001) assumptions and her own series of experiments first identified in the participating left and right handers which hemispheres apparently process words (linguistic, generally left hemisphere processes) and prosody (generally right hemispheres processes) prior to a Stroop analogue task and an integration task similar to Christman's (2001) same-different task. She found that complementarity (whether individuals process the two dimensions in opposite or the same hemispheres) was not related to Stroop interference effects in any way. She also found, contrary to Christman (2001), that left and right handers did not differ on either the interference or integration tasks according to handedness.

Further studies using Stroop tasks by Christman and colleagues (Christman & Garvey, 2003; Christman, 2004) have used right handers only or compared strong right and mixed handers respectively. Both studies invoke the same explanatory mechanisms in relation to interhemispheric interference. Comparisons of strong and weak handers raise other methodological difficulties which are considered in Appendix 20.

To summarise, two studies of handedness in relation to Stroop interference (Christman, 2001; Grimshaw, 1998) show mixed results and evidence in respect of the role of interhemispheric interaction seems more complex than supposed by Christman (2001). Neither of these Stroop studies used an emotional Stroop task. The experiment described here sets out to investigate possible differences in Stroop interference on an emotional Stroop paradigm in left and right handers.

6.1.6 The current study: rationale and hypotheses

In left handers the dominant hemisphere, at least for motor control, is the right hemisphere. If this is preferentially activated in left handers, then responses to fearful stimuli may be exaggerated in left compared to right handers; indeed Tomarken et al (1990) found that in healthy females, asymmetry (increased in right hemisphere) of resting alpha wave (in EEG) predicted subsequent fearful responses to films. If the fear response activates the right hemisphere and deleteriously affects language processing (e.g. Rauch et al., 1996) this may be an exaggerated effect in left handers.

The experiment presented here sets out to test the hypothesis that there will be increased interference effects observed in left compared to right handers in an emotional Stroop paradigm. An effect on an emotional Stroop paradigm is not normally evident in healthy populations. By using a fearful film as a laboratory analogue of fear, it is hypothesised that this will engage fear mechanisms similar to those involved in PTSD with the potential to produce an interference effect.

The film excerpt used has been described in Chapter 5 and has been previously used (in a shorter version) by Gross & Levenson (1995) for the target emotion of fear. In a previous study in right-handed subjects (Choudhary, 2004) significantly higher self-report ratings of fear (by males and females) were made in response to this film compared to a control film. Since interference effects are to trauma-specific words in PTSD, the target condition here is the film-related words.

While some recent research (van Honk et al., 1998; 1999; 2000) has attempted to use more ecologically relevant stimuli than words in an emotional Stroop task of angry faces by using photos prepared as slides and coloured by placing a transparent coloured folio in front of the picture in the slide frame, it would appear that other non-verbal techniques have not been used. As people with PTSD appear to have deficits in processing verbal material, a non-verbal version of the Stroop task, but similar in form was devised using text-like wingdings (a font type available in MS Word) to compare with the standard word Stroop task. In order to control for effects of viewing the film, three different versions, or protocols, of the experimental procedure were devised, and rationales are considered for each protocol separately below. The main hypotheses are:

Hypothesis 1: Left handers will show an increased interference effect specifically to film-related words compared to right handers after watching a fearful film.

Hypothesis 2: If word processing is an important component of the interference effect, any interference will be greater to verbal than to non-verbal stimuli.

Sex differences in performance of colour Stroop tasks have not been found (MacLeod, 1991). There are differences in prevalence of PTSD in men and women, so it is unclear whether a sex difference for an emotional Stroop task will be evident; however, the null hypothesis is tested.

Hypothesis 3: There will be no sex differences in interference effects.

Hypothesis 4 considers results from the recognition test for the words used - the Stroop Word Recognition Task: SWRT. This can only be investigated in participants recruited to the standard and control protocols; the reversed protocol only uses the word Stroop in part two, precluding this test. This test also checks that participants have not adopted a strategy of blurring their vision to avoid seeing the words in order to complete the task more easily.

Hypothesis 4a: The words used in the Stroop task will be processed, despite instructions to ignore them, and subsequently remembered in a recognition test of memory. This effect is hypothesised to be greatest for the film-related words, but not in the control group who do not view the film.

Hypothesis 4b: There are no clear predictions as to possible effects of handedness. If left handers show greater Stroop interference than right handers due to increased processing of the material they may show greater recognition memory; on the other hand, the work presented in Chapter 5 suggests left handers show poorer memory for verbal material than right handers. On balance, it is hypothesised that there will be no differences between left and right handers in recognition memory on the SWRT.

6.2 Methods

6.2.1 Participants

Participants were volunteers, primarily recruited from the psychology undergraduate subject panel for course credit, although postgraduates and staff also volunteered. Participants were offered cash in payment for their time if they did not require course credit. Since the majority of students in the psychology department are female, and only approximately 10% of the population is left handed, recruitment was augmented by appeals through posters and the University's home portal log-in page particularly for males and left handers, drawing on the whole university population. Each protocol of the procedure (*qv*) aimed to recruit 20 left and right handed males and females (total n=80).

6.2.2 Apparatus

The film excerpt, recorded on a DVD, was presented on a HP Compaq nx9010 Pentium 4 laptop, running Windows XP, using Windows Media Player (Version 9 series) and fitted with digital stereo headphones. A Solex digital stopwatch was used for timing the colour naming of Stroop cards.

A Sony cassette recorder (TCM-939) was used to record participants' free recall of the film storyline and events.

6.2.3 Materials

Three standard instruments were used: The Posttraumatic Diagnostic Scale (PDS; Foa et al (1997)) (see Appendix 1); the combined Edinburgh Handedness Inventory (Oldfield, 1971) / Coren lateral preference inventory (Coren et al., 1979) which included additional questions about parental handedness for writing (see Appendix 2) and the PSS10 (Cohen & Williamson, 1988) (see Appendix 3). These have been described in Chapter 2.

Preparation of the film excerpt has been described in Chapter 5. The associated Emotion Rating form was completed after watching the film (see Appendix 4). Subjects indicated how strongly they felt each of the negative emotions (anger, fear, disgust and sadness) during the film, using 10 point Likert rating scales, and also responded on an overall measure of tense emotional arousal.

There were two Stroop tasks used, a word based task, and a novel task using wingdings in place of words. Both were prepared on A4 size white paper and laminated for durability before being comb bound as a booklet; plain pages interleaved between the coloured stimuli pages, so that the content of each following page did not intrude through a see through effect.

The word Stroop task consisted of six white cards presented in a fixed order (practice, control (OOOOO), neutral, positive, negative, film) so that any practice effects ran counter to hypothesized interference effects and to prevent possible reactions to film-related words affecting subsequent sets. The practice set contained six rows of five words; the task cards contained 100 words arranged in 20 rows of five words (see Appendix 5). Each task card contained one set of five words each appearing twenty times, four times in each colour, pseudo-randomly organized so that the same word or colour did not occur in succession.

Other studies have used uppercase letters in presenting the words, but as words in lowercase are easier to read, they were used here in order to maximize any interference effects. The stimuli sets were created using MS Word 2002. Text was left justified, at 1.5 line spacing in Times New Roman font, size 20, using five font colours: red, blue, green, light orange and a purple selected from the 'more colours' font colour drop-down menu (RGB (204, 102, 255)) and were printed out using a Canon i9100 colour inkjet printer. Participants were not instructed to use a particular name for a colour but to be consistent in response to a colour. All named red, blue and green as such but names in response to the orange colour included orange, gold and yellow, and to the purple colour included purple, lilac, violet, pink and magenta.

A pilot study was conducted to identify a set of five film-related words (shouts, darkness, basement, doors, railway) for use in this study (see Appendix 21). A set of neutral words (lifts, inclined, milk, manage, network) was matched to them by word frequency using on online database (Kilgarriff, 1997 - unlemmatised lists). No words were colour related, for example, strawberry would be associated with the colour red, as this can affect interference in colour naming (MacLeod, 1991). Other sets of words were taken from previous studies. Positive words (love, pleasant, loyal happy and friendship) and neutral words (mix, millionaire, fingertips, concrete, input) matched in number of syllables and frequency in usage (of American English) to them were used in three previous studies of the emotional Stroop in PTSD (McNally et al., 1993; McNally et al., 1990; Cassiday et al., 1992). Their neutral words were used as practice stimuli here. Negative words (cancer, funeral, hate, disease, coffin) were chosen from ten used by Foa et al (1991); of the five not chosen, anxiety, stress, guilt and panic were considered to be possibly also relevant to the film excerpt; the remaining two words were similar (tumour and cancer) and the latter was chosen.

A test of memory (SWRT: Stroop Word Recognition Test, Appendix 7) was constructed for the 25 words used in the Stroop task. An additional 75 words were added for the test: 15 valenced distracters (5 each, positive, negative, film); 30 matched neutral words (by frequency and word use: Kilgarriff, 1997) to these and the valenced Stroop words; 30 additional neutral words as fillers (3 matched to each Stroop practice and neutral word) to produce a list of 100 words. The order of the 100 words was randomised, with the proviso that no target word (from the Stroop task) immediately followed another target word. The test was presented to the participant for self-completion, with instructions to indicate YES/NO whether they remembered the word from the Stroop task.

The valenced distracters were chosen as follows. A thesaurus (Dutch, 1966) was used to generate five positive words similar in meaning to the first. Additional negative words were chosen from the general threat and rape-related sets of words used by Foa et al (1991) excluding any that could also be associated with the film (such as ‘trapped’). For the film words, the five next best remembered film words from the pilot study were used.

6.2.4 Procedure

This was a two part study, and the experimental procedure used three different protocols: standard, reversed and control. The standard protocol will be described prior to the rationale for, and changes in, the other protocols.

Study information for recruitment indicated that the study was investigating attention in right and left handers, so as not to prime participants for any of the memory components of the study. To meet ethical requirements, on presentation for the study, and before signing a consent form, participants read an information sheet which specifically drawing their attention to the fact that they were to watch a film rated 18, and while not explicit about content, indicated it was not violent or pornographic in nature. They were also informed that they were free to leave the experiment at any time should they wish; no participant did so.

Participants first completed the PSS10 and the Handedness Inventory, and palmar surfaces of both hands were scanned (for 2D:4D ratios: see Chapter 7). The film was viewed on a laptop, as described in Chapter 5, and immediately afterwards participants completed the rating of subjective emotion (Emotion Rating Sheet: Appendix 4).

The Stroop task immediately followed. Participants were shown the practice set and instructed that they should go through the list of words, as if reading from left to right, but to ignore the words and focus only on the colour of the ink in which each word was printed, naming aloud each colour, as quickly as they could, but trying not to make errors. No test of colour blindness was included but no participant failed to correctly differentiate the colours on the practice set of words. After the practice set and a check made to establish that the participant was comfortable with the requirements of the task, each successive card was presented and timed by the experimenter who followed the participant's performance on colour naming with the correct list of the 100 colour names; any errors made were recorded by the experimenter on the same recording sheet as were times for completion of each card. Since errors did not frequently occur they were not considered further.

Finally, participants filled in the PDS. This concluded the end of part 1 and participants were told that they would return the following week to complete another colour naming task.

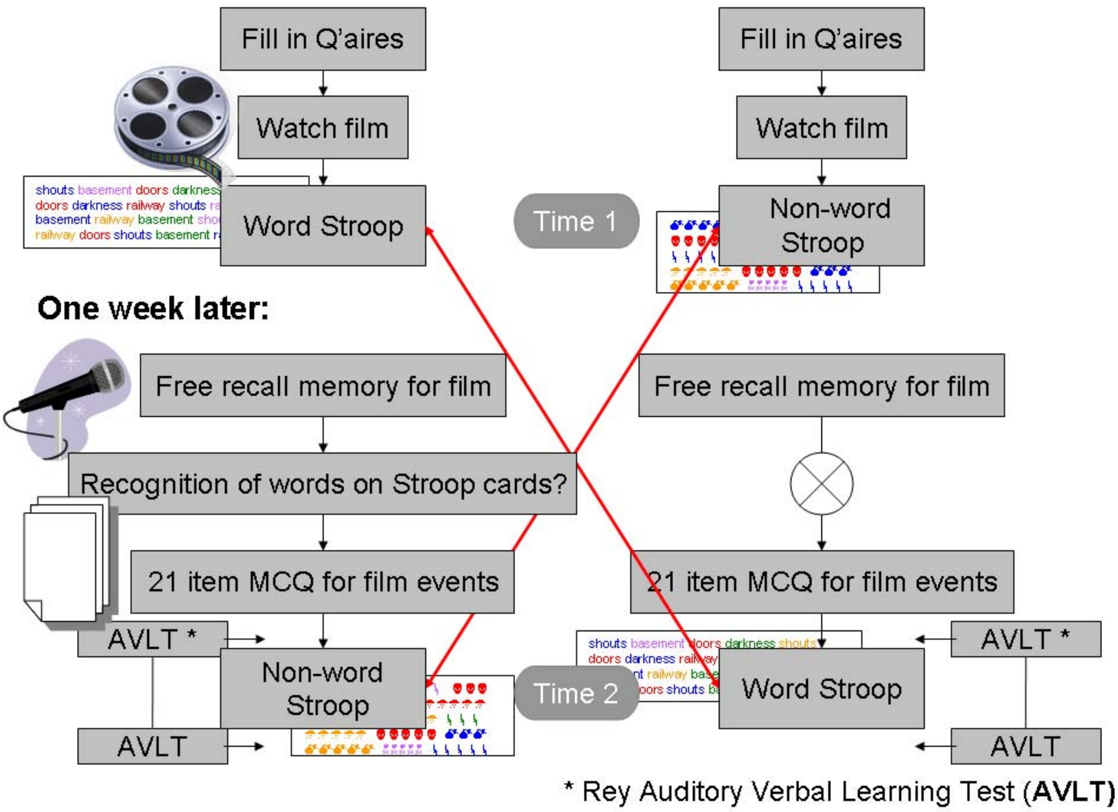
Seven days later participants returned for part 2. Participants were first asked to remember back to the film they had watched the previous week and to try and remember as much as they could about the storyline and any associated details; they were informed that what they said was going to be recorded. The experimenter started the tape recorder and participants allowed to recall freely and uninterrupted, until they indicated they had finished, when the recording was stopped.

Participants then completed other memory tests. First, they were asked to remember back to the booklet of coloured words they had seen the week before, and were reminded that they had been asked to ignore the words. They were then asked to complete the SWRT indicating "yes" if they thought they recognised a word as having appeared anywhere on that list, and "no" if they did not recognise the word. After this they completed the MCQ for the film.

The immediate recall trials of the AVLT were completed prior to the non-word Stroop task which was introduced in the same way as the word-based Stroop in part 1. The delayed recall and recognition trials of the AVLT concluded the procedure and participants were debriefed.

This protocol (hereon, the standard protocol) was designed to test the hypothesis that after watching a fearful film left handers (compared to right handers) would show increased interference effects for film related words (Hypothesis 1). However, if an interference effect is evident, it is important to check whether this is associated with the film or occurs independently of it. This control check was done by using two additional protocols.

Figure 6.1 Flowchart of procedure for standard (left below) and reversed (right below) protocols; arrows indicate the crossover of the two Stroop tasks.



The reversed protocol was designed to control for order effects of seeing the film on the two Stroop tasks, by having participants complete the non-word Stroop task immediately after watching the film and the word Stroop at time2, one week later (producing a between subjects comparison with the standard protocol). This precluded participants completing the SWRT at time2. A flowchart outlining the main features (omitting details of the questionnaires and the PDS at the end of part 1) of the standard and reversed protocols is shown in Figure 6.1 above; the arrows indicate the crossover of the two Stroop tasks.

Despite controlling for order effects, it is still possible that any interference effects occur independently of the film: there may be underlying differences between left and right handers *irrespective* of watching a fearful film. For this reason a control protocol was included that omitted the film. It did not prove possible to recruit complete samples to this protocol (see results section 6.3.2.3 below). Since the film was omitted, the free recall and MCQ memory tests were precluded, although the SWRT could be completed as the protocol otherwise followed the standard protocol.

6.2.5 Design and analysis

In all ANOVAs Greenhouse-Geisser corrections were applied.

Hypothesis 1

For each protocol, a 4x2 (stimulus type x handedness) repeated measure ANOVA was conducted to determine any interference effects (of stimulus type - neutral/positive/negative/film - over baseline control card) and effects of handedness. An *a priori* hypothesis predicting increased interference to film words specifically in left handers was tested for the word Stroop by one-tailed t-tests, since directionality was hypothesised.

Hypothesis 2

A 3x3 (stimulus type x protocol) repeated measure ANOVA was conducted to determine any interference effects (of stimulus type - neutral/positive/negative - over baseline control card) for the non-word task.

A 3x2 (stimulus type x handedness) repeated measure ANOVAs tested whether interference effects were different in left and right handers.

Across the two Stroop tasks, hypothesis 2 predicted greater interference for the word compared to the non-word stimuli. Since the two tasks do not have exactly corresponding sets of stimuli (there is no film related equivalent in the non-word task), for each corresponding stimulus type (neutral/positive negative) paired t-tests between word and non-word tasks were performed for interference effects.

Hypothesis 3

4word/3non-word x2 (stimulus type x sex) repeated measure ANOVAs tested for sex difference in interference effects for the two Stroop tasks.

Hypothesis 4

A 5x2x2 (word type – practice[‡]/neutral[‡]/positive/negative/film – by protocol by word status –target/distracter) repeated measure ANOVA tested for differences in recognition of target and distracter words in the two protocols which differed in respect of viewing the fearful film. 5x2x2 (word type by word status - target/distracter - by handedness) and 5x2x2 (word type by protocol by handedness) repeated measures ANOVAs tested

[‡] Since there were 60 neutral filler items (matched to the various other word sets in frequency of usage) but only 5 of each type of all the other distracter words, scores out of 60 for neutral distracter words were divided by 12 to produce a score equivalent to that of the other distracter sets of words. This score was used for comparison with both practice and neutral words.

for differences between left and right handers in recognition memory for the targets/distracters and according to protocol respectively.

6.2.6 Ethics

Ethical approval for this study was obtained from the Department of Psychology Ethics Committee (see Appendix 23). The ethical issues relevant to this study have been discussed above (in section 6.2.4) in relation to the procedure adopted for the study reported here and for the memory tasks reported in Chapter 5.2.

6.3 Results

6.3.1 The sample

Two individuals were excluded from the study, both in the control protocol: one was a male (control protocol) who laughed all the way through his attempt at the Stroop colour naming tasks and one female (control protocol) who had difficulty with the Stroop tasks and by observation and her own spontaneous admission was badly hung-over, and possibly still under the effects of alcohol.

Six individuals of the remaining 215 (2.8% of the whole sample) reported being made to change the hand used for writing, all in the direction of left to right. Of these, two females were in the standard protocol; one had badly broken her left arm and subsequently learned to use her right, and the other was made to change for cultural reasons. Four males had been forced to change, one in the control protocol was made to change by teachers and the three others (one in reversed and two in control protocols) did not specify a reason for the change. These six individuals were excluded from all analysis considering the possible effects of handedness (leaving a sample size of 209), but were retained for analysis considering sex differences.

There is a robust interference effect on an emotional Stroop in people with PTSD to trauma specific words but the Stroop task used here did not include such words. Nevertheless, all participants were screened for possible PTSD using the self-report PDS and chi squared tests were performed to check that (1) left and right handers, (2) males and females and (3) the three experimental protocols did not contain different proportions of people with possible PTSD. All results were non significant, so it was not felt necessary to exclude these individuals from the analysis, and in order to retain sample sizes for power considerations.

This was a two part experiment. Inevitably some participants (n=14; 6.7%) did not return for Part 2; their data for Part 1 were retained and included in the analysis; sample sizes therefore vary in some of the following reporting of results. Each of the three protocols was intended to recruit 20 right and 20 left handers of each sex, making a total of 80; despite running for 5 semesters (the maximum possible during the timeline of this research project) the full complement of left handers, particularly male left handers were was not recruited. This reflects the greater proportion of female psychology undergraduates forming the subject pool which was the prime source of participants and the fact that only 10% of the population is left handed. A summary of the sample sizes achieved for each protocol is given in Table 6.1 below. The distribution of participants across experimental protocols is significantly different for both handedness [$\chi^2_{(209)}$=10.937, p=.004] and sex [$\chi^2_{(209)}$=6.920, p=.031] as it was particularly difficult to recruit males and left handers and, indeed, there were no male left handers recruited to the third, control, protocol.

The mean age of the total sample was 22.93 years (SD ±7.15) and ranged from 17 years 4 months to 62 years 0 months. There was no significant difference in age between males and females, but an independent samples t-test (with unequal variances) showed that the left handed sample was significantly older and had a higher standard deviation from the mean (24.4 years ± 8.9) than the right handed sample (21.9 years ± 5.3) [$t_{(129.462)}$=2.276, p=.024]. This reflects the wider sourcing of left handed participants than from psychology undergraduates.

Table 6.1 Distribution of total sample for handedness analyses (n=209) across protocols (part samples - no Part 2 – also indicated)

Protocol	*sex*	*right*		*left*		*Total*
		Part1	*Part2*	*Part1*	*Part2*	*no part 2*
Standard	male	20	20	24	21	3
	female	21	19	22	21	4
	totals	***41***	***39***	***46***	***42***	
Reversed	male	20	19	7	6	2
	female	21	19	21	21	2
	totals	***41***	***38***	***28***	***27***	
Control	male	15	14	0	0	1
	female	25	22	13	13	3
	totals	***40***	***36***	***13***	***13***	
Totals		122	113	87	82	14

6.3.2 Hypothesis 1: interference effects in left and right handers

Interference effects were calculated by subtracting the time to complete the control card from each of the other cards. Results are considered separately for each protocol.

6.3.2.1 The word-based Stroop immediately after watching the film (Standard protocol)

The 4x2 (word type over baseline x handedness) repeated measures ANOVA showed a highly significant main effect for type of word [$F_{(2.720,231.220)}$=44.208, p<.001] and a between subjects main effect of handedness which just reached significance [$F_{(1,85)}$=3.947, p=.050] with left handers showing greater interference overall than right handers. The main effect of word type indicates that there were interference effects present, even though these are not usually found in an emotional Stroop task in healthy samples. That the effect was greater in left handers supports the predictions of Hypothesis 1.

Since there was a main effect of word type, a series of paired t-tests were conducted between word types to determine where interference effects were significantly different. All were found to be significantly different to one another, but Bonferroni correction for multiple comparisons (.05/6 for 6 comparisons produces a critical value of p=.0083) was applied. Interference on neutral words was significantly different to all others (all p<.001), on negative significantly different to positive (p<.001) but differences between interference on film words and positive (p=.011) and negative (p=.009) words do not survive correction.

A priori analysis by 1-tailed independent t-test for handedness related differences for film words showed left handers showed significantly greater interference to these words than right handers [$t_{(85)}$=1.888, p=.031]. Since there was a significant main effect of handedness, a 1-tailed independent sample t-test was also performed in respect of the negative words and was significant [$t_{(85)}$=1.988, p=.025]; left handers showed significantly greater interference than right handers for the negative words also. The pattern of interference effects for word type is shown in the left hand graph in Figure

6.2 below. These findings support hypothesis 1 in respect of film words, and in addition find a significantly greater interference effect for negative words in left handers compared to right handers.

6.3.2.2 The word-based Stroop at time2: after completing memory tasks and one week after watching the film (Reversed protocol)

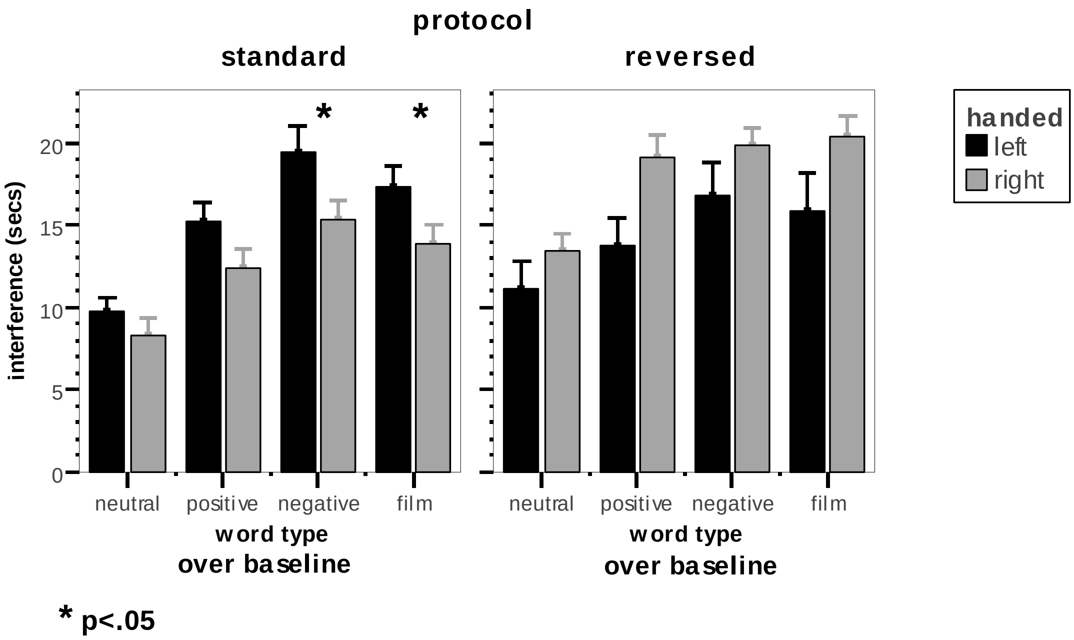
The 4x2 (word type over baseline x handedness) repeated measures ANOVA again showed a highly significant main effect for type of word [$F_{(2.558,161.157)}$=28.958, p<.001] and a between subjects main effect of handedness which just escaped significance [$F_{(1,63)}$=3.781, =.056] but compared to the standard protocol, interference effects were reversed: at time2 the right handers showed greater interference overall than left handers.

Since there was a main effect of word type, a series of paired t-tests were conducted between word types to determine where interference effects were significantly different. All were found to be significantly different to one another, except for film and neutral words (p=.942). After Bonferroni corrections, interference on neutral words remained significantly different to all others (all p<.001), but positive words did not remain significantly different to negative (p=.023) or film words (p=.043).

A priori analysis by independent t-test for handedness related differences in the film-related words showed a trend for right handers to show higher interference to these words than left handers [$t_{(63)}$= -1.731, p=.091]. An independent sample t-test was also performed in respect of the negative words but failed to reach significance [$t_{(63)}$= -1.431, p=.157]. The pattern of interference effects for word type is shown in the right hand graph in Figure 6.2 below. A 2x2 (protocol x handed) repeated measures

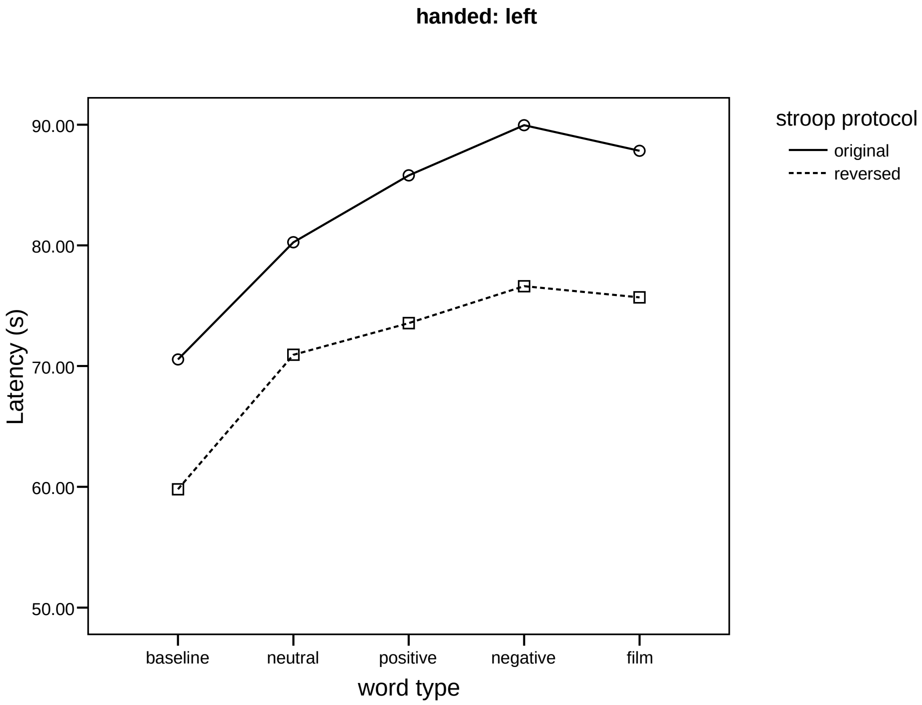
ANOVA showed this to be a significant interaction between protocol and handedness [$F_{(1,148)}$=7.828, p=.006]: left and right handers produced different interference effects according to protocol.

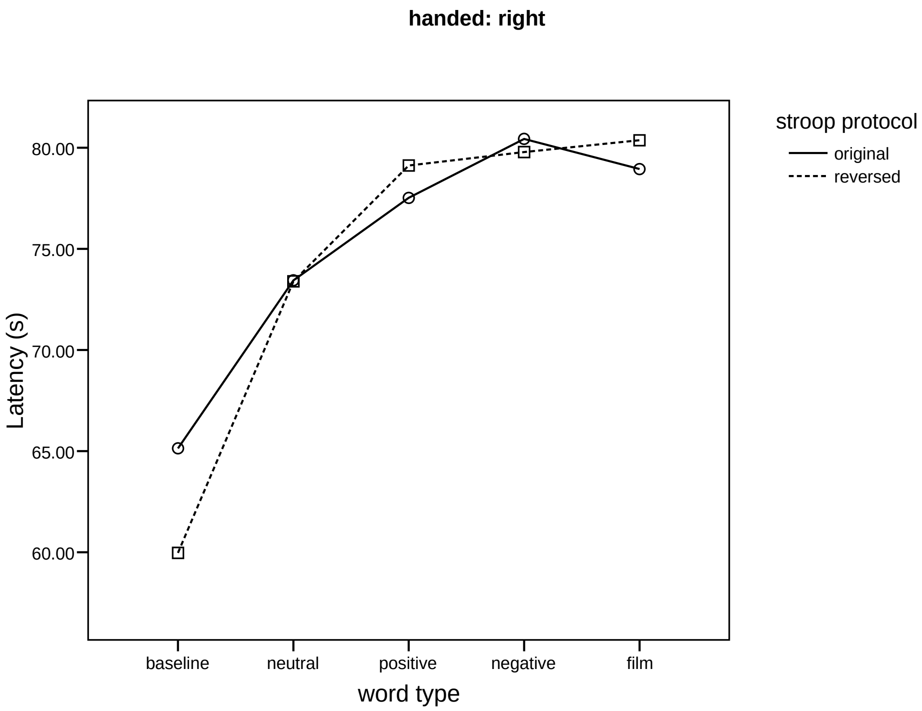
Figure 6.2 Mean interference effects on the word based Stroop immediately after watching the film (standard protocol, below left: main effect of handedness: p=.05) and when performed one week after watching the film (reversed protocol, below right); interaction between protocol and handedness is highly significant (p=.006). Error bars show mean +/- 1.0 SE.



To investigate these differences further, the response latency (the actual times taken to complete each card) of left and right handers was also compared across the two protocols. 5x2 (word type x protocol) repeated measures ANOVAs conducted separately for left and right handers showed a highly significant effect of protocol for left handers [$F_{(1,71)}$=12.647, p=.001], but performance of right handers on the two protocols was not significantly different [$F_{(1,77)}$=.045, p=.833]. Figure 6.3 below shows the performance of left and right handers for each protocol.

Figure 6.3 Response latency for word stimuli in standard and reversed protocols for left handers (top graph) and right handers (bottom graph)





Taken together these results suggest that increased response latencies in left handers occur in relation to watching the fearful film, rather than reflecting underlying differences between left and right handers and are supportive of Hypothesis 1.

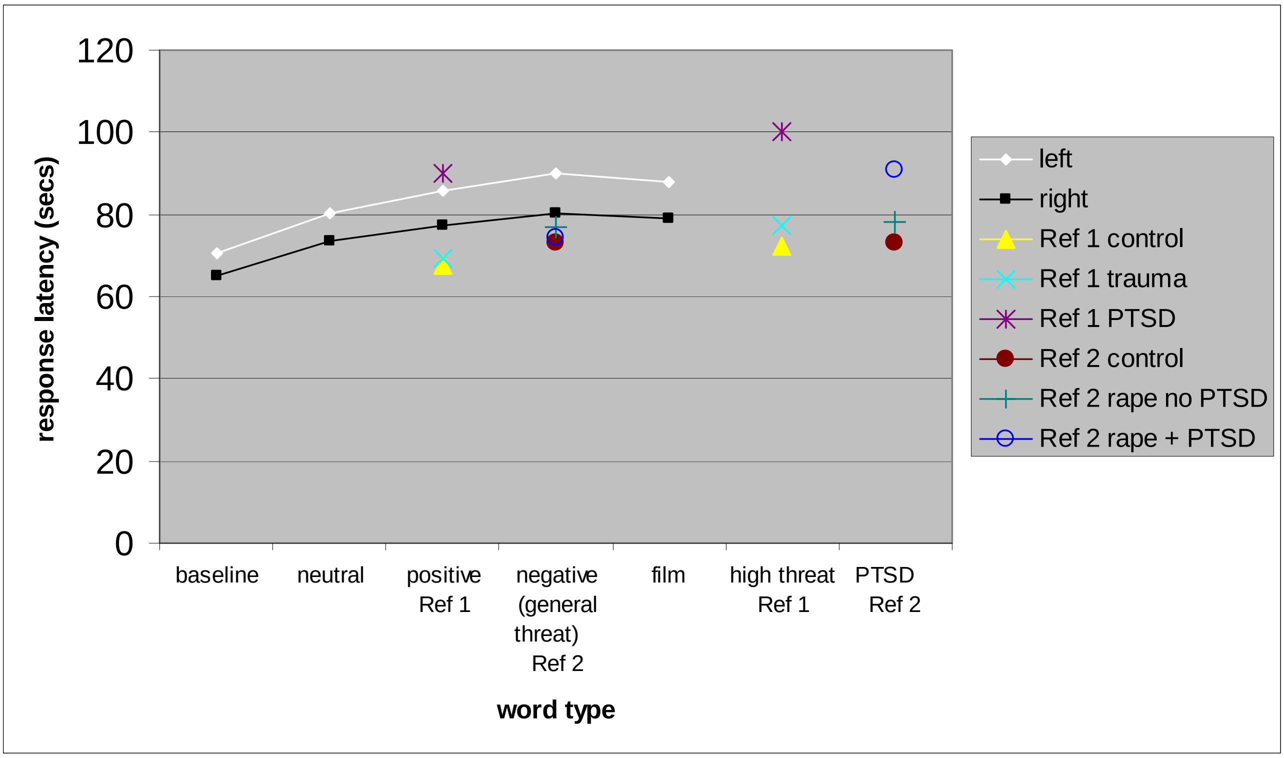
6.3.2.3 No film and the word based Stroop at Time1 (Control protocol): problems with this comparison group

This protocol was intended to control for viewing of the film. While running this study it was felt that the students recruited to the control protocol were of lower ability and/or were less motivated than the other samples and absolute levels of interference appeared high. This was further investigated and findings are reported in Appendix 22; these apparent difficulties with the control group compromise the intended control for watching the film. The absence of this control prevents definitive support for relating findings from the standard and reversed protocols to the film; however, the differences in patterns of interference and response latency in the latter two protocols suggest that watching the film may be responsible for the effect. The next section presents further evidence that this may be the case.

6.3.2.4 Comparisons of findings with PTSD and control groups in the literature

The negative words used in the present study were five of the ten used by Foa et al (1991) as "general threat" words and which were presented as individual stimuli with response latency measured; of the three studies using the same positive words as this study, Cassiday et al (1992) also used this method. By multiplying their mean scores x100, an equivalent measure to the response latency to the cards (containing 100 words) used in the present study can be calculated. Foa et al's (1991) study used a larger set of words (10) per condition instead of the five used here, but with this caveat, comparisons are presented in Figure 6.4. Overall, values for the current study lie between those for controls and PTSD patients in the clinical studies. Importantly, left handers response latencies for negative (general threat) and film words are greater than those of women with rape related PTSD to the larger set of general threat words and are approaching those of people with PTSD, at least in the Foa et al (1991) study.

Figure 6.4 Comparison of response latency for the word Stroop in this study (white: left handers and black: right handers) with values in the PTSD literature using the same words (positive/negative) and with their PTSD trauma related words (high threat/PTSD)



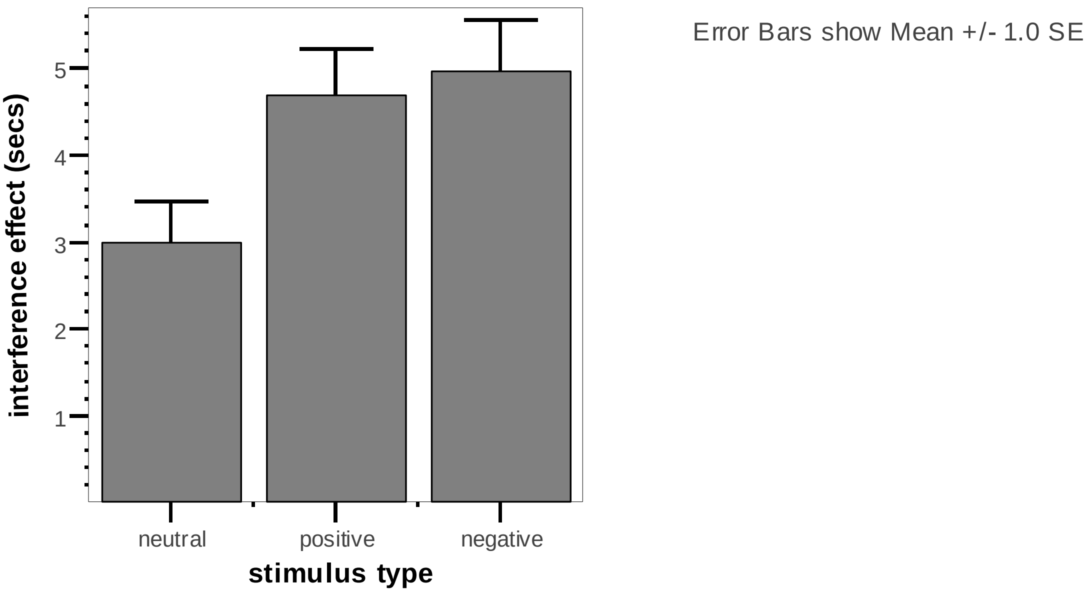
Key: Ref 1: Cassiday et al (1992); Ref 2: Foa et al (1991)

It has been suggested that there may be specificity effects in emotional Stroop tasks with clinically anxious individuals, that is, only particular words that are relevant to an individual's current concerns cause Stroop interference (Mathews & Klug, 1993). It was the negative words in the present study which produced a significant difference between left and right handers, and the five words used: funeral, cancer, coffin, disease and hate, could perhaps be considered to have specificity to someone who had lost a loved one, or if either themselves, or someone known to them, had cancer. Many individuals reported traumatic events on the PDS even if these did not meet Criterion A; of the 35 entries in the "other" category (which required a description), 18 of these (just over 51%) made reference to death or attempted suicide of a loved one. There were 29 entries for "life-threatening illness" and 19 of these were chosen as the index trauma and thus further described; of these 19 entries 15 (79%) related to cancer. In order to check for possible specificity effects, these two trauma categories were examined for possible differences in distribution between left and right handers. Chi-square tests were non significant in both cases (p = .323: other; p = .990: life threatening illness) and also when a distribution of all index trauma categories was examined [$\chi^2_{(10)}$=7.782, p=.650]. This suggests that the increased response latency observed for negative words in the current study were not associated with specifically relevant traumatic experiences.

6.3.3 Hypothesis 2: the non-word Stroop

Due to an inadvertent omission, the first participants (in the standard protocol) did not repeat the control OOOOO card in the non-word Stroop performed at time2. The standard measure of interference (a subtraction of the time taken to colour name the control card from the other cards) could not therefore be calculated for a majority of the participants in the standard protocol. Since participants in the control protocol also seemed significantly different to those in the other two protocols, at least in respect of the AVLT test of standard memory, overall interference effects were not compared by protocol. However, when the interference effect for non-word stimulus type over the control card is calculated for the sample completing the baseline condition, the absolute values of interference effects (Figure 6.5) appear low (between 3-5 seconds) compared to 15-20 seconds for the largest effects in the word Stroop. When non-word mean values were used as test values in one sample t-tests against interference observed for the equivalent stimulus types in the word Stroop, interference effects for the non-words were all found to be highly significantly lower, all with $p<.001$: [$t_{(204)}=16.238$, $p<.001$: neutral]; [$t_{(204)}=19.208$, $p<.001$: positive]; [$t_{(204)}=21.246$, $p<.001$: negative].

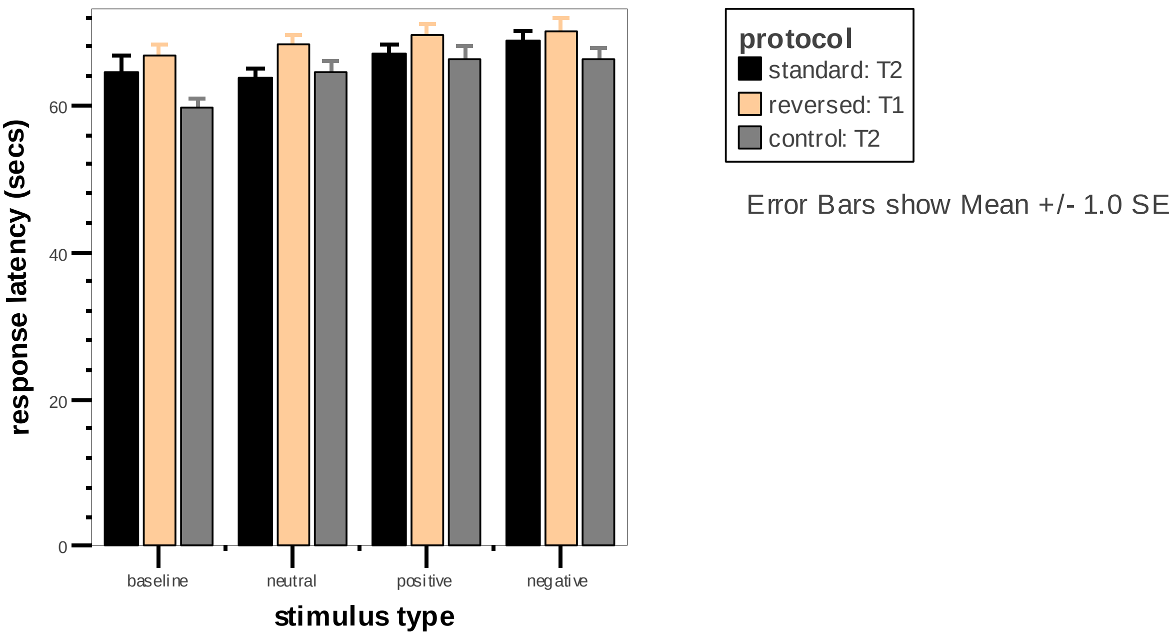
Figure 6.5 Mean interference effects for non-word stimuli: means are considerably (and significantly) lower than for the equivalent word type in the word-based Stroop



When each protocol was considered separately, 2x2 (stimulus type x handedness) repeated measures ANOVAs revealed no significant differences between left and right handers.

Although analysis of interference effects was compromised by omission of the control condition, response latency data was available for the full sample in respect of neutral, positive and negative non-words. A 3x3x2 (non-word type x experimental protocol x handedness) repeated measures ANOVA was conducted in respect of these non-word types. There was no significant main effect of experimental protocol (p=.204), no significant main effect of handedness (p=.294) and no interaction (p=.222). Figure 6.6 shows response latency across experimental groups (and includes the partial sample completing the control card).

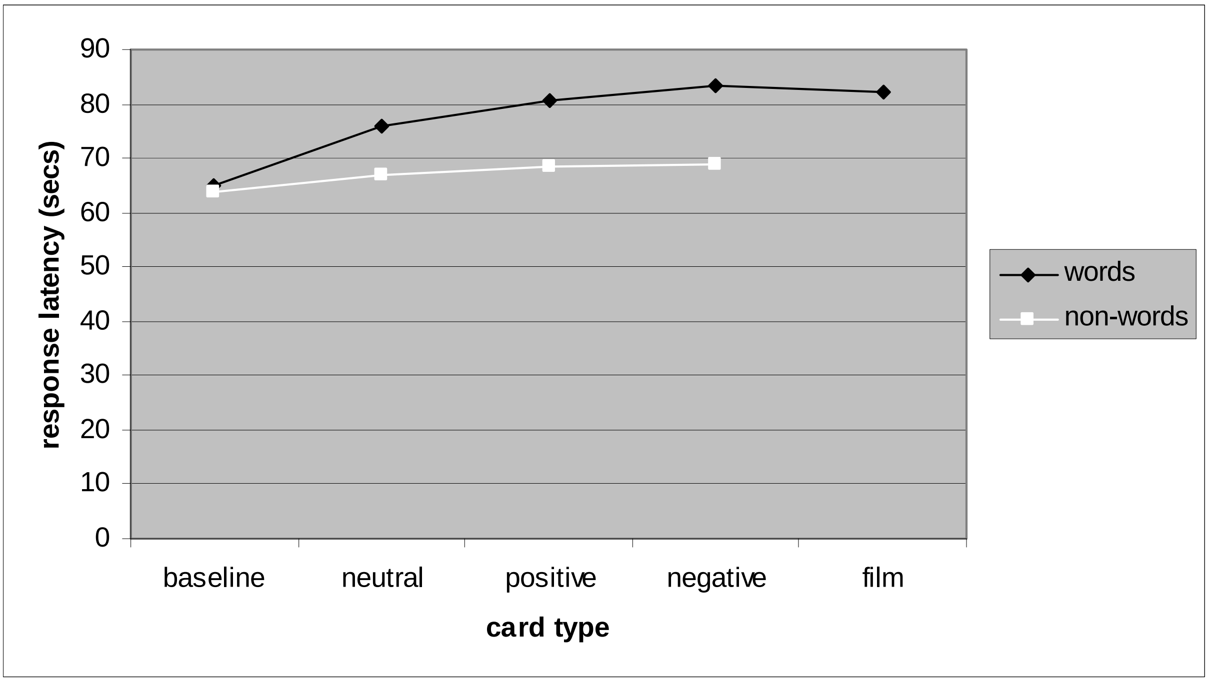
Figure 6.6 Response latency across experimental protocols (main effects and interaction all NS)



The compromised analysis of interference effects, nevertheless suggested that Stroop interference effects were significantly reduced in respect of non-words compared to words. In order to examine this further, in the full sample, response latency was compared for word and non-word Stroop tasks using paired t-tests (excluding film words which had no comparable non-word type).

There was no significant difference between the control card, which was exactly the same in both Stroop tasks, [$t_{(133)}$= -.450, p=.654] but response latency was significantly lower for all non-word equivalents to words at the p<.001 level: [$t_{(194)}$=16.267, p<.001: neutral]; [$t_{(194)}$=19.792, p<.001: positive]; [$t_{(194)}$=21.241, p<.001: negative]. These comparisons are illustrated in Figure 6.7.

Figure 6.7 A comparison of response latency for word and non-word based Stroop tasks: response latency for words is significantly higher than response latency for non-words for all types other than baseline



These findings support Hypothesis 2 and suggest that the verbal nature of the word Stroop task is important in accounting for interference effects and increased response latency.

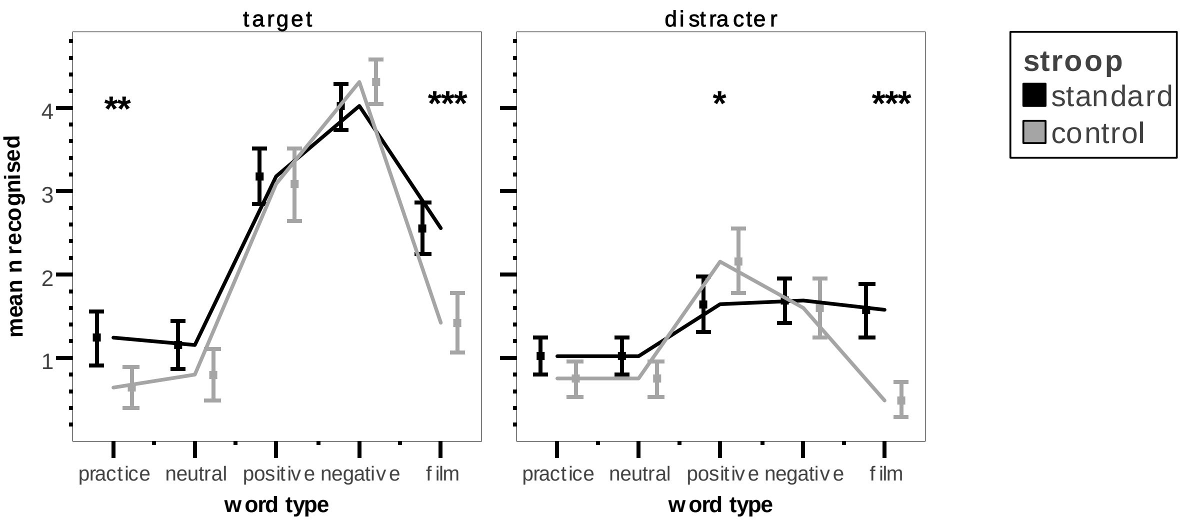
6.3.4 Hypothesis 3: sex differences

Using the full sample size, not excluding participants forced to change the hand they used for writing; no sex differences were found in any of the experimental protocols for either the word or non-word Stroop colour naming tasks. This supports Hypothesis 3.

6.3.5 Hypothesis 4: are words in the Stroop task cards remembered?

In order to test the first part of hypothesis 4, a 5x2x2 (word type – practice/neutral/ positive/negative/film – by protocol by word status –target/distracter) repeated measure ANOVA tested for differences in recognition of target and distracter words according to protocol.

Figure 6.8 Correctly identified responses (maximum possible score = 5) on SWRT: highly significant main effects of word type, protocol and word status. Error bars show 95% CI of mean.



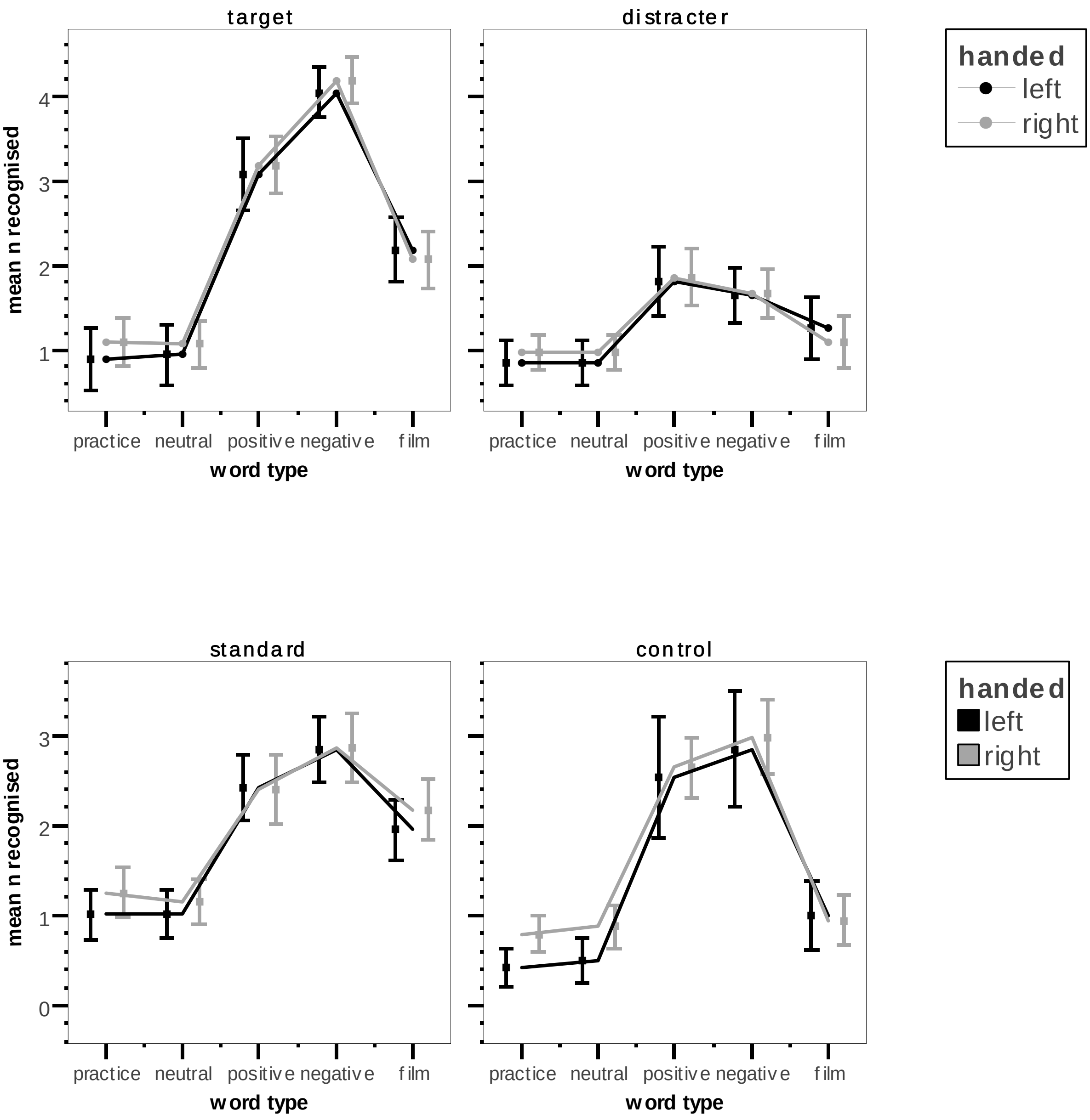
* p<.05; ** p<.01; *** p<.001

There were highly significant main effects of word type [$F_{(3.245,1024)}$=212.711, p<.001], protocol [$F_{(1,256)}$=7.713, p=.006] and word status [$F_{(1,256)}$=76.565, p<.001], but no significant interactions. Planned comparisons using paired sample t-tests for type of word showed no differences in recognition memory for practice and neutral words, but scores for all other word types were significantly different from one another and from practice/neutral words (all p < .001, surviving Bonferroni correction with critical p=.005). Significant differences between protocols were found in relation to practice words (significantly better recognised in the standard protocol) and as predicted by hypothesis 4a, participants in the control protocol recognised significantly fewer film words. This was also the case for the film distracter words which confirms that these words also had no salience for the control group. Overall, participants recruited to the standard protocol recognised correctly more target words than those recruited to the control protocol (standard: mean = 12.13 +/- 4.566 SD; control: mean = 10.24 +/- 3.706 SD: $t_{(128)}$=2.456, p=.015).

The target distracter words (the words related to the "emotional" sets in the Stroop task) were falsely recognised as present compared to neutral distracter words: participants recruited to the standard protocol falsely recognised significantly more positive, negative and film words than practice/neutral, and participants recruited to the control protocol recognised significantly more positive and negative words than practice/neutral and film. In the control protocol, significantly more positive words were falsely recognised than either negative words or the standard protocol. The distribution of correct responses on the SWRT to target and falsely recognised distracter words is shown in Figure 6.8.

There were no significant differences between left and right handers in recognition memory of target and distracter words, or according to protocol (see Figure 6.9).

Figure 6.9 No significant differences in recognition memory in left and right handers for targets/distracters (above) and according to protocol (below). Error bars show 95% CI of mean.



6.3.6 Summary

To summarise the results presented in this chapter, when completing a word-based Stroop task immediately after watching a fearful film, compared to right handers, left handers showed a significantly greater interference effect on film and general threat words, supporting Hypothesis 1. This effect on the word-based Stroop was not evident after completing memory tasks related to watching the film one week previously. Theses findings were supported by a consideration of response latency: only left handers showed a significant difference between protocols, with significantly greater response latency on the task when performed after watching the film compared to one week later after performing the memory tasks. In addition response latencies of left handers for the general threat words were greater than values reported in the literature for PTSD patients and response latencies for these and film-related words in left handers were approaching values reported in the literature for PTSD patients to trauma related words.

In contrast, and supporting Hypothesis 2, the novel, non-word version of the Stroop task produced significantly reduced interference effects and significantly lower response latencies than the word-based Stroop task. There were no significant differences between left and right handers for this non-word Stroop task.

There were no sex differences in performance of the Stroop tasks supporting Hypothesis 3.

With respect to Hypothesis 4, in a recognition memory task, the "emotional" words used in the Stroop task were better remembered than practice/neutral words, but the film related words were only better remembered by those participants who had watched the film, suggesting that the words, particularly the emotional and film related words, are semantically processed during a Stroop task rather than ignored as instructed, supporting Hypothesis 4a. This was also the case for falsely remembered target distracter words. There were no effects of handedness on the recognition memory test for words used on the Stroop supporting Hypothesis 4b.

6.4 Discussion

The experiments presented here found a significant interference effect in left handers for general threat (negative) and film-related words after watching the film; this effect in an emotional Stroop task is not normally found in healthy populations. This in itself is an interesting finding. Tentatively this could be related to the specific use of a laboratory analogue of fear, and replication of this finding is required before firmer conclusions can be made.

Hypotheses predicting greater interference effects for film-related words in left handers in a word Stroop task after watching a fearful film were supported; although effects were at a slightly higher level of significance for the negative words. Although referred to here as a “negative” words, in the study from which they were taken (Foa et al., 1991) these words constituted “general threat” words, and are perhaps better seen in this context: it is therefore not surprising after watching a fearful film these words also caused significantly greater Stroop interference in left handers compared to right handers.

That the “general threat” words, were associated with a higher level of significance in respect to these interference effects in left handers, may be due to a decision about stimuli inclusion that with hindsight was probably unduly conservative. That the interference effect in left handers to film words which were chosen to be *neutral* other than by their association with the film was significant is perhaps remarkable. Since trauma related words used in PTSD Stroop studies are likely to be *negative* words in themselves, it would be a better comparison, if film related, negative words (such as gun, trapped, killer) were used in future studies and on the basis of results here, would be hypothesised to produce effects at a higher level of significance.

While left handers show overall increased interference compared to right handers in the standard protocol (immediately after watching the film), there was a significant interaction in interference effects between the two protocols (see Figure 6.2). However, when the actual times taken to complete the Stroop tasks are examined (in Figure 6.3) this apparent effect disappears. In right handers response latencies were not significantly different in the two protocols, whereas the left handers show a highly significant main effect of protocol with increased response latency when the word Stroop task was performed directly after the film, compared to one week after the viewing when preceded by various tasks requiring recall of the content of the film.

Closer examination of Figure 6.3 reveals the reason for this: the time taken to complete the control (baseline) card, but not the other word cards, differs in the two protocols. Due to the design of this experiment, which also considered a non-word form of stimuli in a separate Stroop task, these findings reflect between-subject differences, as different samples of left and right handers were recruited to each protocol, and constitutes a limitation of the current study. Future research using within-subject comparisons for the same Stroop task repeated in both protocols would be useful in confirming these observed differences.

Both the standard and reversed protocols made reference to the film prior to the word Stroop task. In the standard protocol, which produced significant differences in Stroop interference effects between left and right handers, the film was used as a laboratory analogue of fear, while the reversed protocol involved several tasks which required memories of this experience to be re-visited. The control protocol was intended to control for effects of the film. Not only was there a failure to reach recruitment targets of all but female right handers, but this protocol also appears to have recruited students different to those recruited to the other protocols, as reflected in significantly lower scores on the AVLT, and by comparing performance on the word Stroop with another group of female right handers (the PG group). This highlights the difficulties of recruitment of left handers generally, since they represent only 10% of the population, and raise questions of motivation when subjects are required to perform experiments in which they might otherwise not have chosen to participate. That this may be a valid account of the results obtained is supported by Kaspi et al (1995) who point out that lower intelligence in subjects may contribute to poor concentration and hence longer response latencies in the colour naming task. The design of this experiment was such that the control protocol was intended to control for viewing of the film and clearly this intended control has failed.

Nevertheless, there is other evidence suggestive of the film being implicated in the increased Stroop interference effect observed in left handers. Firstly, the effect did not occur one week after watching the film (in the reversed protocol). Secondly, an interference effect to an emotional Stroop is not normally found in healthy subjects. Thirdly, and more importantly, the actual size of the response latency effects when compared to the PTSD literature suggests that the film manipulation is producing an effect in left handers immediately after the film approaching that of PTSD patients, and these effects are greater than in their healthy control groups. This is an important finding since emotional Stroop effects do not usually occur at all in healthy samples, and the magnitude of this effect is considerable. Taken together, despite the failed control for watching the film, this evidence suggests that viewing this film appears to be associated with the effect. This also suggests that the film is a useful laboratory manipulation targeted to fear, which may be important in studying underlying processes relevant to PTSD.

The two part nature of this study afforded the testing of a novel version of the Stroop task. Crucially, this task used stimuli that appeared to look like the word stimuli on the cards, but contained no linguistic forms within them (as would strings of letters used as non-words). As hypothesised, this significantly attenuated response latencies across all protocols and importantly produced no significant main effects of protocol or handedness, or an interaction. This is a potentially important finding as it provides supporting evidence for models of the Stroop effect that suggest interference arises in word response selection. Unlike other emotional Stroop tasks which do produce interference to pictorial representations of threatening faces (van Honk et al., 2000), the stimuli used here, even though rated according to valence, did not generate a significant increase in response latency. The nature of the stimuli may be such that they encode verbal representations to a much lesser extent. It might have been interesting to include a free recall test for the stimuli content, to assess this (and indeed to include a recall test for the word Stroop stimuli prior to the supported retrieval recognition test, for comparison). This study can not make definitive statements about this, as activations have not been measured, but the results here are suggestive and amenable to explanations based on ERP findings. It would be interesting to investigate this possibility further using imaging or ERP techniques which may be able to assess more directly the nature of any processing of the non-word stimuli. This finding is important, however, because it potentially also lends support to the idea that a subjective state of fear involves reduced ability to process verbal material, resulting in interference effects in the word Stroop task but not the non-word task.

In summary, these results suggest that left handers are responding differently to right handers to a laboratory analogue of fear in ways that are analogous to people with PTSD and which appear to affect verbal processing. These results support Hypotheses 1 and 2. As predicted, there were no sex differences in any variables of the Stroop tasks, supporting Hypothesis 3.

The SWRT was primarily included to check that participants had not adopted strategies, such as blurring vision, which ignored the words in the Stroop task (Hypothesis 4). That more than 50% of positive, negative (and film in the standard protocol) target words were recognised in the test suggests this was not the case. This also provides additional evidence that the Stroop effect is not due to avoidance of threat-related material, since the negative (general threat) words were the most recognised set of words for all participants. Differences in recognition scores of the film words by protocol also suggest that the film words were no more memorable than practice/neutral words used, unless their salience was made relevant by watching the film.

Results suggest that the "emotional" words are better remembered in the Stroop task compared to neutral words, whether or not participants viewed the film. This is consistent with results of a similar test of recognition memory for words used in an emotional Stroop task in PTSD (Vrana et al., 1995); the emotion words were significantly more likely to be recognised than control words. They found that their PTSD group was more accurate overall than the No-PTSD group; in the present study participants who watched the film (the standard protocol) accurately recognised significantly higher total number of words than the control protocol, suggesting that the manipulation of fear had a similar effect to the differences observed between the PTSD/No-PTSD groups.

There were no differences between left and right handers in this recognition task, irrespective of viewing the film immediately prior to the word Stroop task. However, there was a clear difference in Stroop interference effects: left handers showed both an overall significant slowing of response latency compared to right handers, and a specific interference effect for negative (general threat words). This suggests that the underlying mechanism operating in respect of accurate recognition of the words is not the same as the mechanism involved in generating the Stroop interference effect, that is, "attention" to the stimuli which results in correct recognition, is not responsible for Stroop interference. Findings in relation to false memory illuminate this further, so these are next discussed before returning to this point.

That distracter words (related to the "emotional" word sets in the Stroop task) were falsely identified as present in the Stroop task is consistent with the Deese (1959)/Roediger-McDermott (1995) paradigm. The DRM paradigm is an extremely robust and persistent phenomenon: when subjects hear a list of related words (for example, thread, haystack, eye, sewing etc) all of which are associated with a critical non-presented word (in this case, needle) and are then given a test of memory (recall or recognition) subjects often falsely report the presence of the critical non-presented word. The words presented here in the practice and neutral sets were not related to one another and significantly less false recognitions were made for additional neutral words in the SWRT; within the "emotional" sets of words, the words were clearly related to one another and significantly more false recognitions were made for related distracters in each case.

Evidence suggests that implicit association (with non-presented items) occurs at encoding; any subsequent retrieval at test also simultaneously re-encodes both the correct and false items so that they are both more likely to be retrieved at re-testing (McDermott, 1996). Recent investigation of the false recognition phenomenon in a DRM paradigm using ERP's, suggests that increased semantic associative processing is associated with those items falsely remembered at test with patterns at retrieval showing some common and some differential processes in respect of correct and false recognition (Geng et al., 2007). The same associative mechanism may occur for apparently "positive" words - they may also be associated with their negative opposites. For example, in this study, love appeared in the positive set and hate in the negative set of words; it is likely that associative networks of one include the other.

Taken together, evidence from DRM paradigms and the results here suggest that in the Stroop paradigm, the words presented are not ignored, as instructed, but are semantically processed, to the extent that the "emotional" words are capable of generating false recognitions to semantically related words. In contrast, other evidence, reviewed in the introduction to this chapter, suggests that Stroop interference arises at a relatively late stage, indicative of word processing conflict at response output. Any effects of watching a fearful film on left handers appear to operate at the late stage, in relation to verbal processing, rather than on implicit associative processes that occur early on in response to the coloured words.

If the film targeted fear, and there are reasons to think that it contained all the correct ingredients to do so (see Chapter 5), then this appears to have affected the left handers in the Stroop task, firstly to a greater extent than right handers, and secondly, in a way that people with PTSD are affected. In PTSD and in the fear response, there is hypoactivation of language processing areas; if this is occurring in left handers, to a greater extent than in right handers, consistent with their relatively greater right hemisphere dominance, then this explains the pattern of results observed here.

Chapter 7

The 2D:4D: is testosterone related to left handedness and PTSD?

Background: One theory proposed to account for left handedness is exposure to high levels of *in utero* testosterone (Geschwind & Galaburda, 1985). Since sex differences exist in aetiologic routes to PTSD with respect to substance abuse and risk taking, it was hypothesised that this may be related to higher levels of *in utero* testosterone in males with PTSD.

Methods: The apparent ease of measuring the 2D:4D as an indicative measure of *in utero* testosterone afforded the opportunity to test these hypotheses in the large general population sample reported in Chapter 3 and in participants of the experimental studies of Chapters 5&6.

Results: The larger sample did not support associations of *in utero* testosterone with left handedness, but the smaller sample, which contained a high proportion (30%) of left handers, did in respect of the 2D:4D in the right hand only. Contrary to hypotheses in relations of *in utero* testosterone to PTSD, the larger sample suggested that males with PTSD had a higher 2D:4D indicating a more-female-like digit ratio; the second sample attempted replication failed to reach significance likely due to inadequate power.

Conclusions: There continues to be mixed evidence in respect of the Geschwind-Galaburda hypothesis. This study identifies methodological difficulties in measuring

the 2D:4D which have not been previously reported in the literature. Relations between the 2D:4D and PTSD require further replication, but this is a potentially important new finding relevant to observed sex differences in prevalence of PTSD.

The rationale for this study was introduced in Chapter 2 where the use of the second to fourth digit ratio (2D:4D) was introduced as a possible indicative measure of *in utero* testosterone level. This chapter first discusses the evidence in relation to Geschwind & Galaburda's (1985) hypothesis that *in utero* testosterone may be linked to left handedness before presenting data on the 2D:4D collected from participants in the large general population sample reported in Chapter 3. Since testosterone may be associated with risk taking behaviours that may lead to increased risk of trauma, relationships of the 2D:4D with PTSD are also considered.

7.1 Introduction

The suggestion that levels of *in utero* testosterone are implicated in left hand preference has been debated for the last twenty years, since Geschwind and Galaburda's (1985) seminal paper on this subject presenting a series of hypotheses about biological mechanisms of lateralisation. They proposed that, whilst there may be genetic factors involved, there are shortcomings of genetic models of lateralisation (considered further in Chapter 9) and that the chemical environment *in utero* may alter lateralisation patterns. Oldfield (1971) had found higher prevalence of left-handedness in men than women and Geschwind and Galaburda (1985) suggest developmental disorders of childhood such as dyslexia, stuttering and autism are more common in males and left-handers. They therefore proposed that testosterone, one of the hormones implicated in sex related prenatal development of cortical asymmetry in comparative studies (Lewis & Diamond, 1995; Andrew, 2002; Cowell & Denenberg, 2002) was a possible cause of left handedness. Findings since then have, however, been mixed.

Although animal studies can manipulate levels of *in utero* testosterone, this is not possible in humans. Opportunities to explore possible links between *in utero* testosterone and lateralisation are therefore afforded by clinical conditions in which prenatal levels of testosterone are abnormal. One such instance is prenatal exposure to diethylstilboestrol (DES, a non steroidal oestrogen) *in utero*, when this was widely prescribed in the post-war years to prevent miscarriages (Schachter, 1994). While at first seeming paradoxical, since DES is an oestrogen, testosterone is converted to oestradiol (an oestrogen) and may consequently act via oestrogen receptors in the developing cerebral cortex (Lewis & Diamond, 1995). Hines and Shipley (1984) considered 25 women exposed pre-natally to DES and although they found a more masculine pattern on a dichotic listening task in the exposed women compared to their non-exposed sisters, they report that only one subject (a control) was not right handed. Schachter (1994) specifically examined handedness in 77 women with prenatal exposure to DES compared to 514 female controls and found a significant shift from strong right handedness to weaker right handedness amongst the DES exposed women. Smith and Hines (2000) assessed handedness in 40 women exposed to DES and 25 unexposed sisters. Whilst significantly more left handers were found in the DES exposed group using Fisher's exact test, an independent samples t-test on handedness inventory scores of exposed and non-exposed women did not produce significant differences, although earlier onset of exposure to DES in the gestational period appeared to be linked to left hand preference. Small numbers of DES exposed women in these studies may have limited the findings, but there is only mixed support for increased left handedness in these women.

Another line of enquiry has focussed on individuals, particularly females, with Congenital Adrenal Hyperplasia (CAH). This is a genetic disorder in which the foetus produces excess androgens and is consequently exposed to atypically high levels of androgens *in utero*; in women this leads to physical virilisation. Several studies have hypothesised that increased left handedness will be found, particularly in women with this condition, but again findings have been mixed. For example, Helleday et al (1994) in a study of 22 CAH women and 22 healthy controls did not find any differences in handedness whereas Kelso and Nicholls (1999) in a study of 6 males and 7 females with CAH and 13 controls found a higher incidence of left handedness in individuals with CAH. Mathews et al (2004) in a study of 40 females and 29 males with CAH compared to unaffected relatives (29 females and 30 males) found that males with CAH were less consistently right handed for writing than their unaffected male relatives, but all other tests of hand preference produced no significant differences. All of these studies also had relatively small sample sizes which may have limited the possibility of establishing sex or handedness differences. While results for handedness are inconsistent, a study of 2D:4D in a sample of CAH children, did, however, find a lower digit ratio in female patients with CAH compared to healthy girls, and their mean 2D:4D was not different to male controls (Okten et al., 2002). In summary, evidence based on these opportunistic samples has not provided strong evidence in support of the Geschwin-Galaburda hypothesis.

However, Okten (2002) measured the 2D:4D in patients with CAH and found that women with CAH had a low 2D:4D, not significantly different to healthy males and men with CAH had significantly lower 2D:4D than healthy males. This suggests the 2D:4D is influenced by *in utero* testosterone and shows expected differences in patients with CAH.

Use of the 2D:4D provides a means to test further, and perhaps more directly, the Geschwind-Galaburda hypothesis that left handedness is linked to *in utero* testosterone. Manning et al (2000) considered 2D:4D in 285 rural Jamaican children in relation to hand performance on an Annett peg moving task. Though performance may be related to lateral preference (Annett, 1985), this study did not measure lateral preference *per se*. In the right hand 2D:4D, there was a significant negative relationship with lateralised hand performance (time for right hand performance divided by time for left handed performance). While a right hand performance advantage was related to higher 2D:4D and left hand performance advantage to low 2D:4D, in accordance with the Geschwind-Galaburda hypothesis, the study was not directly concerned with lateral preference.

The present study was designed to provide a test of the Geschwind-Galaburda hypothesis in the large general population sample who were also screened for possible PTSD as reported in Chapter 3 above and elsewhere (Choudhary & O'Carroll, 2007). The study protocol included a scan of participants' hands in order to determine 2D:4D from the scanned image. Although a non-clinical sample, 8.6% of the population met all criteria for diagnosis of probable PTSD on the self report measure (the Posttraumatic Diagnostic Scale; Foa et al., 1997) a prevalence similar to the estimated lifetime prevalence of 7.8% found in the (US) National Comorbidity Survey (NCS; Kessler et al., 1995) and 8.7% projected lifetime risk in the NCS DSM-IV Replication (Kessler et al., 2005a).

In the context of the present study which uses an indirect measure indicative of prenatal gonadal hormone status, it is relevant to consider typical sex differences in PTSD as outlined in Chapter 1. To recap, experience of a traumatic event is a relatively frequent event, with 61% of men and 51% of women (a significant difference) reported experiencing at least one traumatic event in the NCS (Kessler et al., 1995). The widening of the criteria for qualifying events in Criterion A1 of the DSM-IV has increased the prevalence of exposure such that 92.2% of males and 87.1% of females are estimated to experience lifetime trauma (Breslau & Kessler, 2001). Despite this sex difference in exposure, epidemiological studies have typically found PTSD prevalence rates twice as high in women than in men (for example 11.3% compared to 6% in Breslau et al, 1991; 10.4% to 5% in Kessler et al, 1995). For both sexes, the event with highest conditional risk of developing PTSD is rape; this is experienced by more women than men, but in a review, Norris et al (2002) conclude that this exposure alone is not sufficient to explain women's excess risk for PTSD which remains to be fully explained.

Considerations of sex differences in co-morbid PTSD and substance use disorders suggest that there are potentially different aetiologic routes to PTSD in men and women (Stewart et al., 2002). For example, Deykin et al (1997), in a study of 297 chemically dependent adolescents, not only found extremely high lifetime prevalence of PTSD in this population (45.3% of females and 24.3% of males), but also a different time course in the onset of the two conditions. In females, chemical dependency appeared to be secondary to PTSD, resulting from repeated substance use in an attempt to deaden the symptoms of PTSD, whereas in males, substance dependence appeared to be primary, resulting in behaviours with consequent risk of trauma.

In this respect, while there is clear evidence linking levels of aggression with testosterone in animals, this relationship is not so clear, and is more complex, in humans (O'Carroll, 1998) though higher levels of testosterone in response to a competitive challenge (Archer, 2006) are generally supported. However, it may be that other factors moderate the relationship between testosterone and aggression. Recent evidence suggests that there may be an interaction between production of cortisol and testosterone in animals (Pivina et al., 2007). The hormone cortisol, produced by the HPA-axis stress response, inhibits sex steroid release during stress; in delinquent male adolescents there was a strong positive relationship between testosterone and aggression only in those with low, but not high cortisol levels (Popma et al., 2007), which may be relevant in explaining mixed findings. In a fMRI study examining neural responses to social threat (angry faces) in females, stronger activation was found in baseline high testosterone and low cortisol individuals and responses were stronger after administration of testosterone compared to placebo, suggesting that testosterone enhances responses in neural circuits related to social aggression (Hermans et al., 2008).

Higher testosterone levels have been found in violent male offenders compared to less violent individuals (Archer, 1991), in males with delinquent or deviant behaviour (Banks & Dabbs, 1996; Mazur, 1995) although perhaps dependent on social settings (van Bokhoven et al., 2006) and to be related to sensation seeking in some cases (Daitzman et al., 1978; Daitzman & Zuckerman, 1980; Gerra et al., 1999) but not others (Rosenblitt et al., 2001; Wang et al., 1997). These behaviours could, even in the absence of substance abuse, predispose such men to higher levels of risk of experiencing trauma. It might therefore be proposed that higher levels of testosterone in males (reflected in a lower 2D:4D) may be associated with risk of experience of trauma and consequently higher prevalence of PTSD. The measurement of 2D:4D and PTSD diagnostic criteria in a large general population sample provided the opportunity to test this hypothesis.

This study therefore had two main aims. The primary aim was to test the Geschwind and Galaburda (1985) hypothesis and secondly, to investigate associations between an indicative measure of testosterone and meeting diagnostic criteria for PTSD. There were two hypotheses tested:

Hypothesis 1: higher levels of *in utero* testosterone, indicated by a low 2D:4D, is related to left handedness.

Hypothesis 2: males fulfilling diagnostic criteria for PTSD will have a lower 2D:4D, indicative of higher levels of testosterone, than men who did not fulfil diagnostic criteria for PTSD, but there would be no difference in 2D:4D in women with and without PTSD.

7.2 Methods

7.2.1 Participants

The study population consisted of a subset of the study population reported in Chapter 3 and elsewhere (Choudhary & O'Carroll, 2007) recruited from two main sources: students (mainly psychology undergraduates) and some staff of the university (n= 286) and a general population drawn from weekend visitors to the Glasgow Science Centre (n=310). Of the 596 volunteers recruited, 200 had images of the hands which were not usable (see Appendix 18). Of the remaining 396 individuals forming this study population, 359 (90%) had digit ratios calculated for the right hand, 294 (74%) for the left hand and 257 (65%) for both hands. The two sources each contributed 50% of this sample (University: n=199; Glasgow Science Centre: n=197). No participants were actively excluded.

7.2.2 Materials

The lateral preference inventory and PDS were completed as described in Chapter 3 above. On each measure, maximum negative scores indicate consistent left hand preference and maximum positive scores, consistent right hand preference.

7.2.3 Procedure

Participants were approached and asked to consider participating in the study by providing a scan of the ventral (palmar) surface of both hands to determine the 2nd to 4th digit ratio (Manning, 2002) and filling in a handedness inventory and a questionnaire about experience of certain life events so that the investigation could consider possible relationships between these factors in a healthy general population.

7.2.4 Apparatus

Scans of the ventral surface of both hands were made using a Dell AIO (All-In-One) Printer A920 attached to a Compaq nx9010 laptop computer running Windows XP. Scanned images were sent to file, named with the unique identifier appearing on a participant's questionnaire and stored as .jpg files. Subsequent measurement of the length of 2nd and 4th digits from the basal crease (at the palm) to the tip of the digit was made using AutoMetric software (DeBruine, 2003). Adobe Photoshop v7.0 (running in Windows XP) was used for further analysis of scanned images; a Sealey digital caliper, measuring to 0.01 mm, was used for assessment of these images (see Appendix 18). SPSS v 12.0.1 (running in Windows XP) was used for data analysis.

7.2.5 Analysis

There is evidence suggesting that the right hand is more susceptible than the left to the effects of testosterone (e.g. McFadden & Shubel, 2002; Williams et al., 2000) and many of the behavioural traits examined in relation to the 2D:4D have been found to correlate more strongly with the right hand (Williams et al., 2000; Williams et al., 2003). Analysis was therefore performed separately for the digit ratio of each hand and of a combined mean.

7.2.6 Ethics

Ethical approval for this study was obtained within the application to the Department of Psychology Ethics Committee (see Appendix 23); information to participants was included in an Information Sheet, which participants read before giving informed consent to participation. Since completing the PDS may have caused distress to anyone reminded of their traumatic experiences, the front cover included a reminder that should this occur they may wish to seek help from their GP (or student support services for the student participants).

7.3 Results

7.3.1 Characteristics of the sample

The full sample has been described in Chapter 3; the subset of this sample with usable scans (N=396) is described here. The university sample was significantly younger than the science centre sample with a mean (± S.D.) age of 21.6 ±4.63 years (range: 17.0-49.7) compared to 37.8 ±9.73 (range: 17.9-70.1) [$t_{(276.7)}$=21.071, p<.001]). There were significantly more females than males in both samples, 147 (74%) in the university group [$\chi^2_{(1)}$=45.352, p<.001] and 122 (62%) in the science centre group [$\chi^2_{(1)}$=11.213, p=.001] and overall (269 females - 68% of the total sample - and 127 males) [$\chi^2_{(1)}$=50.919, p<.001].

Analysis of the full sample (Choudhary & O'Carroll, 2007) found no significant differences between groups in respect of variables relating to lateral preference and experience of trauma and the groups were combined for all further analysis.

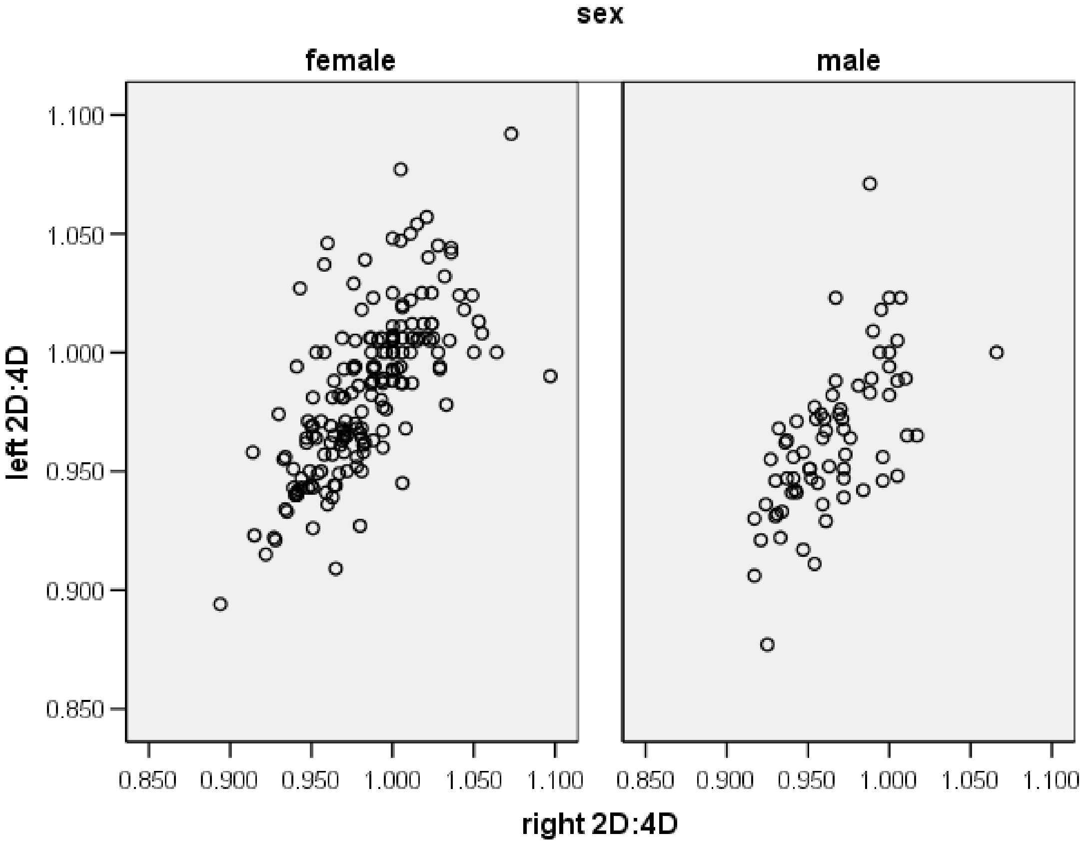
7.3.1.1 Digit ratios

A significant positive correlation was found between the digit ratios of the left and right hands [$r_{(257)}$ = 0.701, p < 0.001]. This relationship is shown in Figure 7.1 below which also illustrates the relatively lower value of the 2nd to 4th digit ratio for males (although there is considerable overlap between the sexes).

7.3.1.2 Prevalence of left handedness

When classified by hand used for writing (the first question on the Oldfield 10 measure), 90% (n=358) were right handed, 9% were left handed (n=34) and 1% (n=4) reported using both hands equally. The latter two groups, as non-right handers, were combined for further analysis.

Figure 7.1 Scatterplots to show relationship between digit ratios of right and left hands (by sex)
Digit ratios of left and right hands are positively correlated; in males (below left) the points cluster nearer to the origin (a low 2D:4D) than in females (below right) where points cluster further towards the top right, indicating a relatively higher 2D:4D.



7.3.1.3 Prevalence of trauma and PTSD

More than half (56%, n=219) of the participants reported experiencing a trauma; in 149 cases (38.9% of the population) this trauma met Criterion A (requiring the trauma to be both appraised as life threatening or incurring physical injury and with subjective experience of terror or helplessness). Of these, approximately one in four (n=39: 10.0%

of the total population) met all DSM-IV diagnostic criteria for PTSD and have a possible diagnosis of PTSD. Chi square tests revealed no significant differences in the distribution of those with PTSD between the university and science centre groups, or between males and females.

7.3.1.4 Sex differences in 2D:4D ratios

Since not all the images of participants hands could be used, right and left hands were analysed separately, as well as a mean value where both hands were measured.

Table 7.1 Sex differences in 2D:4D (p<.001 in all cases)

	***2D:4D Ratio**:* *Left hand*	*Mean (SD) [n]* *Right hand*	*Mean (both)*
Males	.963 (.031) [93]	.964 (.030) [105]	.964 (.028) [71]
Females	.985 (.033) [201]	.985 (0.33) [254]	.984 (.030) [186]

For all digit ratios, shown in Table 7.1 males had highly significantly lower 2D:4D ratios than females, that is, they had relatively long 4^{th} digits compared to their 2^{nd} digit (left hand [$t_{(292)}$=5.323, p<0.001]; right hand [$t_{(357)}$=5.782, p<0.001]; mean (both hands) [$t_{(255)}$= .871, p<0.001]).

7.3.2 Hypothesis 1: Left handedness is related to lower 2D:4D

Independent sample t-tests were performed to compare digit ratios in left and right handers. Mean values are shown in Table 7.2; no significant differences were found in digit ratio according to handedness (for writing). Hypothesis 1 was not supported.

Table 7.2 2D:4D in relation to handedness (all ns)

	handed	*N*	*mean*	*SD*	*t*	*df*	*p*
L 2D:4D	left	24	.98321	.032968	.824	292	.411
	right	270	.97726	.033966			
R 2D:4D	left	36	.97406	.031324	-.927	357	.354
	right	323	.97947	.033459			
mean 2D:4D	left	22	.98232	.028156	.556	255	.579
	right	235	.97847	.031294			

In order to test laterality more widely, rather than handedness alone, correlations were performed between the various measures of laterality derived from the questionnaires and digit ratios. These are shown in Table 7.3 below. Significant, positive correlations were found only in relation to Coren foot score and right 2D:4D [$r_{(347)}$=0.132, p=0.013] and, at a higher level of significance, between Coren ear score and (a) left 2D:4D [$r_{(287)}$=0.169, p=0.004] and (b) mean (both hands) 2D:4D [$r_{(251)}$=0.176, p=0.005]. These relationships indicate that higher, that is more rightward, laterality scores are found with higher, that is more typically female, digit ratios, and that conversely, lower, more leftward, laterality scores are found with lower, more typically male, digit ratios, for (a) footedness, and more strongly, (b) for ear preference.

These correlations were repeated for males and females separately (also in Table 7.3). None of the correlations remained significant in males. The significant, positive correlations in females were with Coren foot score and mean (both hands) 2D:4D [$r_{(180)}$=0.151, p=0.043] with right 2D:4D approaching significance [$r_{(248)}$=0.116, p=0.069] and with Coren ear score and left 2D:4D [$r_{(195]}$=0.150, p=0.036] with mean (both hands) 2D:4D approaching significance [$r_{(181)}$=0.142, p=0.056].

These are weak relationships and would not survive correction for the number of analyses conducted. In conclusion, these results do not support hypothesis 1.

Table 7.3 Correlations between 2D:4D and measures of laterality (significant correlations are emboldened within the table)

		Whole sample			*Males*			*Females*		
	2D:4D	L	R	mean	L	R	mean	L	R	mean
Oldfield handedness	r	.011	.082	.033	-.045	-.043	-.040	-.002	.104	.019
	p	.859	.127	.600	.677	.674	.750	.980	.104	.800
	N	283	345	248	87	100	67	196	245	181
Oldfield 12	r	.003	.090	.035	-.067	-.049	-.072	-.006	.111	.027
	p	.960	.099	.581	.538	.628	.568	.931	.085	.716
	N	279	340	244	86	99	66	193	241	178
Coren hand score	r	.025	.092	.030	.008	.054	-.001	.020	.085	.021
	p	.675	.087	.638	.943	.586	.990	.783	.186	.780
	N	282	347	247	91	103	70	191	244	177
Coren foot score	r	.054	**.132***	.122	-.128	.046	-.077	.108	.116	**.151***
	p	.361	.013	.054	.225	.642	.524	.132	.069	.043
	N	286	351	250	92	103	70	194	248	180
Coren ear score	r	**.169****	.093	**.176****	.191	.097	.191	**.150***	.059	.142
	p	.004	.082	.005	.068	.328	.113	.036	.356	.056
	N	287	353	251	92	104	70	195	249	181
Coren eye score	r	-.033	-.035	-.037	.087	.116	.107	-.055	-.050	-.058
	p	.582	.518	.556	.411	.245	.376	.451	.435	.439
	N	285	348	249	92	103	70	193	245	179
Coren laterality score	r	.087	.090	.100	.070	.108	.074	.085	.059	.086
	p	.149	.097	.119	.512	.284	.542	.248	.361	.261
	N	279	340	244	91	101	70	188	239	174

* p<.05; ** p<.01

7.3.3 Hypothesis 2: Males with PTSD will have a lower 2D:4D

In order to investigate possible sex differences between (a) participants meeting the criteria for diagnosis of PTSD (the PTSD group), (b) those that reported experiencing trauma on the PDS and (c) those that did not, the various digit ratios each formed a dependent variable in a series of one-way ANOVAs with males and females analysed separately. In females, the one way analyses of variance did not produce any significant results.

Table 7.4 Digit ratios in relation to experience of trauma for males (left) and females (right)

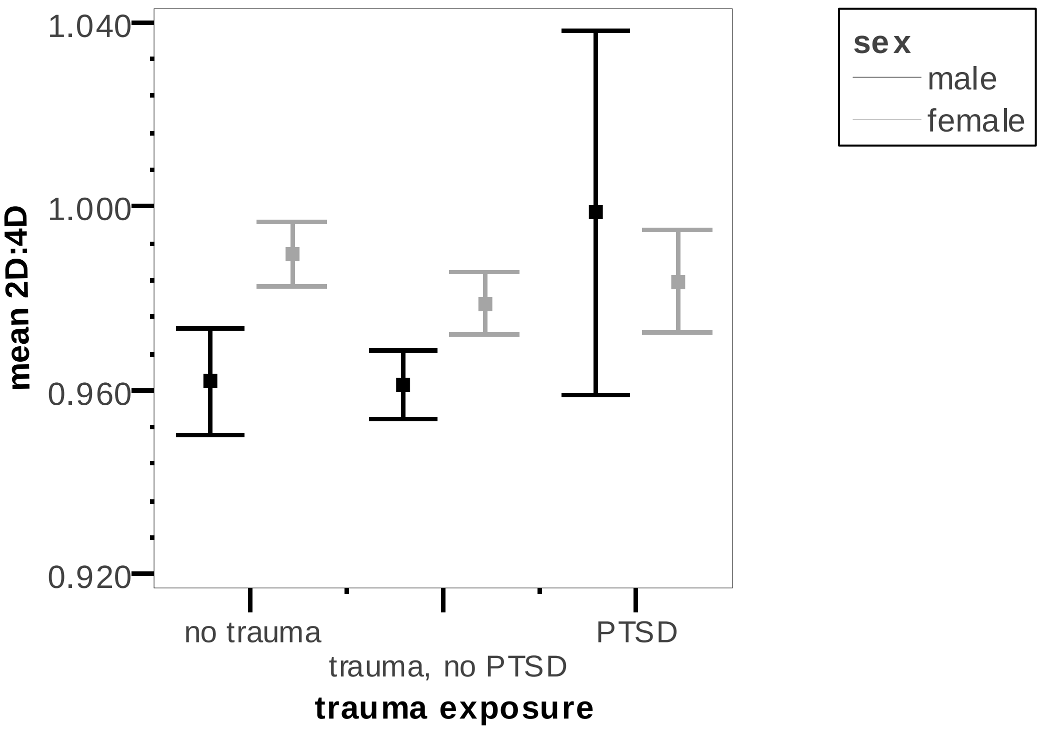
	:	*MALES*				*FEMALES(all ns)*		
Digit ratio	Trauma	n	mean	SD	Trauma	n	mean	SD
L 2D:4D	None	36	.961	.031	None	90	.988	.036
	Trauma	49	.959	.025	Trauma	85	.981	.030
	PTSD** ‡‡‡	8	.100	.042	PTSD	21	.989	.032
	Total	93	.963	.031	Total	196	.985	.033
R 2D:4D	None	41	.963	.033	None	117	.988	.035
	Trauma	56	.961	.024	Trauma	107	.982	.032
	PTSD * ‡	8	.987	.037	PTSD	24	.982	.022
	Total	105	.964	.030	Total	248	.985	.033
mean 2D:4D	None	27	.962	.029	None	86	.990	.032
	Trauma	39	.961	.023	Trauma	78	.979	.030
	PTSD ** ‡‡	5	.999	.032	PTSD	17	.984	.022
	Total	71	.964	.028	Total	181	.985	.031

* p<.05, ** p<.01 (PTSD vs none)
‡ p<.05, ‡‡ p<.01, ‡‡‡ p<.01 (PTSD vs trauma)

In males, significant effects were found for left digit ratio [$F_{(2,92)}$=6.933, p=0.002] and mean (both hands) digit ratio [$F_{(2,70)}$=4.605, p=0.013] while the right digit ratio approached significance [$F_{(2,104)}$=2.644, p=0.076]. Planned comparisons revealed that the difference was due to the PTSD group having higher, or less male-like, digit ratios when compared to either of the other groups (Table 7.4).

The male PTSD group was compared to female digit ratios, using a series of one sample t-tests against the mean female value (0.985 in each case). The values, in each case, were not significantly different (left 2D:4D: [$t_{(7)}$=1.006, p=0.348]; right 2D:4D: [$t_{(7)}$=0.113, p=0.913]; mean (both hands) 2D:4D: [$t_{(4)}$=0.964, p=0.390]). Figure 7.2 indicates these relationships for the mean (both hands) 2D:4D (as typical also of right and left hand 2D:4D).Findings were opposite to those predicted by hypothesis 2 and instead raise interesting questions, as it seems that males with PTSD have a more female-like digit ratio.

Figure 7.2 Mean digit ratios (by sex) in relation to trauma exposure (error bars show 95% CI of mean)



7.4 Discussion

There were more females than males in this population. The incidence of left handedness (for writing) at 10% in this population is comparable to other findings of around 10% in the general population (Coren, 1992). The incidence of current PTSD in this ostensibly healthy population, at 10% of the sample is similar to the estimated lifetime prevalence of 7.8% found in the (US) National Comorbidity Survey (Kessler et al., 1995). This study did not find the expected sex difference in prevalence of PTSD, probably due to a low incidence of rape and sexual assault in this sample.

7.4.1 Digit ratios

This study found the typical sex difference of lower digit ratios in men compared to women. However, in 200 of the original participants the scanned images of their hands were unusable. This occurred for a variety of reasons (see Appendix 18) most of which would have pertained if photocopies, rather than scans had been taken of participants' hands. The inclusion of older, and married, adults in the science centre sample generated particular problems and accounts for the greater number of right hands included in the sample. Importantly, these measurement difficulties do not appear to have previously been reported in the literature in relation to measuring the 2D:4D from scanned or photocopied images. *In vivo* measurement, using calipers, may be a more suitable method, to avoid some of these difficulties, but does not address the issues in relation to the wearing of rings on the fourth digit. This will no doubt have biased the science centre sample towards exclusion of married women and men. This issue is not likely to be relevant in relatively younger populations, such as the majority of a university sample or in children.

7.4.2 Digit ratio and lateral preference

Hypothesis 1 predicted that lower digit ratios would be associated with increased left handedness. Evidence in support of the Geschwind-Galaburda hypothesis that levels of *in utero* testosterone are related to left handedness has not been consistent in the literature. Use of the 2D:4D as a more direct measure indicative of levels of *in utero* testosterone in this large, adult, sample did not find any relationships between 2D:4D and left hand preference. While genetic theories remain inadequate in explaining origins of left handedness, it would appear that there is little evidence for explanations invoking levels of *in utero* testosterone on brain development and organisation as a cause of left handedness either. While positive correlations were evident between digit ratios and both foot and ear preference in the whole sample, this relationship disappeared in the male sample when males and females were considered separately. This suggests that only in the female sub-sample were higher levels of testosterone (indicated by a low digit ratio) associated with leftward foot and ear preference. There does not seem to be an obvious explanation of why this should be so. Relationships were not highly significant ($p< 0.05$) and would benefit from data collection in another similarly large sample to examine the robustness of this finding.

7.4.3 Digit ratio and PTSD

Hypothesis 2 proposed that in males, low digit ratios indicative of high levels of testosterone, would be associated with PTSD, but instead an unexpected finding, opposite to that proposed, emerged. This study consistently found, for right and left hands, strong relationships between high 2D:4D values in males, indicative of low *in utero* and adult testosterone levels (Manning et al., 1998), and fulfillment of diagnostic criteria for PTSD. This suggests males with PTSD are showing a *female-like* digit ratio implying exposure to levels of testosterone *in utero* similar to that found in the female group. Indeed, there was no significant difference between the mean digit ratios of left, right (and both) hands in males with PTSD compared to the respective female mean digit ratio.

This must be considered a tentative finding in view of the small size of the PTSD group. There are other indications, however, that men with higher digit ratios may exhibit more female-like behaviour. Relationships with *in utero* testosterone assayed in amniotic fluid (rather than with sex) were found with various behaviors relevant to social development such as amount of eye contact; *in utero* testosterone correlated negatively with vocabulary size (Knickmeyer & Baron-Cohen, 2006) and with quality of social relations in these children when four years old (Knickmeyer et al., 2005). In a study examining the ability of childless males to generate the prosody of child-directed speech, Kempe et al (2004) found the degree to which young men displayed these prosodic adjustments was related to high digit ratios (indicative of low prenatal testosterone). The prosodic features of child-directed speech are considered not only important in regulating the child's affect and facilitating of their development, but also as a signal of emotional responsiveness and empathy in the caregiver. Lutchmaya (2004) found that *in utero* testosterone is related to circulating testosterone in the child; it is not clear how far this is true for the adult. Nevertheless, and of possible relevance to PTSD, studies have found that a single dose of testosterone administered to healthy females, diminishes preconscious selective attention to threat but not consciously experienced anxiety (van Honk et al., 2005) and reduces fear-potentiated startle (Hermans et al., 2006). The latter suggest that testosterone may mediate sex differences in fear; this may be a factor relevant to the higher prevalence of PTSD in women. If the current finding is replicated in a larger sample, this might suggest a new direction for research into sex differences in PTSD.

Although sex is normally treated as a male/female dichotomy, it is likely, as in the overlap of values of 2D:4D between males and females (Figure 7.1), that many sex-related characteristics are continuously variable rather than dichotomised. Research on gender and PTSD is presently focused on differences between males and females - in fields such as neurobiology (e.g. Rasmusson & Friedman, 2002), psychophysiology (e.g. Peirce et al., 2002) and cognition (e.g. Tolin & Foa, 2002) - that may explain their apparent differential predisposition to PTSD once exposed to a trauma. The present finding suggests as a hypothesis to be tested, that men who develop PTSD may, at least in some respects, be more female-like, and that perhaps the *in utero* hormonal milieu may be affecting development of the central nervous system differentially to affect subsequent risk for PTSD.

7.5 Replication in a further sample?

As reported in the second part of Chapter 3, all participants (mainly students) in the experimental studies were screened for PTSD using the PDS self report instrument, and completed the combined handedness inventory. In addition the 2D:4D was measured in these participants, initially using a scanned image, but once the methodological problems became apparent (see above and Appendix 18) a digital caliper was used. Since the finding of an apparently higher digit ratio in males with PTSD in the study reported above was intriguing, the opportunity presented itself for a replication in this second sample, but using only caliper measurements of the second and fourth digit length instead of scanned images. There were 410 participants in experimental studies but not all of these had digit length measured with calipers. Of these 410, 237 had been measured using the caliper and were included in this sample.

It was intended to augment this sample with a second general population sample recruited at the Glasgow Science Centre over another Easter weekend. However, for reasons not understood, this sample turned out to be extremely unusual in terms of a very different prevalence of left handedness between males and females, neither of which approached general population norms, and the remarkable lack of a sex difference in the 2D:4D. The characteristics of the sample are included for completeness in Appendix 19. Since this appeared to be a very unusual and unrepresentative sample this generated concerns about attempting hypothesis testing and generalising from this sample and precluded any meaningful analysis.

For the experimental sample, analysis was performed separately for the digit ratio of each hand and of a combined mean. The same two hypotheses were tested:

Hypothesis 1: a higher level of *in utero* testosterone, indicated by a low 2D:4D, is related to left handedness.

Hypothesis 2: males fulfilling diagnostic criteria for PTSD will have a lower 2D:4D, indicative of higher levels of testosterone, than men who did not fulfil diagnostic criteria for PTSD, but there would be no difference in 2D:4D in women with and without PTSD.

7.5.1 Results

The sample comprised 76 males (32.1%) and 161 females (67.9%). Since left handers were selectively recruited for the Stroop experiments (reported in Chapter 6), the prevalence of left handedness in the total sample was higher than in the general population (30.0%: n=71 out of 237). There were significant differences in digit ratios in males and females, with males having lower 2D:4D values consistent with higher levels of *in utero* testosterone. These results are summarised in Table 7.5.

Table 7.5 Expected sex differences in 2D:4D

	sex	*N*	*mean*	*SD*	*t*	*df*	*p*
L 2D:4D	male	76	.9756	.03163	-2.305	236	.022 *
	female	162	.9853	.02993			
R 2D:4D	male	76	.9732	.03207	-3.167	236	.002 **
	female	162	.9874	.03223			
mean 2D:4D	male	76	.9743	.02857	-3.013	236	.003 **
	female	162	.9863	.02862			

* p<.05; ** p<.01

7.5.1.1 Hypothesis 1: Left handedness is related to lower 2D:4D

Independent t-tests were performed to compare digit ratios in left and right handers; results are shown Table 7.6. There were no significant differences between the 2D:4D in the left hand and the mean 2D:4D, while the 2D:4D in the right hand showed a trend towards significance.

Table 7.6 2D:4D in relation to handedness: only the 2D:4D in the right hand shows a trend toward significance

	handed	*N*	*mean*	*SD*	*t*	*df*	*p*
L 2D:4D	left	71	.9841	.02654	.686	235	.493
	right	166	.9812	.03238			
R 2D:4D	left	71	.9765	.03026	-1.909	235	.058
	right	166	.9853	.03351			
mean 2D:4D	left	71	.9802	.02615	-.700	235	.484
	right	166	.9831	.03023			

In order to test relationships with the measures of laterality, correlations were performed between these and the 2D:4D for right and left hands and the mean (of both hands) 2D:4D. These results are shown in Table 7.7 below and significant correlations highlighted in bold.

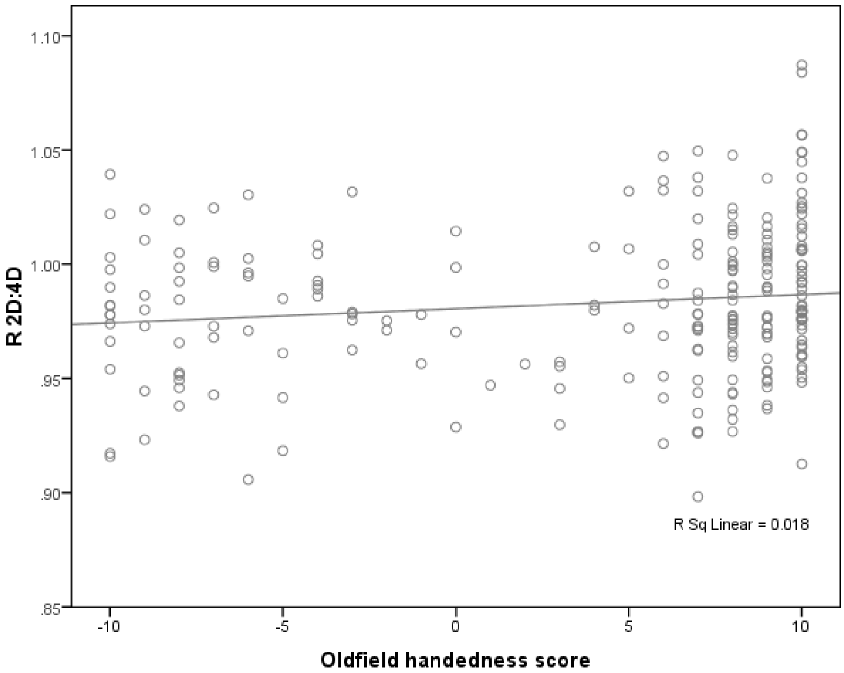
Table 7.7 Correlations of 2D:4D with laterality scores: associations are only significant in the right hand 2D:4D

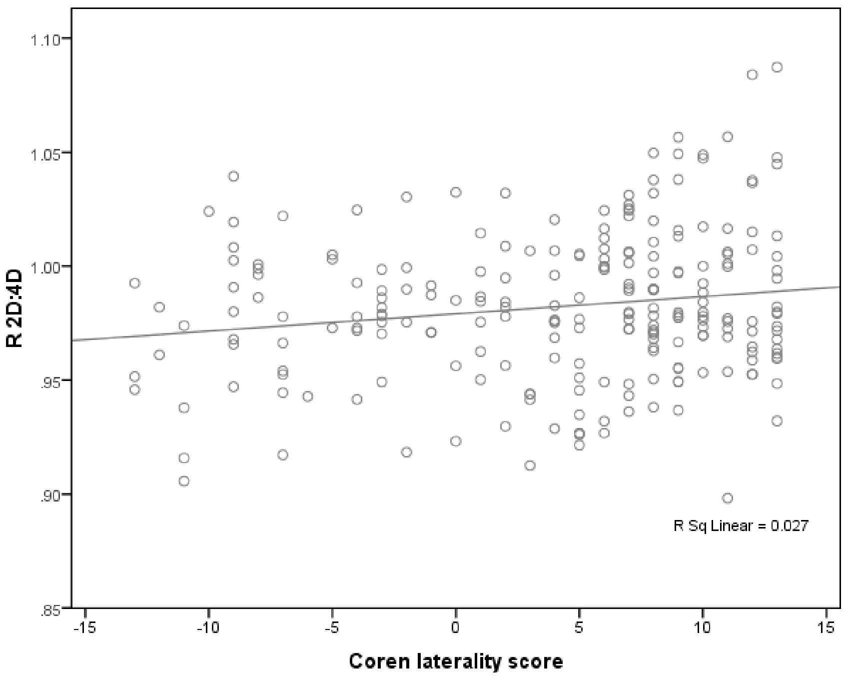
		Whole sample			*Males*			*Females*		
	2D:4D	L	R	mean	L	R	mean	L	R	mean
Oldfield handedness	r	-.009	**.134***	.071	-.007	.104	.053	-.020	.140	.069
	p	.894	.041	.284	.954	.374	.649	.807	.079	.389
	N	233	233	233	75	75	75	158	158	158
Oldfield 12	r	.003	**.141***	.081	.013	.106	.066	-.011	.150	.079
	p	.964	.031	.219	.911	.364	.575	.894	.059	.322
	N	233	233	233	75	75	75	158	158	158
Coren hand score	r	.009	**.150***	.089	.022	.122	.080	-.006	**.156***	.085
	p	.885	.022	.173	.848	.294	.494	.941	.050	.288
	N	234	234	234	76	76	76	158	158	158
Coren foot score	r	.024	**.137***	.090	.126	.171	.165	-.010	.144	.076
	p	.712	.035	.169	.279	.140	.154	.902	.070	.341
	N	235	235	235	76	76	76	159	159	159
Coren ear score	r	.005	.123	.072	.018	.078	.052	-.023	.118	.054
	p	.935	.060	.274	.879	.506	.656	.777	.140	.496
	N	234	234	234	75	75	75	159	159	159
Coren eye score	r	.031	.064	.053	.062	-.049	.008	.020	.123	.080
	p	.635	.328	.417	.597	.677	.944	.802	.123	.318
	N	233	233	233	74	74	74	159	159	159
Coren laterality score	r	.027	**.164***	.107	.078	.108	.104	-.002	**.182***	.102
	p	.686	.012	.105	.513	.364	.383	.982	.022	.203
	N	231	231	231	73	73	73	158	158	158

* p<.05

There are weak positive correlations between overall handedness laterality scores, Coren hand and foot scores and right hand 2D:4D which are significant, but there are no significant correlations of laterality measures with left hand or mean 2D:4D. Since the correlation is positive, this means that higher 2D:4D values indicative of lower *in utero* testosterone levels, are associated with higher, more rightward, laterality scores and leftward laterality scores with higher levels of *in utero* testosterone. This provides some support for hypothesis 1. Figure 7.3 below shows these relationships for right hand 2D:4D. When these correlations were performed separately by sex, Table 7.7 shows that any significant correlations are only found in females and not in males.

Figure 7.3 Scatterplots to show significant positive correlations of right hand 2D:4D with Oldfield10 (above) and Coren13 (below) laterality scores

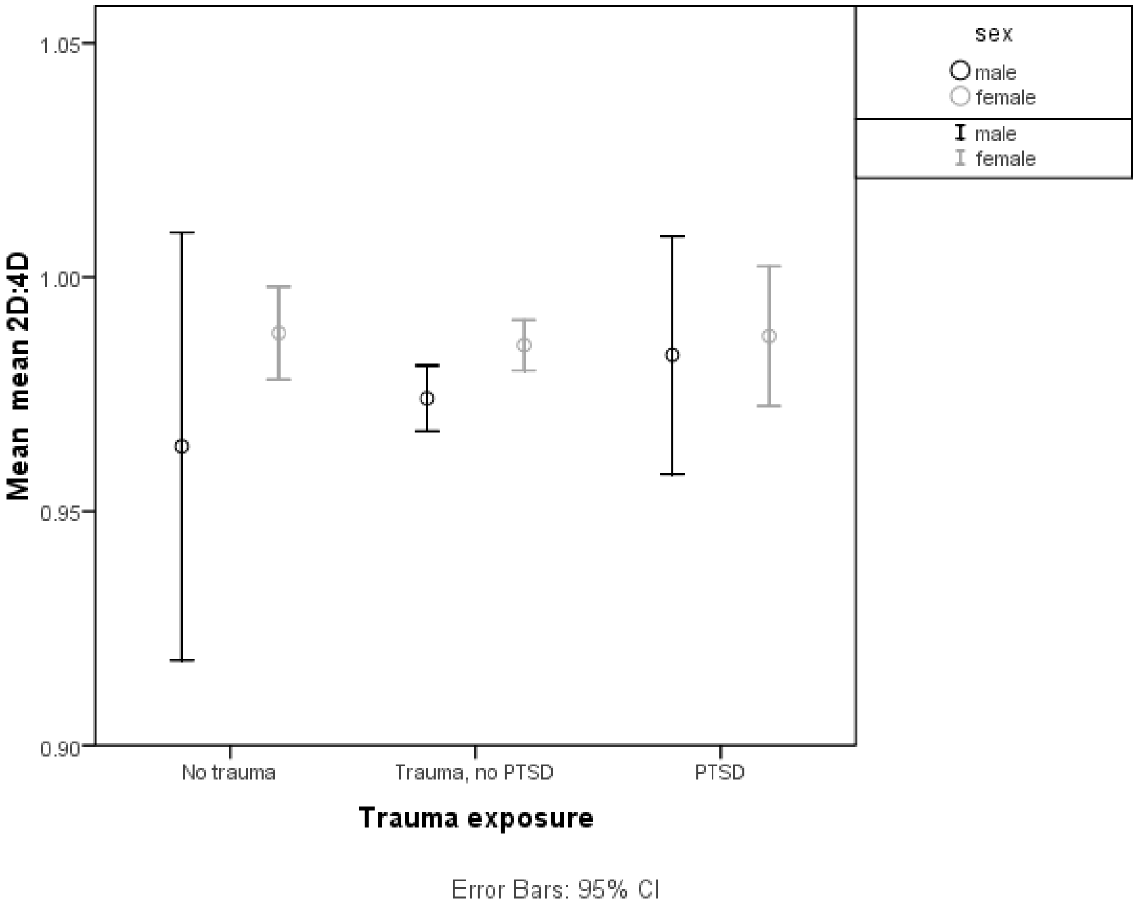




7.5.1.2 Hypothesis 2: Males with PTSD will have a lower 2D:4D

In order to investigate possible sex differences between (a) participants meeting the criteria for diagnosis of PTSD (the PTSD group), (b) those that reported experiencing trauma on the PDS and (c) those that did not, the various digit ratios each formed a dependent variable in a series of one-way ANOVAs with males and females analysed separately.

Figure 7.4 Digit ratios (by sex) in relation to trauma exposure: ns in this replication (error bars show 95% CI of mean).



One way analysis of variance performed on each 2D:4D variable in relation to trauma exposure with the sample split by sex failed to find a significant effect in females (all p>.10) or males (all p>.10) on each digit ratio although the pattern shown in Figure 7.4 (for the mean 2D:4D) is suggestive of the finding reported in the large community sample. That is, the value of the mean 2D:4D in males with PTSD appears higher than for other males (indicative of lower testosterone) and more similar to female values which are more similar across trauma conditions.

Further investigation of relationships between prevalence of PTSD and digit ratio in males awaits a suitably large sample, since this experimental sample numbered only 237 individuals.

7.5.2 Discussion

A further test of Geschwind and Galaburda's (1985) hypothesis of a relationship between levels of *in utero* testosterone and left handedness did not show any significant differences in 2D:4D measures between left and right handers, although there was a trend towards significance for the right hand 2D:4D. There were significant, but relatively weak, correlations in the expected direction between the indicative 2D:4D measure and laterality scores from the handedness questionnaires, but only for the right hand and only in females when analysed separately by sex (which may be possibly to do with the larger female than male sample). This is consistent with other findings that show correlations of this indicative measure of *in utero* testosterone with other behavioural variables of interest only in the right hand (Williams et al., 2000; Williams et al., 2003).

There has been inconsistent and mixed support for this hypothesis from studies of individuals with clinical conditions that are known to have been exposed to abnormal levels of testosterone *in utero*, and the two tests of this association reported in the present chapter show mixed findings. Only in the smaller sample are significant correlations found between right hand 2D:4D and handedness scores, suggesting at face value that this is not due to power issues. However, the smaller sample did include a higher proportion of left handers (30% of the sample) due to the recruitment of left handers to the Stroop experiment and this may mean that high proportions of left handers are required to demonstrate the effect, again suggesting that these relationships, if they exist, are weak relationships.

These very mixed findings from the clinical literature on conditions affecting exposure of the foetus to testosterone levels and the studies reported here suggest that any effects of *in utero* testosterone on brain organisation pertaining to handedness there may be are not large and are insufficient as an explanation of observed prevalence rates of left handedness.

The sample available to test further possible relationships of the 2D:4D with prevalence of PTSD was smaller than intended; while the pattern appears similar to that reported in the first part of this chapter, that is, that males with PTSD seem to show a higher, more female-like digit ratio than males without PTSD, the ANOVA did not produce a significant result. There is other evidence linking female-like 2D:4D in males with depression (measured as trait depression) in a student sample of 298 individuals (Bailey & Hurd, 2005). Since depression has a higher prevalence than PTSD, and since Bailey and Hurd (2005) measured an indicator of trait depression in students rather than clinical depression, this may reflect their sample's greater power to detect relationships. This possible relationship between a high, female-like 2D:4D in males with PTSD remains an intriguing finding awaiting further testing in another, larger, sample.

The failure to find a sex difference in 2D:4D in the Glasgow Science Centre sample (Appendix 19) is not unreported; Hönekopp et al (2006) failed to find sexual dimorphism in this trait in one of their two student samples investigating relationships of digit ratio with physical fitness, and publication bias may operate in under-reporting of such failures. Nevertheless, mixed and contradictory findings are not unusual in the literature attempting to relate the 2D:4D to other putative sex-hormone mediated behaviours and replications often produce mixed findings as is the case here.

Putz et al (2004) pose the question of how the 2D:4D can be a predictor of sex hormone levels and yet fail to be consistently related to many traits that depend on sex hormones for their development? However, although Manning et al (1998) found a significant correlation between 2D:4D and adult levels of circulating testosterone, but only in males, an attempted replication failed (Neave et al., 2003). Putz et al (2004) suggest that if it turns out that there is no consistent relationship between 2D:4D and circulating testosterone, the 2D:4D may represent only the levels of sex hormones that were present when digit length differentiates in males and females. Since sexually dimorphic traits differentiate at different stages in development, then although they each depend on sex hormones, they may remain uncorrelated if their developmental timing differs. It therefore seems that further investigation is required to be certain of what the 2D:4D signifies.

Chapter 8

General Discussion

This studies presented in this thesis are an eclectic mix in terms of experimental approach and theoretical backgrounds. The unifying and underlying theme is of lateralisation phenomena in relation to trauma and the fear response. This is examined theoretically in the Introduction (Chapter 1). An historical perspective shows that aspects of the disorder, named as PTSD only in the DSM-III (1980), which modern neuroscience techniques are now being shown to be lateralised in the brain, have long been acknowledged by clinicians working closely with those with the disorder. These observations have, like the disorder itself, been subject to periodic forgetting and rediscovery by psychiatry, which like society, is challenged by the idea that randomly occurring traumatic events can so affect the functioning of any individual. Other than gender, there are few differences intrinsic to the individual (and these are only weak predictors: Brewin, 2003) which account for who will develop PTSD following trauma.

8.1 General observations

This thesis does not use neuroscience techniques in its experimental work, but its hypotheses are framed by these findings and they set the context for the conclusions which may be drawn from experimental results presented here. This is important as converging findings from different approaches are more likely to reflect robust phenomena. The core concern of this thesis is with apparent differences between left and right handers, not just in prevalence of PTSD, but also in deficits that are consistent with those observed in PTSD and which involve lateralised functions in the brain. These relate to the experience of emotion, specifically fear, in which the right hemisphere is preferentially involved, and memory functions, particularly those related to verbal processing in which the left hemisphere is preferentially involved. These are important because though PTSD is currently classified as an anxiety disorder, its place in the classification scheme has been questioned since its inclusion in 1980. It seems increasingly apparent that PTSD is fundamentally a disorder of memory: in fear conditioning, which sets up dysregulation of arousal networks, and in the apparent paradox between intrusive, involuntary memories of the trauma, and the inability to remember, or at least to verbalise, key aspects of the trauma.

8.2 Methodological issues

The issue of handedness involves methodological problems not just related to the relatively low prevalence (10%) of left handedness in the population and these are discussed in Chapter 2, along with the other methods used throughout the study to identify individuals in ostensibly healthy populations with possible PTSD. In everyday use of the term, handedness is defined by the preferred hand used for the fine motor task of writing and is treated as a categorical variable. As researchers have tried to examine handedness as a continuous measure, critiques of their methods have exposed the inherent confounds between strength and direction of handedness, often unacknowledged and ignored by researchers outside the handedness field using their measuring instruments. This is particularly so in attempts to define “strong” and “weak/mixed” handers. These distinctions can only be arbitrary, and the work presented here suggests that hand use for writing (and not foot, ear or eye preference) is sufficient to define groups that are significantly different in relation to PTSD prevalence and symptomatology. The problems of sample sizes remain: the samples used here illustrate the magnitude of the research effort required to demonstrate appropriate associations of variables and null findings in smaller samples are perhaps to be expected rather than of importance.

Another important methodological point relevant to the work here is that the study of emotion, only relatively recently enjoying a resurgence of research interest, is best served by treating each emotion separately, as they have different physiological and neural circuitry underpinnings. Much has been learned in respect of fear by this approach, contributing directly to understanding of PTSD. If laboratory research is to further clarify processes involved, then it too must approximate the particular emotion concerned: in this case fear. It is not sufficient to consider "emotion" in general not least because, as Lazarus (1964) points out, physiological end points may arise from different processes. What matters is manipulation of the psychological *mechanisms* (processes that occur between stimulus and response) by which these effects are produced. These considerations have been applied here in using a fearful film as a laboratory analogue of fear for the experimental studies presented in this thesis.

8.3 Left handedness and PTSD

In respect of relationships of handedness with PTSD, the starting point for this thesis was findings in two papers in male Vietnam combat veterans (Spivak et al., 1998; Chemtob & Taylor, 2003) that suggested that an increased prevalence of PTSD was associated with a mixed pattern of hand preference rather than a consistently right handed preference. The first experimental chapter (Chapter 3) extended these findings to a large community sample, of students and members of the general public, including women. Low population prevalence rates of left handedness will always make analysis of variables of possible relevance problematic (Bishop, 1990a) and sample sizes in the earlier studies had precluded inclusion of left handers, hence the limitation of the finding to “mixed” handers. The use of this large (N=596) sample included sufficient left handers, and extended findings to suggest that it is the leftward bias towards left handedness, rather than “mixed” handedness patterns, that are associated not only with prevalence of PTSD, but also with symptom severity. Prevalence rates of PTSD in left handers at 15% was almost double that found in right handers at 8%. Differences in laterality scores between the PTSD group, and both trauma exposed but with no PTSD and no trauma groups showed medium effect sizes of just over .40 (Cohen, 1992). Differences in symptom scores between left and right handers were found in respect of arousal and avoidance scores and were at a higher level of significance for arousal symptoms, which are those increasingly thought to be at the core of the disorder and that differentiate those with the disorder from those without (McFarlane, 1998).

An attempted replication of these effects using a sample compiled from all experimental studies, whose participants also completed the PDS, failed due to insufficient sample size (at N=410) to generate the power required to detect these effects. However, a potentially important finding emerged in relation to the types of trauma disclosed. The large community sample was recruited on an opt-in basis to a study advertised as related to trauma whereas participants completed the PDS as part of experimental procedures in studies that made no mention of trauma and, although according to ethical requirements were aware that they could opt-out of any part of the study, none did so. Significant differences emerged in this experimental sample with higher reporting of trauma, particularly sexual trauma “missing” in the opt-in community trauma study. This has consequences for methodologies such as the large community samples used to establish likely prevalence rates of PTSD in the population (e.g. Kessler et al., 2005a; Kessler et al., 1994) and is consistent with other evidence that reporting of sexual traumas (which differentially affect more women than men) is avoided when participation is on an opt-in basis. Indeed, the NCS-R identified possible sources of bias (see section 1.3), all of which render the estimates conservative (Kessler et al., 2005a). Consequently, established rates of PTSD (around 8%) are likely to be under-estimates. Kessler et al (2007) also point out that mental disorders are distinct from physical disorders in being most prevalent in youth, rather than later in life; indeed the NCS-R found an apparent increasing prevalence generally in recent cohorts and cites evidence for this being at least in part real rather than a methodological artefact. In this context, rates of PTSD of between 8-10% in the two studies here are not unexpected.

One limitation of the community sample study of Chapter 3 was however, the self-report nature of the instrument on which a diagnosis of possible PTSD was based. Although the instrument has good construct validity and has shown to be reliable and valid against clinician interview and maps directly to DSM diagnostic criteria for PTSD, nevertheless diagnoses were not determined by a clinician. A second, large scale collaborative study, reported in Chapter 4, therefore pooled samples of trauma exposed patients, in whom diagnosis was established (PTSD, other psychiatric disorder or no PTSD) and assessed handedness in these samples by questionnaire. In order to examine the specificity of the relationship with handedness to PTSD, samples of other clinician-diagnosed anxiety disorders (GAD and panic disorder) were included as a control sample.

In this second, clinical, sample left handedness was again found to be significantly associated with increased prevalence of PTSD (81% in left handers compared to 64% in right handers). While it had been hoped to repeat the analysis in respect of strong versus “mixed” handedness, this sample was not sufficiently large (despite N=364, a very large sample in clinical studies) to have sufficient power to detect any effects. An unexpected finding emerged in respect of the other anxiety disorders. While the prevalence of left handedness in the PTSD sample was 13.2%, in the other anxiety disorders it was only 5.1%. This suggests that whatever the mechanisms are by which left handedness and PTSD are associated, they are not the same in these other anxiety disorders; this is potentially of interest as it provides further evidence that PTSD is unlike other anxiety disorders. A limitation of this study was that due to differences in clinician practices there was no uniform measure of symptom severity across samples precluding investigation of possible differences in symptomatology associated with left handers which were established in the first, non-clinical population study.

8.4 Experimental studies: the film and memory

The first experimental study, reported in the first part of Chapter 5, set out to test whether fearful film stimuli are capable of generating both a self-report measure of fear (compared to other emotions) and an ANS response, the SCR, known to be associated with a fear response. Results supported their use as laboratory analogues of fear; all films generated significantly higher self reports of fear (and overall tense arousal) than a dynamic, neutral stimulus. In relation to SCR, there were differences in the way the three films varied significantly from the neutral stimulus.

ANS responses in arousal are reactive (rather than sustained) and this is apparent from visual inspection of the chart tracings of SCR (available in Appendix 16 and Appendix 17) in which peaks of response are seen to be multilayered. In short excerpts (comprising one scene each) from The Shining, mean, maximum and minimum values were raised compared to the neutral film clip, reflecting the emphasis on one fearful experience within each scene. In the longer excerpt from Silence of the Lambs, which contained a segment of the film able to stand alone from the film in respect of the unfolding story, it was measures of SCR variability (standard deviation, peak value and range) that were significantly different to a neutral stimulus. Mean scores hide the peaks and troughs of reactions that unfold over the extended time course of this longer excerpt. The films generated effects for self-reported fear and SCR, but correlations between these two variables although in the expected direction (positive) were not significant.

This experiment succeeded in demonstrating that fear responses, as measured by SCR and self-report, were produced by the Silence of the Lambs excerpt used as a fearful stimulus in experiments reported in the second part of Chapter 5 and in Chapter 6. That a movie can deliver this response is perhaps unsurprising when the techniques used in this excerpt are considered in relation to the mechanisms acting to produce anticipation of danger and threat considered in the introduction to this first part of Chapter 5.

It seemed likely that, since this is a highly rated film, many participants would have viewed the whole film previous to participating; indeed 47% had previously viewed Silence of the Lambs and 53%, The Shining. It was hypothesised that this may have lead to a reduction in fear on subsequent viewing, but neither measure (self-report or SCR) was found to differ significantly. In contrast, in the experiment reported in the second part of Chapter 5, having previously viewed the movie did result in significant attenuation of fear (and overall tense arousal) ratings. It is not clear why these findings should differ for the same excerpt.

The second experiment in Chapter 5 established that there were subtle but significant differences in memory for events in the Silence of the Lambs film when left and right handers were compared on recall and recognition memory tests and on the AVLT, intended as a standard test of verbal memory. Hypotheses that left handers would perform better than right handers on memory for sensory (mainly visual) items and less well on verbal material were supported by a variety of measures from both recall and recognition test of memory, suggesting these are to do with encoding processes, rather than retrieval (since otherwise the support for memory retrieval afforded in recognition tests would be expected to produce different results when compared to recall tasks). These findings are consistent with neuroimaging evidence in people with PTSD which show relative hyperactivation of the right hemisphere and visual cortex and relative hypoactivation of language processing areas in the left hemisphere when people with PTSD are exposed to their trauma narrative (e.g. Rauch et al., 1996), an inherently fearful situation.

This explanation may also be relevant to the unexpected sex differences in memory for the film which emerged opposite to the direction hypothesised and to the literature on sex differences in memory. Females showed poorer recall and recognition memory than males for events of the film on almost all of the measures used, again suggestive of a mechanism operating at encoding. Superior performance of the females on the standard test of verbal memory, the AVLT, suggest that this experimental effect is not due to general memory deficits in the particular females recruited to this experiment.

In other studies of memory using “emotional” material, females have shown superiority rather than inferiority of memory when compared to males (Canli et al., 2002) but these authors, consistent with other evidence, suggest that women, but not men, may use a left lateralised, language based encoding strategy. If language processing is adversely affected in situations of fear, then the encoding strategy used by women, but not men, will also be adversely affected, perhaps explaining their relatively poorer performance on the test of memory used in this experiment. Not only that, but the explanation, based on lateralised responses to fear, is parsimonious in explaining both the sex and handedness effects in memory for events of the fearful film. Thus it can be suggested that the differences observed between left and right handers and, unexpectedly, between males and females, may be explained by the same underlying process: a relative hypoactivation of left lateralised language areas in a situation of fear, as demonstrated in people with PTSD.

This finding is important and intriguing and merits further investigation, to establish whether specifically fear responses do affect verbal processing in women. If they do, this may be an important factor in understanding the distinctive sex differences in prevalence of PTSD. This is another illustration of how “emotional” responses may need to be more clearly defined with respect to specific emotions in order to fully understand the relevant processes involved.

In relation to sex differences, females reported higher subjective ratings of fear (and overall tense arousal) as predicted. These findings accord with evolutionary accounts of why females may experience increased fear compared to males to the same objective risk (Campbell, 1999).

8.5 Experimental studies: emotional Stroop paradigms

In the experiment reported in Chapter 6, an emotional Stroop paradigm which produces robust and distinctively large effects in people with PTSD was adapted for use with the fearful film as a laboratory analogue for the fear experienced in trauma. Findings from this experiment provide converging evidence that the conclusions in respect of handedness and sex differences in memory, may also apply to these results.

After viewing the fearful film, left handers showed overall increased response latency, and a specific interference effect to "general threat" and film-related words compared to right handers, which approached response latency values in people with PTSD to trauma related words. That effects were at a higher level of significance for general threat rather than film-related words is likely due to a conservative, and with hindsight probably unjustified decision to use only words relating to the film that were otherwise *neutral*, and not inherently *negative* as are trauma related words. That significant interference effects occurred to otherwise neutral film words suggests this is an important effect and one that could be expected to be greater if negative film words were used.

Theoretical accounts of the emotional Stroop interference phenomenon have evolved from erroneous conceptions as "attention to threat" occurring at early stages to current views of the effect arising during language processing conflict at the response output stage, as indeed Stroop (1935) suggested; these processes are lateralised to the left hemisphere. Results from the SWRT designed to test whether the words appearing in the Stroop task are processed, rather than ignored, suggest that they are. Scores on correct word recognition and patterns of false recognition (in accordance with the DRM paradigm) do not differ in left and right handers, suggesting that this encoding stage is not where the interference effect arises. However, if it is language processing that is responsible for the Stroop interference effect, and language processing is adversely affected in situations of fear, as rehearsed above, then since left handers already have a relatively more dominant right hemisphere than right handers, this may be preferentially activated and a response to fearful stimuli exaggerated with relatively increased consequent disruption to language processing.

Of particular interest in this respect is the finding that the non-word stimuli, which on the printed page had the general appearance of words, but contained no linguistic content, in contrast to the word Stroop, failed to generate significant main effects of handedness and stimulus type (with respect to valence) and minimal levels of interference *per se* when compared to the word Stroop. This appears to provide more converging evidence that it is language processing that is (1) involved in the Stroop interference effect (2) compromised in left handers relative to right handers and (3) known to be adversely affected in people with PTSD in fearful situations.

Further research using a fearful film as a laboratory analogue specifically of fear prior to Stroop tasks while probing these effects using ERP's would seem to be important in clarifying whether these are indeed the underlying mechanisms as suggested here. A within-subjects procedure design is also necessary to confirm that the interference effects observed in the current study are indeed related to the fearful film stimulus. Results here are between–subjects and were compromised by questions of ability and/or motivation to what is an attentionally demanding procedure, in those recruited to the control protocol which was intended to control for effects of viewing the film.

8.6 Testosterone, left handedness and PTSD

The final experimental chapter (Chapter 7) examined one theory of left handedness (Geschwind & Galaburda, 1985) which postulates that levels of *in utero* testosterone may be associated with increased levels of testosterone, using an indicative measure, the 2D:4D. In the large community sample reported in Chapter 3, no support was found for this hypothesis. Contrary to hypotheses in respect of possible associations between levels of high levels of testosterone, risk taking and consequent PTSD, evidence was found that males with PTSD exhibited more female-like digit ratios. Due to small sample sizes in PTSD cells, this finding should be considered tentative, but is consistent with other evidence that testosterone is protective of stress in respect of fear responses. This remains an intriguing possibility for future study, which might focus on populations with diagnosed PTSD to examine its utility as a possible explanatory factor of sex differences in prevalence of PTSD. Indeed, with respect to the Geschwind-Galaburda theory, if testosterone is implicated in left handedness and protective against stress, this generates opposite predictions about left handers than those found: they should be more resistant to PTSD rather than more vulnerable.

The smaller, experimental sample (also reported in Chapter 3 as a replication of the association of left handedness with PTSD) failed to replicate 2D:4D relationships with PTSD due to inadequate power. In addition and contrary to the larger sample, there was some evidence that levels of *in utero* testosterone were related to left handedness, at least in respect of the digit ratio of the right hand which is thought to be more susceptible to the effects of testosterone. This reflects the generally mixed findings in the literature with respect to the 2D:4D and as one commentator observes it may be that the 2D:4D may represent only the levels of sex hormones present when digit length differentiates in males and females (Putz et al., 2004). It seems that further research is required to be certain of the status of the 2D:4D, particularly since the current studies also identified methodological difficulties in measuring the 2D:4D which have not been previously mentioned in this literature.

8.7 Implications for clinical practice

The studies reported in this thesis are distant from clinical practice and hence any clinical interpretations should be made with caution. However, the work of this thesis adds to the evidence base about possible individual vulnerabilities for developing PTSD following exposure to trauma, and suggests that left handedness is an important variable in this context. Perhaps left handers known to have been exposed to trauma should be subject to a more focussed assessment to evaluate whether they are exhibiting symptoms of PTSD; however, being left handed is likely to account for only a small amount of variance in determining exactly which individuals will develop PTSD. The use of left handedness as a variable to be considered not just in relation to other mental disorders besides PTSD but also within psychology, particularly in evaluating how emotional material is processed and remembered would seem to be potentially important. The work of this thesis suggests that treating handedness as a binary variable is sufficient for this purpose, and that handedness, rather than lateralisation of foot, eye and ear, is relevant.

A consideration of the underlying neurobiology in PTSD in Chapter 1 (in section 1.3) discussed differences between fear and anxiety and how any form of exposure therapy may need to balance the re-experiencing of fear in order to potentially resolve the memory of trauma against the possibility that fear mechanisms may prevent extinction and cause disruption to verbal processes. In the light of the experimental findings of this thesis which potentially confirm that conditions of fear may lead to difficulties with verbal narratives, then the use of therapy which engages other modes of expression may be useful. In this context the use of Art Therapy in treating people with PTSD may be beneficial (e.g. Greenberg & van der Kolk, 1987) and may warrant wider use.

8.8 Summary

To summarise, the research work of this thesis has extended previous work in demonstrating that left handedness is associated with increased prevalence of PTSD and greater symptomatology. The experimental work with ostensibly healthy populations of left and right handers suggests that left handers exhibit various differences in memory and emotional Stroop interference phenomena that are reminiscent of deficits identified in people with PTSD and which can be hypothesised as related to deficiencies in language processing which is known to be adversely affected by fear. The question remains about why this should be the case: the rationale presented here so far has been based on relative right hemisphere dominance in left handers (as a group relative to right handers) that may serve to bias responses to threat, since it is the right hemisphere which is sensitive to threat, and to exaggerate biases to hypoactivation of left hemisphere language processing areas in left handers as a consequence.

Chapter 1 briefly indicated that current theories of left handedness are inadequate in accounting for empirical observations and it is to this question that the next and final chapter returns. Evidence is reviewed in relation to the intriguing possibility that left handedness is not just an apparently robust risk factor for PTSD, but may arise from traumatic experience at or around birth which may, at this early stage in development, set in motion the lateralisation effects observed in people with PTSD which become fixed patterns in the developing brain of the neonate. This, like many of the questions posed by the results presented in the studies here, will be further informed by future research efforts.

Chapter 9

Is left handedness linked to trauma at or around birth? A new Birth Trauma Model

There are broadly two types of theory of the origins of predominant right handedness, considered below, and these give rise to different predictions about the incidence of dextrality through history. Theory based on an environmental or social pressure would predict a steady increase in dextrality through history to the present, reflecting more complex societal organisation and tool use. Conversely a biological theory would predict that dextrality will have remained constant over time. The determination of handedness throughout the evolutionary span of human species may at first sight appear problematic; however, there are some sources of evidence that can be examined.

The available archaeological and fossil evidence suggests that mankind's ancestors were predominantly right handed. Amongst man's closest relatives, the subfamily Homininae, the split of first the Gorilla (gorillas) and then Pan (chimpanzee) genera from the Homo genus is thought to have occurred between 8MY – 4MY (million years before the present); this predates the evidence for Homo right handedness. It is now accepted that the human ancestor Australopithecus (extinct from 1.0MY) became bipedal and walked erect approximately two million years before enlargement of the brain occurred and the hands were used to fashion tools (Campbell, Reece & Mitchell, 1999); the popular idea that the human brain and upright posture evolved together is not supported.

Archaeological evidence of fractures in skulls of baboons killed by Australopithecus (in the Pliocene Epoch, 5.3MY – 1.8MY) are consistent with weapons wielded by the right hand in face to face confrontations (Dart, 1949) and asymmetry in the left parietal-occipital regions was already evident in these hominid ancestors (Gundara & Zivanovic, 1968; cited by Levy, 1974). Flakes of stone produced in the making of stone tools from the Pleistocene Epoch (1.9MY – 1.4MY) are suggestive of right handedness in hominid species (Homo habilis and its presumed descendent H erectus) and were consistent with results from experiments conducted with naïve stone makers (Harvard undergraduates) to replicate the processes involved (Toth, 1985).

Written references to handedness in the historical record are rare. Possibly the earliest quantitative record of handedness is reported in Judges 20: 15-16: the mustering of armies by the Benjaminites included 26 000 swordsmen and 700 from Gibeah; "among all these were seven hundred picked men who were left handed; every one could sling a stone at a hair, and not miss" [The Bible: Revised Standard Version]. The specialised left handed slingers in this Biblical population may not represent all left handers in the army but at 3% form a substantial yet relatively rare minority.

Artistic representations of individuals performing unimanual tasks, which likely reflect common practices of the time have also been examined (Coren & Porac, 1977). In over 12 000 works of art, dating back to 15 000 BC, from European, African, Asian and American sources, 92.6% of all scorable instances were representations of right handedness, with no evidence of any trends towards increasing dextrality in more recent samples, or cross-cultural differences. Together these findings argue against a social learning explanation and are suggestive of some form of stable biological basis.

This is not to say there are no cultural pressures on handedness. In eastern cultures where the left side is considered less favourably and used for unclean activities such as bottom wiping (Bishop, 1990a), writing with the left hand is not permitted, as it was not during the last century in western cultures. Underlying preferences for other unimanual tasks are unaffected and when cultural differences are taken into account, the underlying prevalence of left handedness is still found to be around 10% (e.g. Iwasaki, 2000).

The various theories that have been advanced in explanation of (human) dextrality are presented in Table 9.1 and due to pressure of space the details of each are not pursued further here. None have proved satisfactory as explanations of all known facts about handedness, let alone why prevalence of PTSD appears to be related to non-right handedness. Though genetic theories are generally invoked, they face particular challenges, particularly from twin data: “twins continue to show a clean pair of heels to any genetic model” (Corballis, 1997; p716). Alterations to genetic models (eg Annett’s) have occurred to accommodate empirical data, but mechanisms to justify the required alteration are not proposed (Boklage, 1981). Ashton (1982) comments that “these [hypotheses] are notable more for the ingenuity of their alleged fit to an investigator’s data than for their experimental verification” (p125). Table 9.2, which follows Table 9.1, presents the factors which require explanation from any theory attempting to explain handedness.

In considering the factors in Table 9.2, a short digression on the subject of twins may be helpful. There are different types of twins. Fraternal or dizygotic (DZ) twins arise when two eggs implant in the uterine wall at the same time; they are equivalent to brothers and sisters with the same age and may be more common in older mothers.

Table 9.1 Summary of proposed theories of the origin of human predominant dextrality in hand preference

Theory/model	*Summary*	*References*	**Weaknesses**
Warfare shield	better protection of heart – survival value for right handers	discussed in (Bishop, 1990a)	Tenuous advantage; insufficient time since Bronze Age for RH proportion
Cultural learning	learned behaviour + imitation	(Collins, 1975)	no support from adoption studies (Carter-Saltzman, 1980)
Genetic*			**** see also Table 9.2***
2 gene	dominant & recessive alleles; for language and handedness; influences writing posture	(Levy & Nagylaki, 1972)	does not fit evidence on recovery from aphasia; writing posture not indicative of lateralisation (Bishop, 1990a)
1 gene	normal distribution between R/L with added effect from right shift allele (RS+); in RS- language & handedness random; RS+ may be semi-dominant	(Annett, 1972)	several revisions to accommodate data from empirical studies
	two alleles – chance and dextral; neither dominant – effects additive	(McManus, 1984)	frequency of C allele has to be low to accommodate data from empirical studies
Intrauterine environment	testosterone predisposes to left handedness - delays L hemisphere development	(Geschwind & Galaburda, 1985)	mixed evidence in CAH: see Chapter 7; right hemisphere more sensitive *in utero*
Birth stress			
Pathological left handedness	damage to left hemisphere	(Satz, 1972)	distribution of hand preference not affected by lesions identified by ultrasound (Marlow et al., 1989) therefore unlikely
	anoxia at birth: left hemisphere more vulnerable – higher metabolism	(Bakan et al., 1973)	mixed evidence for birth stress factors, irrespective of hypoxia

Table 9.2 Factors which theories of handedness need to explain

Factor	*Comment*	
More right than left handers	this remains to be explained	
Problems for genetic theories to accommodate	no putative gene identified	
	segregation analysis fails to find evidence for a significant major gene or polygenes for handedness	this technique works in other conditions known to have a genetic basis (Ashton, 1982)
	left handed children born to two RH parents (& vice versa)	does not fit simple Mendelian inheritance model (Bishop, 1990a)
Apparent rise in proportion of right handers with increasing age	2 explanations: (1) elimination hypothesis (LH die earlier) (Halpern & Coren, 1988) (2) relaxation of cultural pressures against use of left hand	(1) no evidence using correct statistical method (Bland & Altman, 2005) (2) likely explanation (Hugdahl et al., 1993; Iwasaki, 2000)
(Slight) excess of male left handers over females	Predicted by (Geschwind & Galaburda, 1985)	
	Females more likely to conform to social pressure to switch to right hand	evidence of recent relative increase in n of female left handers (Hatta & Kawakami, 1995)
Left handedness in twins:	pose problems for genetic models e.g. genetic models do not fit large twin sample data (Ooki, 2005)	models have been manipulated to accommodate empirical data (Ashton, 1982) – Occam's razor implications
(1) Excess left handedness in twins	compared to singletons	why?
(2) Similar proportions of left handers in MZ and DZ twins	suggest factor is environmental rather than genetic, as it operates on twins in general rather than according to zygosity	why?
(3) Discordance for handedness in twin pairs is similar in MZ and DZ twins	MZ should be more similar (if not identical) than DZ twins	why? (implies genetic mechanism not simple Mendelian inheritance)
(4) Excess left handedness in chimpanzee (*Pan troglodytes*) twins	compared to singletons	genetic theories have to consider extension to chimpanzees
Recent (30-40 years) rise in left handedness to approx 15%	too rapid for genetic model	why?

Duplicate, identical or monozygotic twins (MZ) arise when a single egg forms a single zygote but this then splits to form two embryos. The timing of this split has consequences. An early split, up to four days post fertilisation, results in embryos each with their own chorion (placenta) and separate sacs (amnion); these are known as dichorionic (MZ-DC) twins. A split later than four days post fertilisation, results in two embryos with a shared placenta and usually separate sacs, known as monochorionic (MZ-MC)[‡]. (Rarely, an even later division may result in a shared amnion – monochorionic monamniotic twins.) The proportions of each in a large survey of twins (808 pairs) found the relative proportions to be 54% DZ, 15% MZ-DC and 31% MZ-MC (Derom et al., 1996). Chorionicity can not be retrospectively determined; placental anatomy must be studied at birth. As a consequence, most studies of twins cannot differentiate these two forms of MZ twins. Similarly, correct determination of zygosity cannot rely on an inspection of the placenta at birth: both DZ and MZ-DC twins have separate placentas. To determine zygosity accurately, a variety of measures is needed, such as, fetal sex (although it is not impossible for MZ twins to be of different sexes e.g. if chromosomal abnormalities are present), structure of foetal membranes as discussed above, blood groups, placental alkaline phosphatase isoenzymes and DNA polymorphisms (Derom et al., 1996).

This is a level of assessment only recently possible; early diagnosis of twins was based on criteria of observational similarity, and finger and palm prints were also considered (Newman, 1917; Newman, 1928a). Newman's (1917) ideas on twins were based on his extensive study of the armadillo (*Dasypus novemcinctus*), which routinely produces

[‡] This has (unrecognised) implications for the classical twin method which invokes an equal environment assumption in all twins. Considering MZ twins alone, clearly, MZ-DC twins may experience subtle differences in their *in utero* environment as a consequence of unshared placentas, relative to MZ-MC twins, introducing an environmental confound even before birth. For a critique of the assumptions of the twin method see Joseph (2004).

quads (four embryos) in a single egg, by a particular pattern of rotational splits. It is from his ideas that the erroneous concept of "mirror-twins" arises.

Excess left handedness in twins compared to singletons is a common finding (e.g. Davis & Annett, 1994; Carter-Saltzman et al., 1976). This in itself requires explanation. Intuitively, genetic theories would expect MZ twins to be concordant for handedness, and they are not. Discordance for handedness is similar in MZ and DZ twins, and there are similar proportions of left handers in both types of twins (e.g. Orlebeke et al., 1996). Prior to Derom et al (1996), no study of handedness in twins had considered chorion type; they found 17% of twins to be left handed irrespective of zygosity or chorionicity. Carlier et al (1996) in a smaller sample (n=79) of twin pairs of known chorion type also found no differences in rates of left handedness between the different types of twin. Newman (1917) had proposed mirror-imaging in twins as a criterion of MZ origin to explain the discordance of handedness in MZ twins, relating it to *situs invertus*, the rare occurrence of inversion of the viscera, or internal organs. This idea has been uncritically invoked for decades (Boklage, 1981) and persists in the literature. In a study of *situs invertus* based on the mass radiography of (90% of) the Norwegian population, no relationship was found between *situs invertus* (occurring in 0.011% of the population) and twinning or handedness (Torgersen, 1950). Derom et al (1996) conclude that "the belief that discordant handedness in MZ twins represents mirror-imaging is mythical" (p408).

Related to this issue is the matter of hair whorls. Newman (1917) takes from a case study of the convolutional pattern of the brain in a pair of stillborn supposed MZ twins mention of the hair whorls (on the crown of the head) which were *on opposite sides of the midline*, as a highly significant factor:

> "Were there no other evidence of the monozygotic character of these twins, this condition of the hair whorls would go far to prove it." (p168).

Later (Newman, 1928b), the focus of attention has shifted to the *direction* (clockwise/anticlockwise) of hair whorl rotation; this was considered, along with handedness and head size, in a descriptive account of a series of 50 pairs of (supposed identical) twins, still working from the assumption of mirror-imaging as the basis for asymmetry in MZ twins and an indication of that status. The majority of the population has a clockwise hair whorl (viewed from behind the head); in about 10% the direction is anti-clockwise. The latter was therefore taken as an indication of "asymmetry" and considered along with handedness; no clear patterns can be discerned in the data presented.

These unwarranted assumptions are repeated even in recent work proposing a genetic model linking handedness and hair whorl (Klar, 2003). On the basis of an unobtrusive observational study of hair whorls (which can only be readily observed in short haired males) in 500 members of the unsuspecting general public in a shopping mall, finding clockwise whorls in 91.6%, and the fact that 10% of the population is left handed, Klar (2003) assumes that:

> "Because the predominant proportion of individuals in the general population both in our sample and in an earlier study [reference] are expected to be RH [references], it follows that most RH exhibit a clockwise pattern." despite the earlier statement: "Due to large sample size, collecting the data on their handedness as well as sex was impractical." (p 271)

As a second test of the predictions of his random recessive model, Klar (2003) in an (undefined) sample of 23 individuals chosen for anti-clockwise hair whorls, finds 11 (approximately 50% - the prediction of his model) are non right handed. He states:

> "Therefore, these two results establish that, like hair whorl rotation, handedness is a genetically determined trait. Thus, it is an

> inescapable conclusion that hair-whorl direction and handedness share a common genetic mechanism." (p272).

This sentiment is repeated in the abstract:

> "The cause of handedness and its relation to the biologically specified scalp hair whorl rotation is determined here. …. These findings of coupling in RH and uncoupling in NRH unequivocally establish that these traits develop from a common genetic mechanism" (p269).

A more recent study used neuroimaging to determine language lateralisation, in addition to measuring handedness and direction of hair whorl *in the same population*, a sample of 1212 individuals (Jansen et al., 2007). They found that 81.5% had typical clockwise hair whorls, 11.5% were left handers and, in a smaller sub-sample (n=225) in whom language dominance was assessed, 76.9% had left-hemisphere language dominance, all findings consistent with other literature. However, when relationships between these factors were assessed, there was no evidence for any of the associations between hair-whorl direction and either language dominance or handedness expected by Klar's model and the authors state: "Our results unambiguously show that the predictions of [Klar's] random-recessive model have to be disapproved" (p858).

There is another common misconception about left handedness indicated in Table 9.2 that deserves further mention here. Some reports claim early mortality in left handers (Halpern & Coren, 1988; Coren & Halpern, 1991; Aggleton et al., 1993) but Bland & Altman (2005) point out a common error in such studies considering lifespan. When a cohort of people born recently is considered, only early deaths are included; the long-lived are still alive. In a cohort born a long time ago, there is time for all of them to have died and both long and short lifespans will be included. Anything that is related to birth cohort, that is, any factor which changes over time (in this case such as relaxation of cultural pressures against use of the left hand) will be related to lifespan in the sample. Unless the correct statistical correction is used, it is possible to conclude that nursery education is more dangerous than paratrooper training, since the mean age at death is lower in the former than the latter (Rothman, 1991). When the correct survival technique was applied to the data of one of the above studies, the apparent relationship was not found (Aggleton et al., 1994).

To return to the issue of possible causes of left handedness, other authors have questioned genetic models. An investigation of possible links between left handedness and specific speech and language impairment, using twin studies found no evidence that left handedness was associated with impairment, nor was there any fit with genetic models for handedness data (Bishop, 2001). It seems that there is no adequate explanation for all of the issues identified in Table 9.2.

A reconsideration of the birth stress hypothesis is therefore suggested here. Previous explanations have proposed either pathological left handedness arising from insult to the brain (Satz, 1972) or hypoxia (Bakan et al., 1973). Both of these are mechanisms which will presumably occur in some individuals and can be measured by handedness performance measures, but are unlikely to account for all instances of left handedness.

The argument proposed here, in line with emerging comparative evidence (*qv*) is that across species, the default pattern is for right "handedness" and that predominantly environmental factors act to change this pattern. This is also consistent with evidence that, in terms of brain organisation, the left hemisphere is superior in motor control per se, irrespective of handedness (Pollok et al., 2006). In a reformulation of the birth stress hypothesis, it is proposed that this switch occurs via mechanisms in response to stress and events specifically traumatic to the neonate occurring at or around birth. This hypothesis, referring to "birth trauma" to differentiate it from earlier "birth stress" hypotheses, is offered as it provides a mechanism to explain the relationship of non-right handedness with PTSD, and all of the other factors identified in Table 9.2. Other evidence which supports the basis for this hypothesis is outlined here.

There is emerging evidence of many examples of species, across different classes, in which right side preference occurs, particularly for precision movements. Examples include amphibians: toads (Bisazza et al., 1995), reptiles: most species of lizards (Seligmann et al., 2003), birds: chicks use the right foot preferentially in searching for food and mammals: in male deer (*Dama dama*) the right antler is used more for combat (Alvarez, 1995). This argues against claims of human uniqueness in being (predominantly) right handed (e.g. Levy, 1974; Annett, 1985; Bishop, 2001). However, in four legged animals there may be less scope to develop preference where use of only one limb to perform a manipulative task is not unusually required. In non human primates, evidence for right hand preference in the skilled manipulation in food gathering has been found in gorillas (Byrne & Byrne, 1991) and bonobos (Hopkins & de Waal, 1995).

In chimpanzees, there is mixed evidence. Studies of wild chimps have generally observed no consistent preferences in handedness (e.g. Marchant & McGrew, 1996; McGrew & Marchant, 2001), but captive chimps, performing skilled precision tasks, have been consistently found to show population right hand preference (e.g. Hopkins et al., 2003; Hopkins et al., 2002). These differences may be explained by the nature of the tasks involved and Bishop's (1990a) observations that it is likely that precision movements will be the most likely to show preference effects; co-ordinated bimanual tasks in great apes do exhibit stronger hand preference than simple reaching tasks

(Hopkins, 2006). In addition, excess left handedness is also found in chimpanzee twins (Hopkins, personal communication).

There is also evidence, consistent across at least vertebrate species, of structural and functional lateralisation of the brain (Vallortigara et al., 1999). As mentioned in section 1.3 above, in all vertebrate classes the right hemisphere is associated with escape, attack and sexual behaviour (Vallortigara & Bisazza, 2002). This is consistent with relative hyperactivation within the right hemisphere in people with PTSD when reliving their traumatic experience and simultaneous relative hypoactivation in the left hemisphere, particularly Broca's area. This will be further considered below when possible mechanisms are considered.

It is hypothesised that, instead of considering all general medical risks, as some previous studies of birth stress have done, with mixed support for associations with higher rates of left handedness (e.g. Coren et al., 1982; Nachshon & Denno, 1987; Searleman et al., 1989; O'Callaghan et al., 1993; Powls et al., 1996; Bailey & McKeever, 2004), what matters is the events experienced by the neonate directly. It is possible that some of these may operate during pregnancy, particularly where the mother is stressed, as changes in her stress hormone levels, for example, may influence the *in utero* environment of the developing baby. For example, studies using rats have found that *in utero* exposure to antidepressants has profound consequences on the development of the serotonin system and associated neuronal processes in the developing embryo with long lasting neurobehavioral consequences (Maciag et al., 2005). Factors occurring during pregnancy are more difficult to study, particularly since the embryo may be at least eight weeks old before a pregnancy is discovered. Several studies in humans have found that adverse events and maternal stress in pregnancy are associated with subsequent infant distress: more crying during at least the first six months of life (Wurmser et al., 2006) and increased distress to novelty at four months of age (Mohler et al., 2006). In the latter study, maternal postnatal psychopathology was not so linked. A review also suggests that maternal stress during pregnancy is also associated with greater risk of premature labour (Mulder et al., 2002), thus adding to the risk for the neonate.

In a normal birth, the neonate will be delivered without significant difficulty and mother and child will be together and allowed to form bonds of attachment. In some cases interventions may be required during the birth process, but the neonate is still delivered without harm and stays with the mother in the neonatal period. In other cases of intervention, and particularly in premature babies and twins (who are often premature also and have more obstetric complications than singletons (Siddiqui & McEwan, 2007)) this may need to be more aggressive and the neonate may not be immediately viable without support, or may require monitoring. Twins vary by birth order and this has implications for the birth process. Twin I, especially if born to a primagravida may face risks of more trauma, whereas twin II, whose placenta, irrespective of zygosity, will start to come away as twin I is born, faces greater risks of hypoxia during the birth process. Twin I has a clean passage through the birth canal, but twin II's passage is contaminated with blood and possibly meconium from twin I. Twin II is therefore generally at greater risk of mortality, and any interventions may need to be relatively more aggressive.

If neonates are cared for in some form of intensive care unit (NICU), they will be physically separated from their mother, be incubated and held infrequently, attached to various monitoring devices or more intensive life support devices, such as ventilators, may have intra-venous drips in place, are likely to be fed via a naso-gastric tube, if not intra-venously, and blood will be regularly collected (by heel prick) throughout a 24 hour period for monitoring purposes. Their environment has high noise levels and constant bright light. This is irrespective of any surgical or other invasive procedures, such as intubation, required. (See Perlman (2001) for a full discussion of risk factors in Very Low Birth Weight infants.) It is suggested that events of this kind, particularly in the absence of direct contact with the mother, will be particularly likely to be experienced as stressful by the neonate, resulting in very early and repeated activation of the right hemisphere and initiation of the fear response with all the lateralised consequences discussed earlier in relation to the neurobiology of trauma. These may exert greater and long-lasting effects on the early developing brain; animal studies suggest this is possible.

In infant rats, incubated away from their mother for between 1-24 hours, there was potentiation of the stress response to a novel test (novelty stress) the magnitude of which was related to the length of deprivation, and this was found to be due to the absence of the mother rather than to nutrient deprivation (Stanton et al., 1988). This is consistent with other evidence of maternal regulation of infant physiology, particularly suppression of HPA-axis responses and lowered cortisol (Hennessy et al., 1988).

Rat pups which are repeatedly handled, and/or separated from their dam show altered responses to stress, which can be traced to alterations specifically to the neural circuits involved in the experience of negative emotion discussed in section 1.3 above (Card et al., 2005) and lifelong attenuation of the stress response via reduced CRF expression (Fenoglio et al., 2006). Sensitisation of the fear and defensive responses can be viewed as an adaptation to immediate stress and adversity as they initiate survival mechanisms, as outlined in section 1.3, and thus can be seen as a natural and predictable consequence of early adversity throughout different species, but changes as a result of early neural plasticity through altered regulation of gene expression come with potential long term consequences (Zhang et al., 2006) as these are similar to the alterations to the HPA-axis seen in people with PTSD. These authors argue that development is essentially a process of adaptation that enables the individual to survive in the absence of parental support; increased sensitisation to danger makes sense in this context. They suggest that across all species, there is a common theme: exposure of the mother to environmental adversity alters the infant-mother interaction which in turn affects infant responses to threat (Zhang et al., 2006).

In the human neonate there are several strands of evidence that may be relevant to the hypothesis proposed here. Preferential stimulation of the right rather than late developing left hemisphere (described in section 1.3.1 above) may be sufficient in some for a transfer of language to the right hemisphere which is known to be more common in left handers than right handers. Even if language is not transferred, preferential motor control may transfer to the right hemisphere. Using films of neonates in observational studies, utterances of “protoconversation” were accompanied by raised right hand gestures; when subjected to a mild stressor, such as the presence of a stranger, this pattern changed, either withdrawal and self touching with the left hand and/or raised left gestures were observed in young normal infants (Trevarthen, 1996). It is suggested here that exposure to multiple stressors may create early motor programs that result in a switch to preferential use of the left hand for subsequent hand use; that this may not be a complete switch is reflected in the greater diversity in consistency of handedness observed in left handers, categorised on the basis of writing, a precision, skilled movement.

Until relatively recently, it was a common view that neonates, especially those born premature, were too young to perceive or remember pain in the same way as children and adults (Qiu, 2006). Increasingly methods such as measures of skin conductance (Harrison et al., 2006) or salivary cortisol (Neu et al., 2007) are being used alongside or instead of “pain-coding scales” that have attempted to measure pain using behavioural criteria such as crying and facial expressions, and neuroimaging techniques (near infra-red spectroscopy) suggest that there is cortical activity in response to painful stimuli in even premature babies (Qiu, 2006). NICU neonates have been found to have higher baseline salivary cortisol levels than healthy full-term babies, and in response to nappy changes had higher behavioural pain responses and a higher peak in cortisol response and which returned to baseline more slowly than healthy controls (Morelius et al., 2006); clustered nursing care (concentrating necessary procedures rather than spacing them over time) was also found sufficient to generate ACTH and cortisol responses in preterm babies, while some infants seemed to be showing down-regulation of the HPA-axis (Holsti et al., 2007). Other studies have found changes to HPA-axis functioning in very preterm babies related to frequency of heel pricks (e.g. Grunau et al., 2004; Grunau et al., 2005). Later testing of infants, at 3 months (corrected for gestational age), found lower levels of baseline cortisol in preterm compared to term infants (Haley et al., 2006); this may represent a similar change to baseline cortisol observed in some people with PTSD (e.g. Yehuda, 2002). Similarly, skin conductance responses indicated sensitisation to pain, such that routine tactile stimulation produced physiological stress responses as high as to nociceptive stimulation in preterm newborns, even though behavioural responses were greater to pain (Hellerud & Storm, 2002).

Table 9.3 Trends which are predicted by a birth trauma model related to left handedness

Prediction	*via*	*outcome*	*Evidence*
A) Decreasing peri-natal mortality in:		increases in relative proportions of A1 & A2 in all births	
1) multiple births	improvements in neonatal care	more survivors of high levels of birth stress and peri-natal interventions	(Glinianaia et al., 1998); (Platt et al., 2001)
2) premature neonates	improvements in neonatal care	more survivors of high levels of birth stress and peri-natal interventions	Fig 1: (Alexander & Slay, 2002); (Cooke, 2006); (Colvin et al., 2004)
leading to relatively higher rates of left handedness in:			
3a) premature infants			(Marlow et al., 1989); (Marlow et al., 2007)
3b) extremely/very low birth weight infants			(O'Callaghan et al., 1993); (Powls et al., 1996)
B) Increasing rates of multiple births	Assisted conception techniques since Steptoe & Edwards (1978)	multiples have increased: risk during pregnancy and birth; neonatal care interventions	(Glinianaia et al., 1998); (Platt et al., 2001)
C) Increasing rates of left handedness in recent cohorts	all of A & B above	≥15% left handedness in recent cohorts	(Hugdahl et al., 1993); (Orlebeke et al., 1996); (Iwasaki, 2000)

In relation to these factors, a series of trends that would support the basis for a birth trauma model are outlined, with supporting evidence for their existence, in Table 9.3. Although general factors, these are all consistent with possible associations with left handedness.

There also appear to be transgenerational effects due to maternal influence in relation to stress. Findings of lower baseline cortisol in Holocaust survivors with PTSD (Yehuda et al., 1995) is perhaps not surprising, but lower baseline cortisol was also found in their offspring, and constituted a risk for PTSD (Yehuda et al., 2000). Similar low baseline cortisol levels have been found in the offspring of mothers pregnant when exposed to the events of 9/11 who developed PTSD (Yehuda et al., 2005). These mechanisms may also explain how left handedness can appear to be familial, and appears to be particularly related to maternal left handedness (e.g. Orlebeke et al., 1996). Familial traits can just as likely reflect shared environmental factors as shared genes, and are not considered as direct evidence of a genetic effect (Joseph, 2004). Offspring handedness is also influenced by maternal handedness in the genus *Pan* (chimpanzees and bonobos; Hopkins, 2006)

Perinatal stress in the sense discussed above may not just affect susceptibility to PTSD in the future lives of these neonates (Batstra et al., 2006). Section 1.3 has indicated how dissociative responses as a result of child abuse are linked to dissociative and personality disorders. Models of very early stress are being used to model later development of schizophrenia (Ellenbroek & Riva, 2003), in which early trauma is being recognised as important in the aetiology of this disorder (De Loore et al., 2007; Zornberg et al., 2000; Cannon et al., 2002) and as contributing to diathesis, rather than stress (Read et al., 2001; Rapoport et al., 2005) and which may also be associated with a relative increase in non-right handedness in those with the disorder (Satz & Green, 1999; Cannon et al., 1995; Green et al., 1989; but see Byrne et al., 2004; Buijsrogge et al., 2002).

The birth trauma hypothesis also has the benefit of offering an explanation for why left handers may be at risk for later PTSD. Exposure to previous trauma is known to be one of the more potent risk factors for PTSD. If trauma at birth has gone unrecognised, other than to result in changes in lateralisation, then this may be why left handers are more susceptible.

The experimental work examining differences between left and right handers in memory and using the Stroop paradigm, suggests that left handers, in a variety of ways compatible with what is known about the lateralisation of structures and functions implicated in PTSD, are behaving like people with PTSD. It will be necessary to replicate such findings before such conclusions are justified, but this early evidence is suggestive. This theory of early changes in lateralisation, reflected in handedness, which may also be associated with changes in the HPA-axis, also generates testable predictions, about basal cortisol levels (predicted to be lower in left handers) and about specific lateralisation of processes that can be tested with ERP (or neuroimaging) methods.

In addition, the birth trauma hypothesis remains to be empirically tested. It will be important to separate out risk factors during pregnancy or birth that are not traumatic to the neonate (for example, mothers age - at either extreme - is considered a medical risk factor) from those at or around birth that do directly cause stress and trauma to the neonate. It is hypothesised that the latter, but not the former will be related to left handedness in the developing child. Ideally this would require longitudinal studies through pregnancy, but at least from birth through the first years of childhood until the child's handedness stabilises into a consistent pattern of use. Alternatively, retrospective reports of birth events from the mothers of young children, in whom handedness can be assessed, may suffice, since there is evidence that mothers' reports are consistently remembered and accurate (Reich et al., 2003; Rice et al., 2007).

In summary, the findings of this thesis raise interesting questions, which may help in further understanding how and why it is that some people develop PTSD after exposure to trauma.

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Appendix 1 The Posttraumatic Diagnostic Scale (PDS) Foa et al (1991)

1077

Hand-Scoring Answer Sheet

PDS™

Edna B. Foa, PhD

Name or Identification Number

Test Date

This questionnaire asks about past exposure to stressful or traumatic events.

If you feel able to provide this information it would be very helpful for this study. However, if filling in these answers stirs any unpleasant memories or makes you feel distressed in any way, please make use of support available to you:

Contact SISS (Student Information and Support Service) 01786 (46)7080

Or your own GP

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Part 1

Many people have lived through or witnessed a very stressful and traumatic event at some point in their lives. Below is a list of traumatic events. Put a checkmark in the box next to ALL of the events that have happened to you or that you have witnessed.

(1) ☐ Serious accident, fire, or explosion (for example, an industrial, farm, car, plane, or boating accident)

(2) ☐ Natural disaster (for example, tornado, hurricane, flood, or major earthquake)

(3) ☐ Non-sexual assault by a family member or someone you know (for example, being mugged, physically attacked, shot, stabbed, or held at gunpoint)

(4) ☐ Non-sexual assault by a stranger (for example, being mugged, physically attacked, shot, stabbed, or held at gunpoint)

(5) ☐ Sexual assault by a family member or someone you know (for example, rape or attempted rape)

(6) ☐ Sexual assault by a stranger (for example, rape or attempted rape)

(7) ☐ Military combat or a war zone

(8) ☐ Sexual contact when you were younger than 18 with someone who was 5 or more years older than you (for example, contact with genitals, breasts)

(9) ☐ Imprisonment (for example, prison inmate, prisoner of war, hostage)

(10) ☐ Torture

(11) ☐ Life-threatening illness

(12) ☐ Other traumatic event

(13) If you marked Item 12, specify the traumatic event below.

____

IF YOU MARKED ANY OF THE ITEMS ABOVE, CONTINUE. IF NOT, STOP HERE.

Part 2

(14) If you marked more than one traumatic event in Part 1, put a checkmark in the box below next to the event *that bothers you the most*. If you marked only one traumatic event in Part 1, mark the same one below.

☐ Accident
☐ Disaster
☐ Non-sexual assault/someone you know
☐ Non-sexual assault/stranger
☐ Sexual assault/someone you know
☐ Sexual assault/stranger
☐ Combat
☐ Sexual contact under 18 with someone 5 or more years older
☐ Imprisonment
☐ Torture
☐ Life-threatening illness
☐ Other

In the box below, briefly describe the traumatic event you marked above.

____
____
____
____
____
____

Below are several questions about the traumatic event you just described above.

(15) How long ago did the traumatic event happen? (circle ONE)

1 Less than 1 month
2 1 to 3 months
3 3 to 6 months
4 6 months to 3 years
5 3 to 5 years
6 More than 5 years

For the following questions, circle Y for Yes or N for No

During this traumatic event:

(16) **Y N** Were you physically injured?

(17) **Y N** Was someone else physically injured?

(18) **Y N** Did you think that your life was in danger?

(19) **Y N** Did you think that someone else's life was in danger?

(20) **Y N** Did you feel helpless?

(21) **Y N** Did you feel terrified?

Part 3

Below is a list of problems that people sometimes have after experiencing a traumatic event. Read each one carefully and circle the number (0–3) that best describes how often that problem has bothered you IN THE PAST MONTH. Rate each problem with respect to the traumatic event you described in Item 14.

0 Not at all or only one time
1 Once a week or less/once in a while
2 2 to 4 times a week/half the time
3 5 or more times a week/almost always

(22) **0 1 2 3** Having upsetting thoughts or images about the traumatic event that came into your head when you didn't want them to

(23) **0 1 2 3** Having bad dreams or nightmares about the traumatic event

(24) **0 1 2 3** Reliving the traumatic event, acting or feeling as if it was happening again

(25) **0 1 2 3** Feeling emotionally upset when you were reminded of the traumatic event (for example, feeling scared, angry, sad, guilty, etc.)

(26) **0 1 2 3** Experiencing physical reactions when you were reminded of the traumatic event (for example, breaking out in a sweat, heart beating fast)

(27) **0 1 2 3** Trying not to think about, talk about, or have feelings about the traumatic event

(28) **0 1 2 3** Trying to avoid activities, people, or places that remind you of the traumatic event

(29) **0 1 2 3** Not being able to remember an important part of the traumatic event

(30) **0 1 2 3** Having much less interest or participating much less often in important activities

(31) **0 1 2 3** Feeling distant or cut off from people around you

(32) **0 1 2 3** Feeling emotionally numb (for example, being unable to cry or unable to have loving feelings)

(33) **0 1 2 3** Feeling as if your future plans or hopes will not come true (for example, you will not have a career, marriage, children, or a long life)

(34) **0 1 2 3** Having trouble falling or staying asleep

(35) **0 1 2 3** Feeling irritable or having fits of anger

(36) **0 1 2 3** Having trouble concentrating (for example, drifting in and out of conversations, losing track of a story on television, forgetting what you read)

(37) **0 1 2 3** Being overly alert (for example, checking to see who is around you, being uncomfortable with your back to a door, etc.)

(38) **0 1 2 3** Being jumpy or easily startled (for example, when someone walks up behind you)

(39) How long have you experienced the problems that you reported above? (circle ONE)
1 Less than 1 month
2 1 to 3 months
3 More than 3 months

(40) How long after the traumatic event did these problems begin? (circle ONE)
1 Less than 6 months
2 6 or more months

Part 4

Indicate below if the problems you rated in Part 3 have interfered with any of the following areas of your life DURING THE PAST MONTH. Circle Y for Yes or N for No.

(41) **Y N** Work

(42) **Y N** Household chores and duties

(43) **Y N** Relationships with friends

(44) **Y N** Fun and leisure activities

(45) **Y N** Schoolwork

(46) **Y N** Relationships with your family

(47) **Y N** Sex life

(48) **Y N** General satisfaction with life

(49) **Y N** Overall level of functioning in all areas of your life

Appendix 2 Handedness questionnaire

WHICH HAND DO YOU USE?

Please fill in your: Sex: Age: yrs mths #

Please indicate which hand you prefer to use for the following list of activities by putting + in the "LEFT" or "RIGHT" column below.

If your preference is so strong that you would never try to use the other hand put + + in one column.

If you would really use either hand for an activity please put + in both columns.

Please try to answer all questions and only leave a blank if you have no experience at all of the object or task.

	LEFT	RIGHT
Writing		
Drawing		
Throwing		
Using: scissors		
a toothbrush		
a knife (without fork)		
a spoon		
a broom (the upper hand)		
Striking a match		
Opening a box (lid)		

Which foot do you prefer to kick with?		
Which eye do you use when using only one?		

Have you ever changed, or been forced to change, the hand you would naturally use for writing?

Yes / No *(please circle)*

If Yes, please give details:

Which hand do others in your family use for writing? *(please circle the correct options below)*

Father……R / L / both equally

Mother… R / L / both equally

WHICH SIDE DO YOU USE?

Please fill in your: Sex: Age: yrs mths #

Please indicate your answer to each of the questions below by placing a tick ✓ in one of the three boxes.

	LEFT	RIGHT	BOTH
With which hand would you throw a ball to hit a target?			
If you had to step up on a chair, which foot would you place on the chair first?			
Which eye would you use to peep through a keyhole?			
If you wanted to listen in on a conversation going on behind a closed door, which ear would you place against the door?			
With which hand do you draw?			
With which foot do you kick a ball?			
If you had to look into a dark bottle to see how full it was, which eye would you use?			
If you wanted to hear someone's heart beat, which ear would you place against their chest?			
With which hand do you use an eraser on paper?			
If you wanted to pick up a pebble with your toes which foot would you use?			
Which eye would you use to sight down a rifle?			
Into which ear would you place a single earphone for a tape/CD player or hands free mobile phone?			
With which hand do you remove the top card when dealing from a pack of cards?			

Appendix 3 PSS10

PERCEIVED STRESS SCALE

The questions in this scale ask you about your feelings and thoughts during the **LAST MONTH.** In each case, please indicate by circling the appropriate number on the scale 0below **HOW OFTEN** you felt or thought a certain way.

IN THE LAST MONTH, HOW OFTEN HAVE YOU:	never	almost never	sometimes	fairly often	very often
been upset because of something that happened unexpectedly?	0	1	2	3	4
felt that you were unable to control the important things in your life?	0	1	2	3	4
felt nervous and "stressed"?	0	1	2	3	4
felt confident in your ability to handle your personal problems?	0	1	2	3	4
felt that things were going your way	0	1	2	3	4
found that you could not cope with the things you had to do?	0	1	2	3	4
been able to control irritations in your life?	0	1	2	3	4
felt that you were on top of things?	0	1	2	3	4
been angered because of things that were outside of your control?	0	1	2	3	4
felt difficulties were piling up so high that you could not overcome them?	0	1	2	3	4

Appendix 4 Emotion Rating Form: Silence of the Lambs

FILM RATING

Now that you have watched the film excerpt, would you please indicate on the scale below how strongly you felt any of the following emotions by circling the appropriate number for each:

	not felt at all										felt extremely strongly
anger	0	1	2	3	4	5	6	7	8	9	10
fear	0	1	2	3	4	5	6	7	8	9	10
disgust	0	1	2	3	4	5	6	7	8	9	10
sadness 0	1	2	3	4	5	6	7	8	9	10	

Overall, could you rate how emotionally aroused (eg tense, anxious) you were by the film?

	not felt at all										felt extremely strongly
overall	0	1	2	3	4	5	6	7	8	9	10

Have you seen this film before?

YES NO

Appendix 5 Word-based Stroop cards

These appear in the following order: Practice (below); Baseline; Neutral; Positive: Negative; Film.

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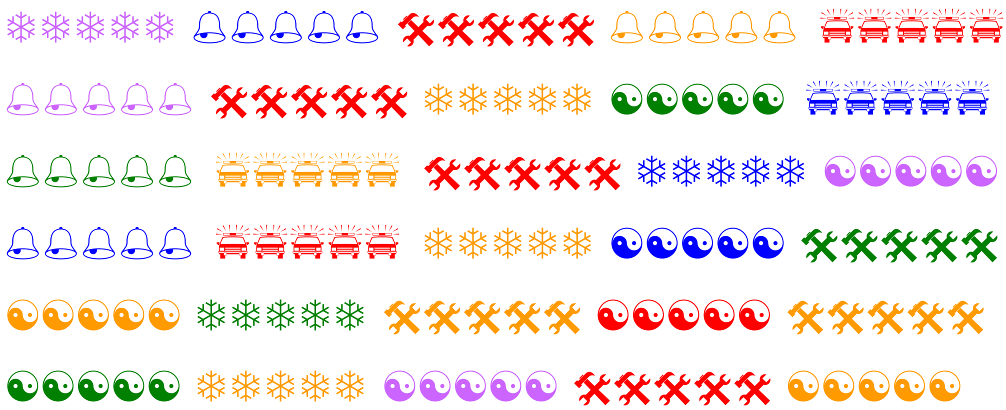
Appendix 6 Non-word Stroop cards

These appear in the following order: Practice (below); Baseline; Neutral; Positive; Negative.



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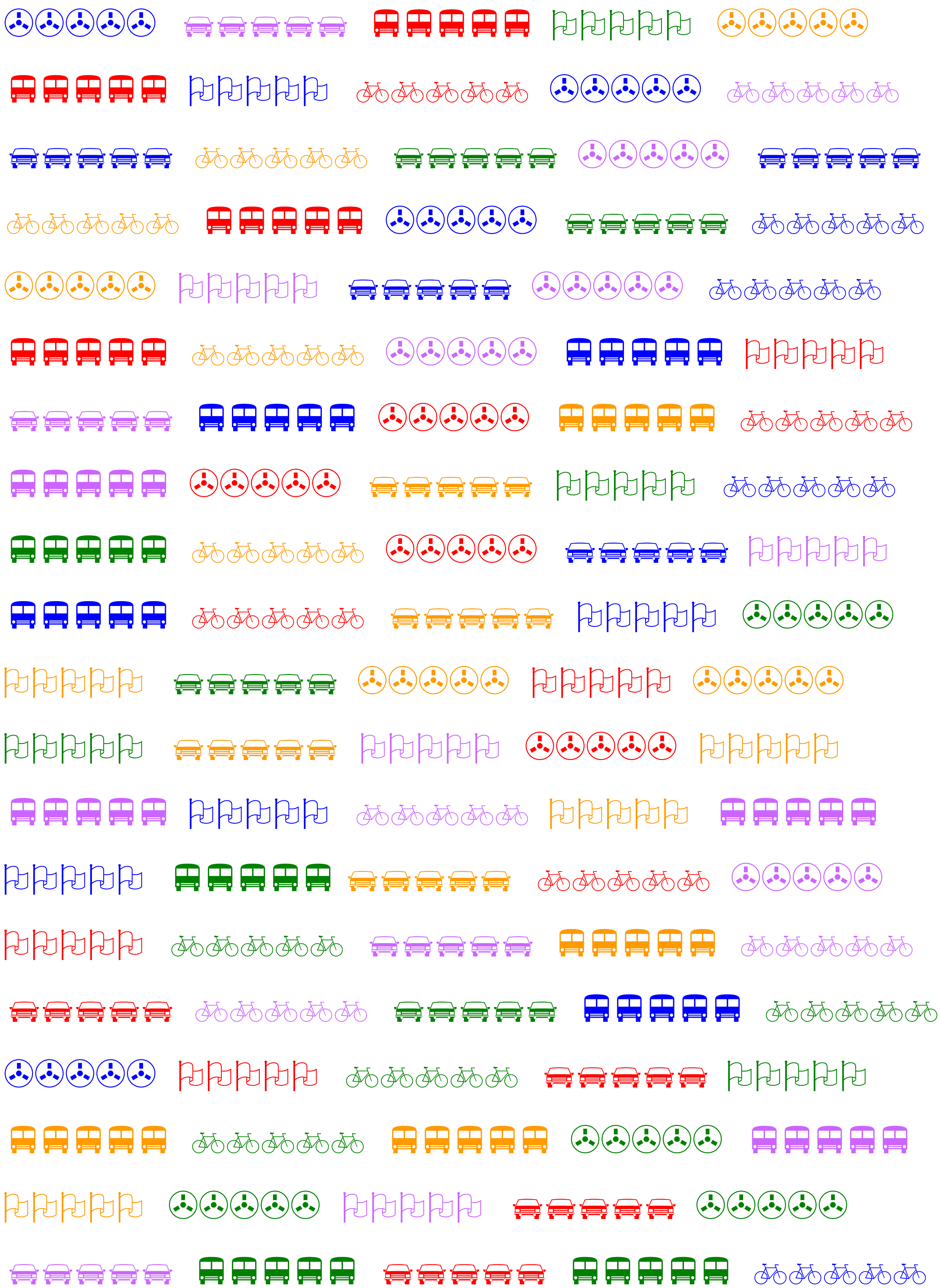

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☼☼☼☼☼ ☺☺☺☺☺ ☼☼☼☼☼ 🕊🕊🕊🕊🕊 ☺☺☺☺☺

♥♥♥♥♥ ♪♪♪♪♪ ☺☺☺☺☺ ☼☼☼☼☼ ♪♪♪♪♪

🕊🕊🕊🕊🕊 ☺☺☺☺☺ 🕊🕊🕊🕊🕊 ♥♥♥♥♥ 🕊🕊🕊🕊🕊

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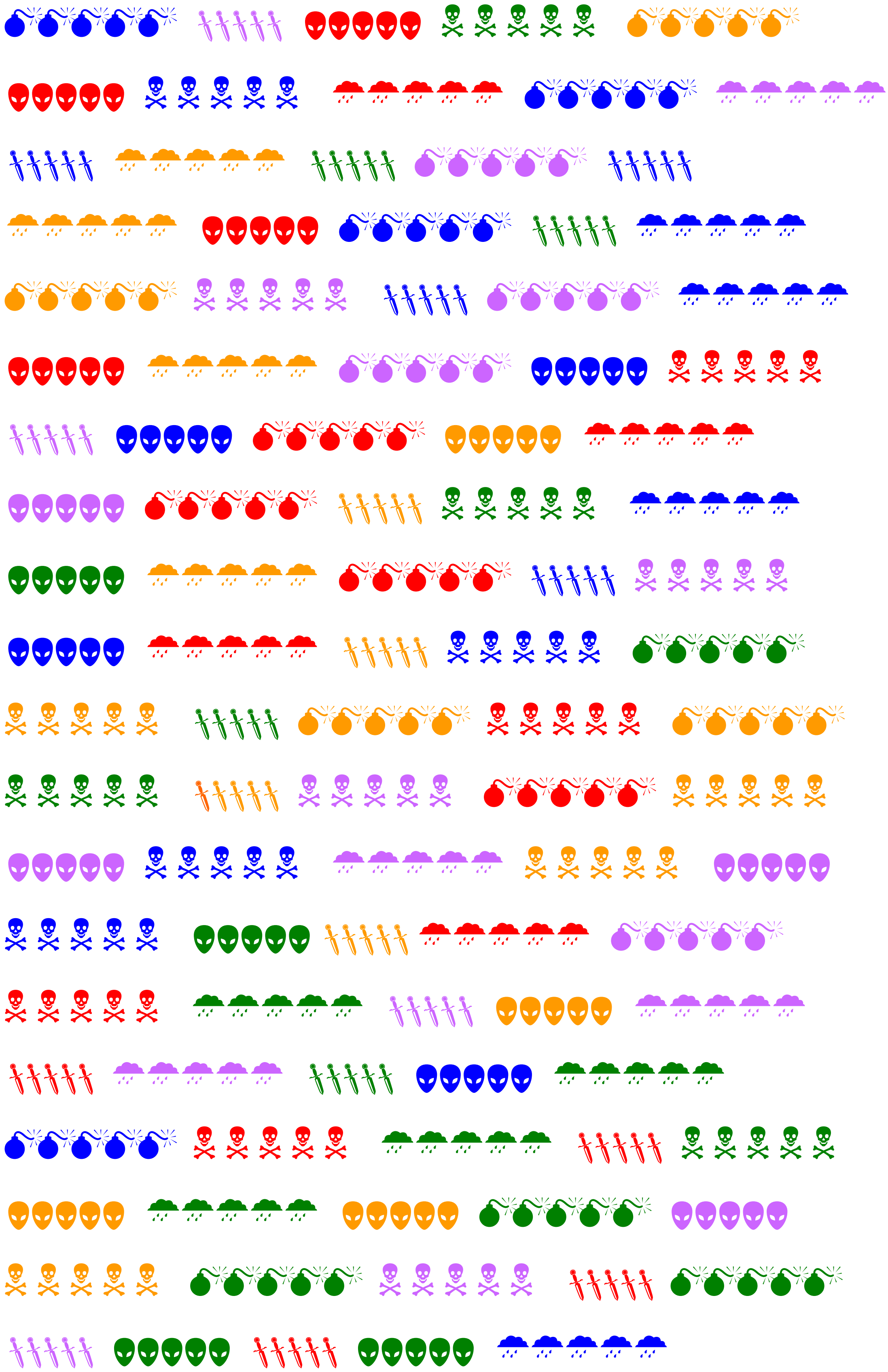


Appendix 7 Stroop Word Recognition Test

SWRT

Please tick YES for any word you think was in the booklet of coloured words last week, otherwise tick NO. If you are not sure, please guess.

	YES	NO		YES	NO		YES	NO
milk			cancer			island		
beans			heat			fourteen		
funeral			moles			railway		
changing			destroy			Danish		
tonight			coffin			campaign		
combine			ground			adore		
enough			widespread			celebrity		
kid			east			suit		
basement			roof			doors		
teeth			snow			monastery		
mix			cap			network		
message			cerebral			expect		
manage			joyful			inclined		
goggles			disease			germs		
expeditions			parade			fingertips		
happy			kidney			cooker		
vacant			column			hate		
sugar			shouts			nearby		
influences			desk			friendship		
moth			ample			enjoyable		
solid			circle			pleasant		
count			loyal			seed		
given			stony			millionaire		
burning			lifts			stand		
cup			decade			concrete		
input			bilingual			pit		
nonsense			closeness			capitalists		
produced			darkness			demand		
design			flint			penny		
reaching			complete			faithful		
guilt			fondant			ladder		
filthy			multiply			ferry		
circa			love			polite		
						earn		

Appendix 8 MCQ for Silence of the Lambs film excerpt

FILM MCQ

ID No…………………..   Date…………………………

Listed below are statements or questions relating to the film excerpt you have watched. Each has a multiple choice style answer. Please place a tick against the answer you think is correct after each question. If you are not sure please guess.

1. The car parked outside the house is
   a……. silver
   b……. black
   c……. blue
   d……. red

2. The woman's coat is
   a……. blue
   b……. black
   c……. brown
   d……. green

3. How long ago did the man buy the house?
   a……. 2 months ago
   b……. 1 year ago
   c……. 2 years ago
   d……. 10 years ago

4. The woman asks the man if the previous owner left behind any
   a……. business records
   b……. business cards
   c……. phone bills
   d……. accounts

5. The woman is wearing
   a……. a ring
   b……. a necklace
   c……. both
   d……. neither

6. On top of a fireplace is a roll of
   a……. clingfilm
   b……. bubble wrap
   c……. aluminium foil
   d……. tracing paper

7. The woman notices an assortment of coloured
   a……. thread
   b……. wool
   c……. sequins
   d……. buttons

8. The man is wearing a
   a……. shirt and jeans
   b……. sweater and jeans
   c……. sweater and trousers
   d……. shirt and trousers

9. The man's gun is resting on a
a……. worktop
b……. fridge
c……. cooker
d……. table

10. The woman follows the man from the
a……. hall upstairs
b……. kitchen downstairs
c……. hall downstairs
d……. kitchen upstairs

11. When the woman follows the man, the first few doors are
a……. brown
b……. black
c……. green
d……. blue

12. The shoes the woman is wearing are
a……. black lace-up
b……. brown slip-on
c……. brown lace-up
d……. black slip-on

13. The walls of the basement are mainly
a……. plaster
b……. wallpapered
c……. painted
d……. brick

14. On one of the walls in the corridor there is a
a……. map
b……. portrait
c……. advertisement
d……. poster

15. What does the woman wedge under a door knob?
a……. an axe
b……. a table
c……. a chair
d……. a shovel

16. What is the last thing the woman tells the person trapped in the pit?
a……. the other officers will be here any minute now
b……. you're alright, Catherine
c……. I've gotta leave this room, I'll be right back
d……. shut that dog up

17. The lights go out when the woman is looking at
a……. a fish tank
b……. a bathtub
c……. tailors' dummies
d……. a fridge

18. The woman trips
a……. against the wall
b……. on a table
c……. against a cupboard
d……. in a doorway

19. Through the night vision goggles everything appears
a……. purple
b……. green
c……. red
d……. grey

20. The woman fires her gun at the man when she hears
a……. a moth fluttering
b……. a dog barking
c……. a gun cocked
d……. a generator vibrating

21. The man is hit
a……. in the shoulder
b……. in the face
c……. once in the chest
d……. twice in the chest

Appendix 9 AVLT

THE AUDITORY-VERBAL LEARNING TEST (AVLT A)

ID no…………………..   Date…………………………

Word List A	I	II	III	recall
drum				
curtain				
bell				
coffee				
school				
parent				
moon				
garden				
hat				
farmer				
nose				
turkey				
colour				
house				
river				

Error				
Words				
TOTAL				

R = repeated recall
RC = S corrects themselves
RQ = S unsure of item
TOTAL = recall order

E = error
EC = error (confabulation)
EA = error (association)

THE AVLT WORD RECOGNITION CHECKLIST (A)

bell (A)	home (SA)	lifts [N]	input [P]	
window (SA)	concrete [P]	curtain (A)	hot (PA)	network [N]
hat (A)	moon (A)	flower (SA)	parent (A)	
barn (SA)	tree (PA)	colour (A)	water (SA)	teacher (SA)
millionaire [P]	balloon (PA)		farmer (A)	fingertips [P]
nose (A)	milk [N]	mix [P]	rose (SPA)	
inclined [N]	crayon (SA)		children (SA)	
school (A)	coffee (A)		house (A)	drum (A)
hand (PA)	mouse (PA)	turkey (A)	manage [N]	toffee (PA)
	river (A)		garden (A)	

A = words from list A
SA = words with semantic association to a word on list A
PA = words phonetically similar to a word on list A
P = words from Stroop practice card
N = words from Stroop neutral words card

A _______

Appendix 10 Non-word Rating Form (Pilot)

SEX: ………………………. AGE:………………….

Please rate your reaction to the following symbols by placing a ✓ in the relevant column:

	very negative	negative	neutral	positive	very positive
💥💥💥💥💥					
☺ ☺ ☺ ☺ ☺					
🚑🚑🚑🚑🚑					
♪ ♪ ♪ ♪ ♪					
☼☼☼☼☼					
🗡 🗡 🗡 🗡 🗡					
🕊 🕊 🕊 🕊 🕊					
🚘 🚘 🚘 🚘 🚘					
👽 👽 👽 👽 👽					
🚍 🚍 🚍 🚍 🚍					
🏆🏆🏆🏆🏆					
☻ ☻ ☻ ☻ ☻					
🚒 🚒 🚒 🚒 🚒					
🛠🛠🛠🛠🛠					
🚲 🚲 🚲 🚲 🚲					
🌧 🌧 🌧 🌧 🌧					
🚔 🚔 🚔 🚔 🚔					
☯☯☯☯☯					
🎁 🎁 🎁 🎁 🎁					
💰 💰 💰 💰 💰					
☢☢☢☢☢					
♫ ♫ ♫ ♫ ♫					
☺ ☺ ☺ ☺ ☺					
🕯 🕯 🕯 🕯 🕯					
💣💣💣💣💣					
♥ ♥ ♥ ♥ ♥					
🏳🏳🏳🏳🏳					
☠ ☠ ☠ ☠ ☠					
❄❄❄❄❄					
🔔🔔🔔🔔🔔					

Appendix 11 Transcript: Silence of the Lambs excerpt

#	STORYLINE	DETAILS
1	Pan across railway to house	quiet orchestral music
2	Voiceover: man asking if they are close to catching anyone	
3	Woman in hallway replies: we may be, asks if he took over place from previous owner	
4	Man by table at end of hall sorting through cards in his hand replies yes	yellow/orange shirt/dark trousers
5	Woman asks if she left any business records	
6	She notices things around the room:	butterfly picture on wall papers on table cling film over fireplace
7	Man replies no; asks if the FBI have learned something	
8	shot of moths on threads in box	
9	man asks if they have fingerprints etc	
10	woman replies they don't but places hand on holster under coat	green coat
11	cut to gun in kitchen	on cooker
12	man finds card and holds it out to woman	
13	she asks to use his phone	
14	he responds: sure you can use my phone	
15	woman pulls out gun and shouts FREEZE	music building + louder
16	Tells man to spread his legs, put his hands in the back Freeze	
17	Man turns away and darts through opening to next room	
18	woman follows through this room	kitchen
19	woman finds door to basement + takes off coat	green door
20	woman looks downstairs sees more green doors	music quietening
21	woman moves downstairs slowly	breathing loudly
22	chooses one of the green doors at bottom of stairs	no music
23	shown coming through door in dingy corridor, looking around	map of US on left hand wall
24	moving down corridor	faint sounds dog barking
25	brick walls and opens another door	photos beside door music changes to drum beats tailors dummies + part skins
26	Hears woman screaming: hello anybody there? I'm down here	
27	down another brick corridor, through another door	music v quiet in background sound of dog barking
28	woman asks Catherine Martin?	Catherine Martin
29	closes door behind her, sees pit in floor	
30	tells other woman: FBI your safe	
31	Woman in pit shouting you get me out of here	
32	woman places shaft of spade under door handle, closes another door	spade
33	Woman tells CM she is alright and where is he	
34	CM: how the fuck should I know..just get me out of here	
35	Woman tells CM she's to be quiet + shut that dog up	
36	woman goes to side of pit	
37	CM: just get me out of here	
38	woman sees CM holding dog	white dog

39	woman tells CM she's going to get her out of there, but to listen to her: she's going to leave the room, and will be right back	
40	CM screams NO, don't you leave me here, you fucking bitch, no don't you leave me here, this guy he's fucking crazy…	
41	woman moving away across room to other doors	
42	woman tells CM the other officers will be here any minute now	
43	CM screams Wait don't go away	
44	woman tells her: Shhhh!! Quiet	
45	CM moans: Oh God	dog still barking
46	Woman chooses a door and opens it	music getting louder
47	sees through another door into room	bats/moths flying around with fishtank + flat work table
48	woman startled by thudding mechanical noise	
49	turns to opening - sees fridge	poster on wall by fridge
50	moves into passageway	moth round light bulb
51	opens another door	yellow wallpaper behind
52	sees body in bathtub	music vol increasing thro above
53	lights go out	silence
	green night vision view of woman against wall, turning round, back to wall, feeling the wall and moving sideways till reaches cupboard door/side of wall	hear loud breathing ↓
54	view of man wearing goggles	
55	woman moves round, turns round, feeling into space, tumbles into doorway, sits up turning round, pointing gun	
56	view of man wearing goggles	
57	woman getting up, moving in another part of room	
58	view of man wearing goggles	
59	woman moving round, faces man, then moves to side, turns her back to man	orchestral music begins
60	man reaches out to her hair, nearly touches	
61	woman turns, man nearly touches her face, woman turns away	
62	view of man wearing goggles, then raising gun, cocks hammer	music louder
63	woman turns, fires her gun	
64	man shot as he falls	shot in chest
65	…in light from shattered window behind him	

Appendix 12 Recall recording sheet (Silence of the Lambs excerpt)

#	WHO	WHAT	LOCATION	SPEECH	SOUNDS	VISUALS
1		pan	railway to house			
2	woman	enters/in house				
3	man + woman	talking	corridor/hall of house	FBI/police		
4	man	looking for something				
5	woman	noticing things/realising				
6	man	realising she knows				
7	woman	hand on holster/gun				
8		cut to gun	on cooker			
9	woman	pulls gun		freeze		
10	man	runs away	downstairs/basement			
11	woman	follows	through doors			
12	woman	looking for him	through corridors			sees tailors dummies + skins
13	woman	finds woman	in pit/well	where is he	barking	dog
14	[+ dog]	conversation		safe but has to wait for backup		
				CM get me outta here		
				be quiet		
15	woman	continues search	through rooms			
16		sees body	in bathtub			
17		lights go out	in room			
18	man's	night vision view of woman				green
19	woman	can't see man				
20		stumbling through room				
21	man	reaching out to touch				
22	man	cocks gun			click	
23	woman	hears him				
24	woman	shoots man				light thro broken window

Introductory Emotion:

Chase 1

Woman in Pit interlude

Chase 2 - resumed

Climax: lights out

Resolution

N Total N t =

Reversals - errors of sequence

errors of fact

repetitions

uncertainties

Appendix 13 Emotion Rating Form: clips for SCR

FILM RATING (v3)

Could you please indicate by circling the appropriate number on the scale below how strongly you felt any of the following emotions while viewing the screen:

	not felt at all										felt extremely strongly
anger	0	1	2	3	4	5	6	7	8	9	10
fear	0	1	2	3	4	5	6	7	8	9	10
disgust	0	1	2	3	4	5	6	7	8	9	10
sadness	0	1	2	3	4	5	6	7	8	9	10

Overall, could you rate how emotionally aroused (eg tense, anxious) you were by the film?

overall	0	1	2	3	4	5	6	7	8	9	10

Could you please indicate by circling the appropriate number on the scale below how strongly you felt any of the following emotions while viewing the film clip:

	not felt at all										felt extremely strongly
anger	0	1	2	3	4	5	6	7	8	9	10
fear	0	1	2	3	4	5	6	7	8	9	10
disgust	0	1	2	3	4	5	6	7	8	9	10
sadness 0	1	2	3	4	5	6	7	8	9	10	

Overall, could you rate how emotionally aroused (eg tense, anxious) you were by the film?

overall	0	1	2	3	4	5	6	7	8	9	10

Could you please indicate by circling the appropriate number on the scale below how strongly you felt any of the following emotions while viewing the film clip:

	not felt at all										felt extremely strongly
anger	0	1	2	3	4	5	6	7	8	9	10
fear	0	1	2	3	4	5	6	7	8	9	10
disgust	0	1	2	3	4	5	6	7	8	9	10
sadness 0	1	2	3	4	5	6	7	8	9	10	

Overall, could you rate how emotionally aroused (eg tense, anxious) you were by the film?

overall	0	1	2	3	4	5	6	7	8	9	10

Have you seen this film before?

YES NO

If YES:

Approximately how many times have you seen it? ………………..……………

Approximately how long ago did you last see it?..

Using the scale below, how does this film rank amongst your most favourite horror movies?

0	1	2	3	4	5	6	7	8	9	10
least favourite										most favourite

Appendix 14 Film editing instructions: The Shining

DVD starts with Warner Brothers Logo- film begins at 12 secs.

Fast forward to scene that starts zooming in on to hotel: start recording as black screen appears with: THE INTERVIEW (2:53)
scene in general managers office
scene back home
scene in general managers office: stop recording after Jack speaks the words “They’ll love it” (6:06) before GM says “Right”
Fast forward to (8:33) start recording as scene fades from office to boy standing at basin:
Continue through to scene of lifts and corridor with blood until screen goes black and then says CLOSING DAY (10.01) Record this screen but stop recording before the next scene (of trees) begins (10:08)
Fast forward to 12:50 - start recording as a group of adults emerge from a lift
stop recording at 1400 (after end of scene with face of boy looking before adults emerge in corridor)
Fast forward to 14:25: start recording as adults are walking outside
scene in kitchen
record to 18:00 stop recording after man says to boy “come on son” before fade to next scene of adults in corridor
Fast forward to 22:33 start recording at black screen ONE MONTH LATER
boy on bicycle - stop recording at end of this scene 23:16
Fast forward to 24:39 start recording as scene changes from man in bed to view of typewriter on table
scenes in maze
TUESDAY boy riding bike
man typing and argument with wife
continue to SATURDAY view of hotel
man typing
stop recording 32:46 before this scene cuts to a woman in a yellow jacket
Fast forward to end of the scene with the woman with the radio/rangers
start recording 34:47as this scene cuts to boy riding bike
MONDAY
scene of boy entering bedroom and talking with man sitting on bed - after boy says “I am Dad” and man holds him stop recording at 38:40 before the boy continues “Dad do you feel bad”
Fast forward to end of this scene
Start recording at 40:55 - black screen: WEDNESDAY
End recording at 46:21 after woman has taken boy away and at the end of face on view of man in chair before the scene fades to the man in a corridor

CLIP 1: Instructions from Gross & Levenson (1995)

Clip length: 1'22"

Advance to the first frame of the film, which shows a body of water surrounded by mountains. Reset the timer to 00:00:00:00 (hours:minutes:seconds:frames).

Begin the clip at 00:56:51:15. At this point, a boy's hands are visible (one flat on the floor and the other in a fist). There are toy trucks and cars on a red, brown, and orange carpet.

End the clip at 00:58:12:18. At this point, an open door with a key in the lock is visible, and one full second has passed since the boy has said "Mom, are you in there?"

CLIP 2

Clip length: 1'52"

From start of film (as above)

Begin the clip at 00:34:48 (hours:minutes:seconds). The previous scene of a woman smoking and ending a conversation on a radio ends at this point; the new scene begins with a sudden cut to a boy riding his tricycle in a green corridor. The clip should begin at this point (Scene 12 on DVD).

End the clip at 00:36:40. This is after the boy has been talking to his finger and looks to camera with a scared expression. Stop the clip before the sudden transition to a black screen with the word MONDAY in white text.

Appendix 15 Film editing instructions: Silence of the Lambs excerpt

[Note: timings may vary slightly on a different recorder.]

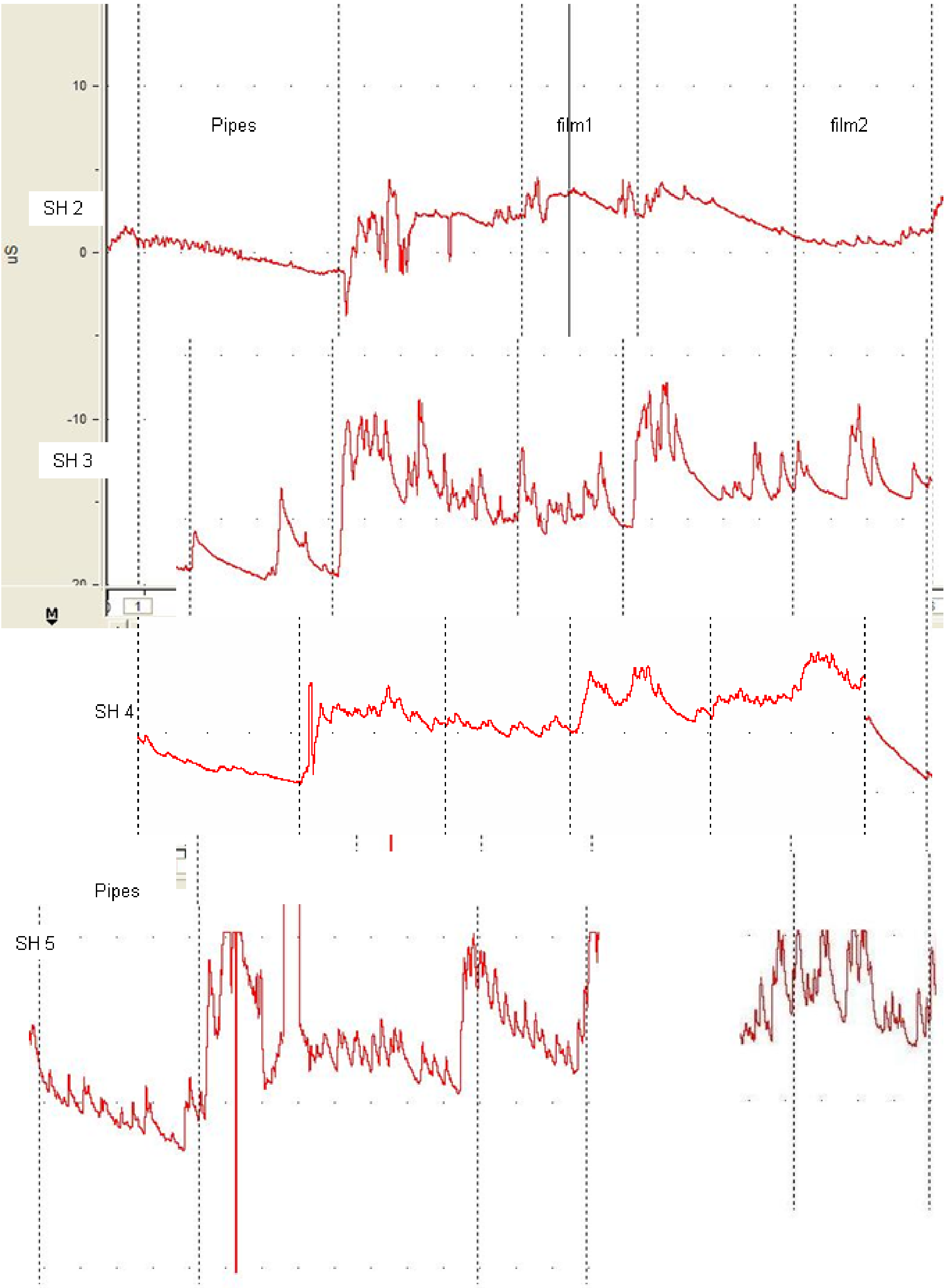
Advance to the first frame of the film in which the words "A STRONG HEART DEMME PRODUCTION" appear. Reset the timer to 0:00:00. (hours:minutes:seconds).

Begin the clip at 1:36:13. At this point a dirt road and trees are in the foreground and a mint green trailer is in the background.

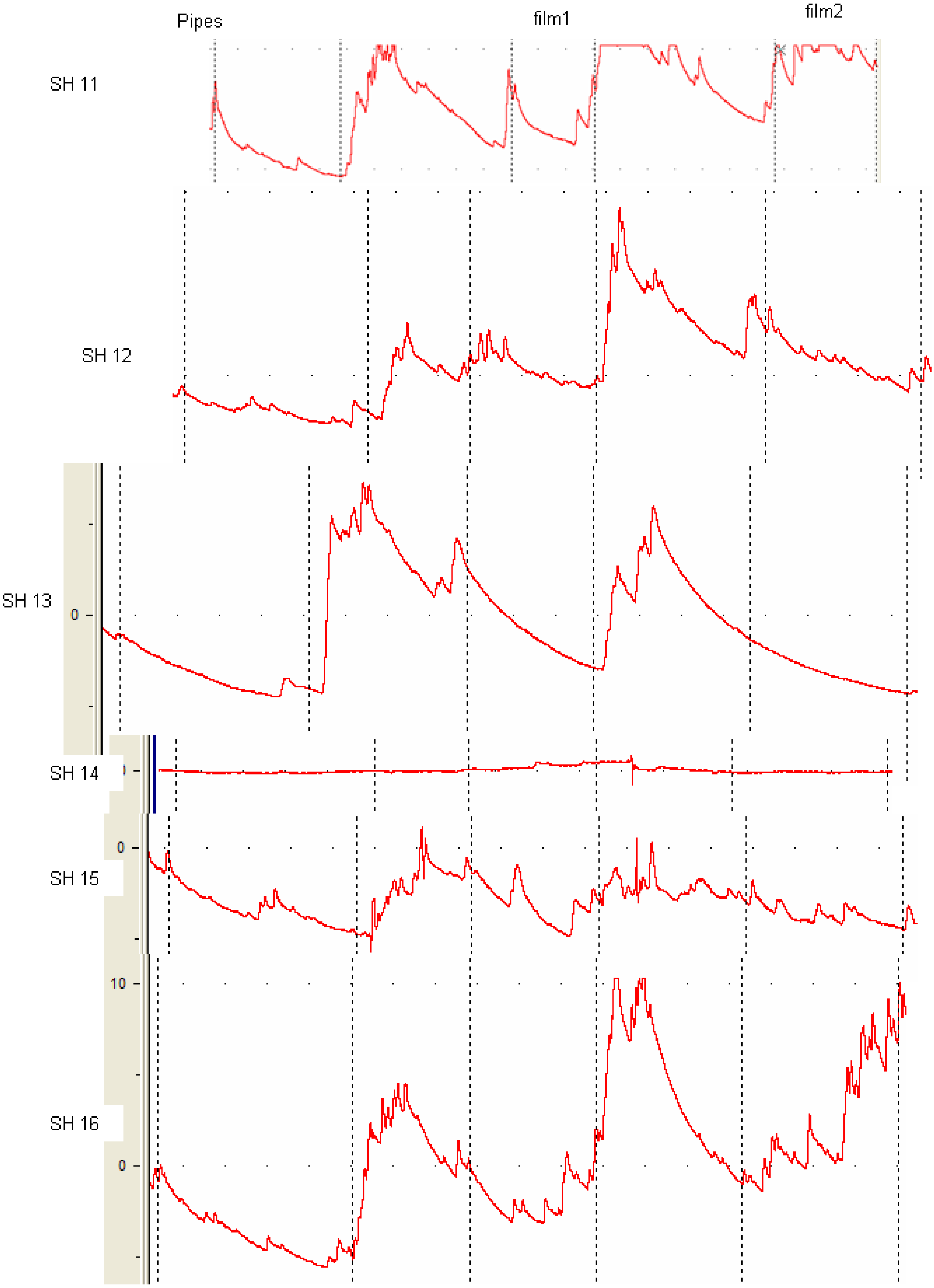
Record the film until the man and woman both fire their guns at each other and the man is seen in daylight; stop the recording at 1:44:04.

Appendix 16 Chart recordings (The Shining)

(SH# refers to participant ID number)



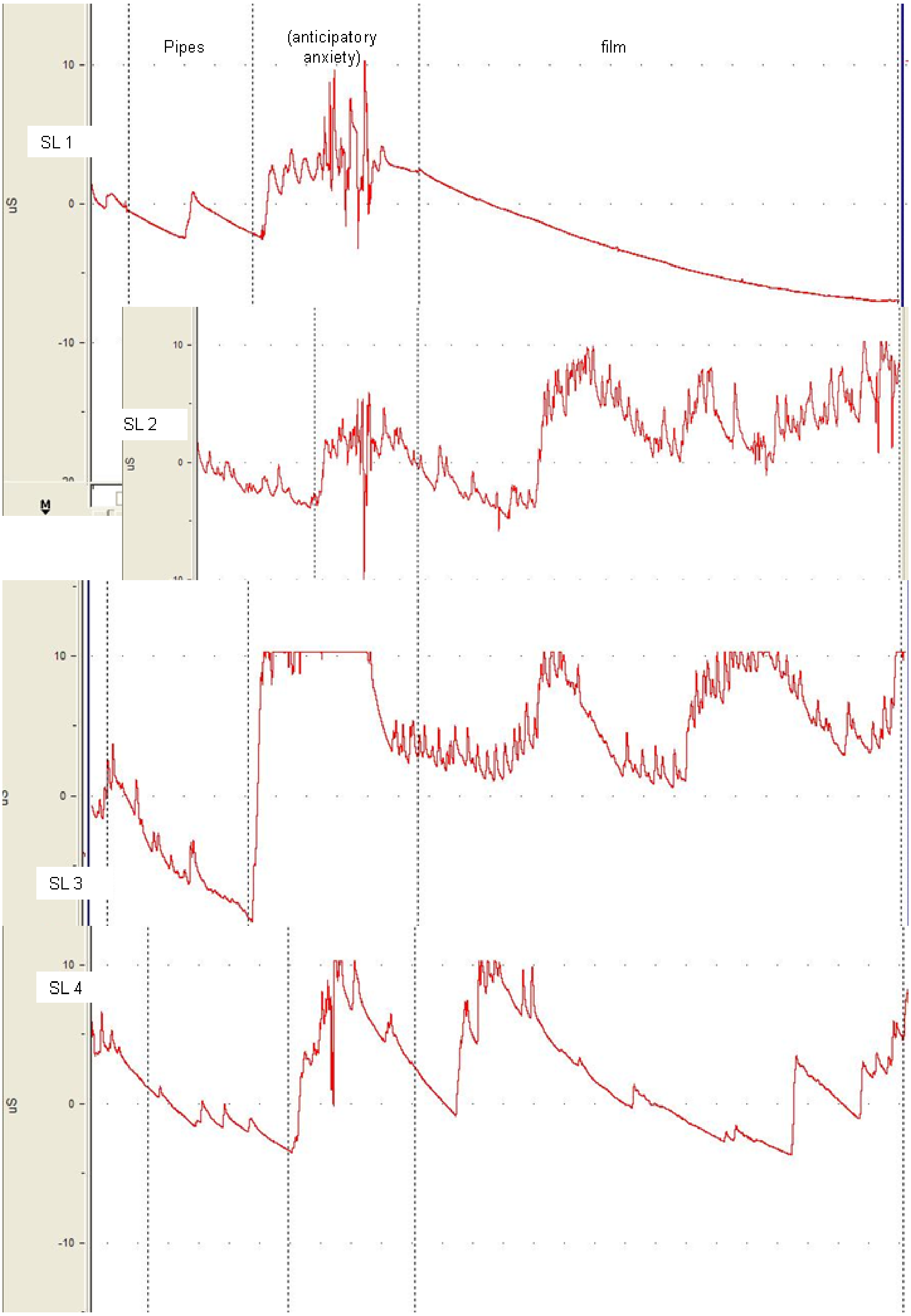

Pipes
film1
film2
SH 6
SH 7
SH 8
SH 9
SH 10

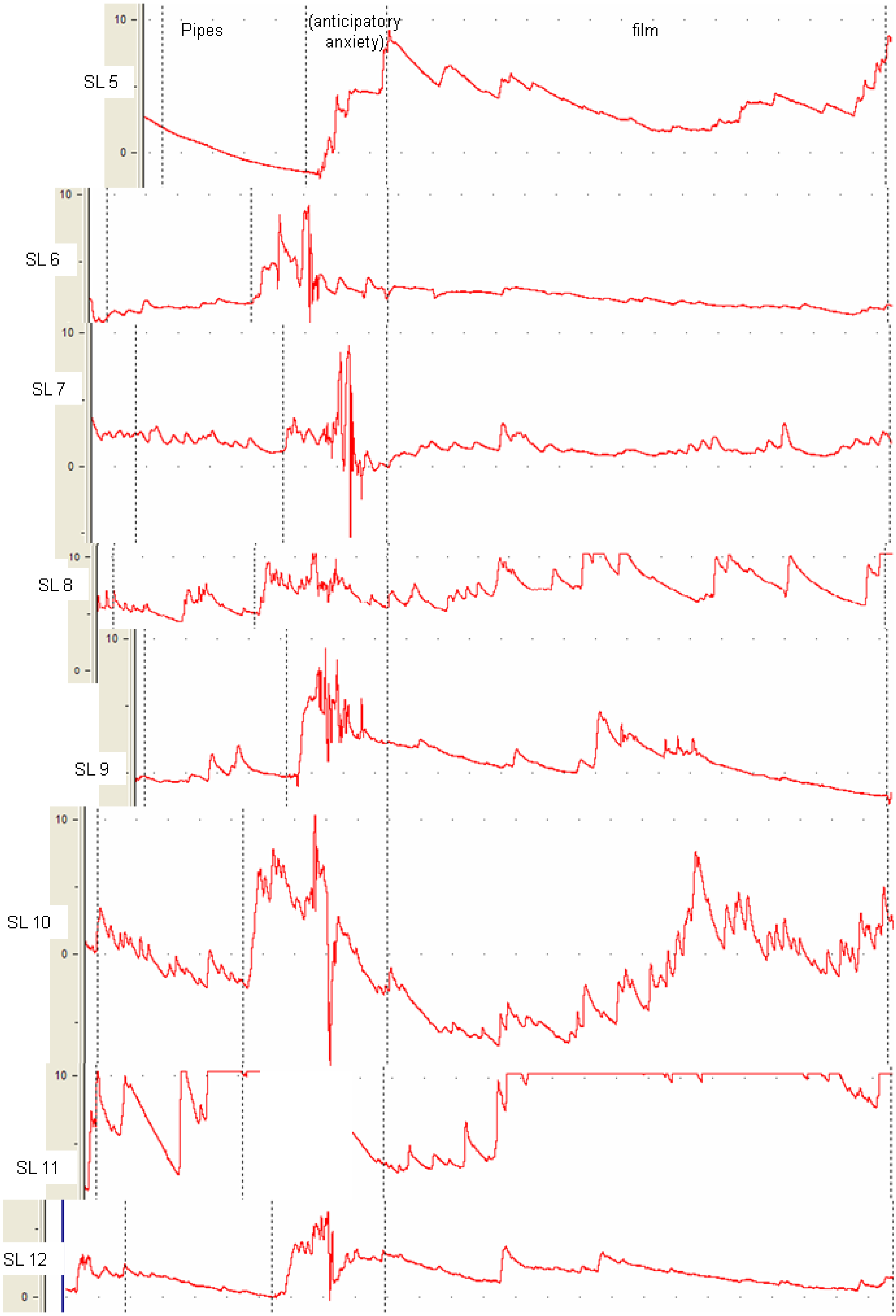

Pipes
film1
film2
SH 11
SH 12
SH 13
0
SH 14
SH 15
0
10
SH 16
0

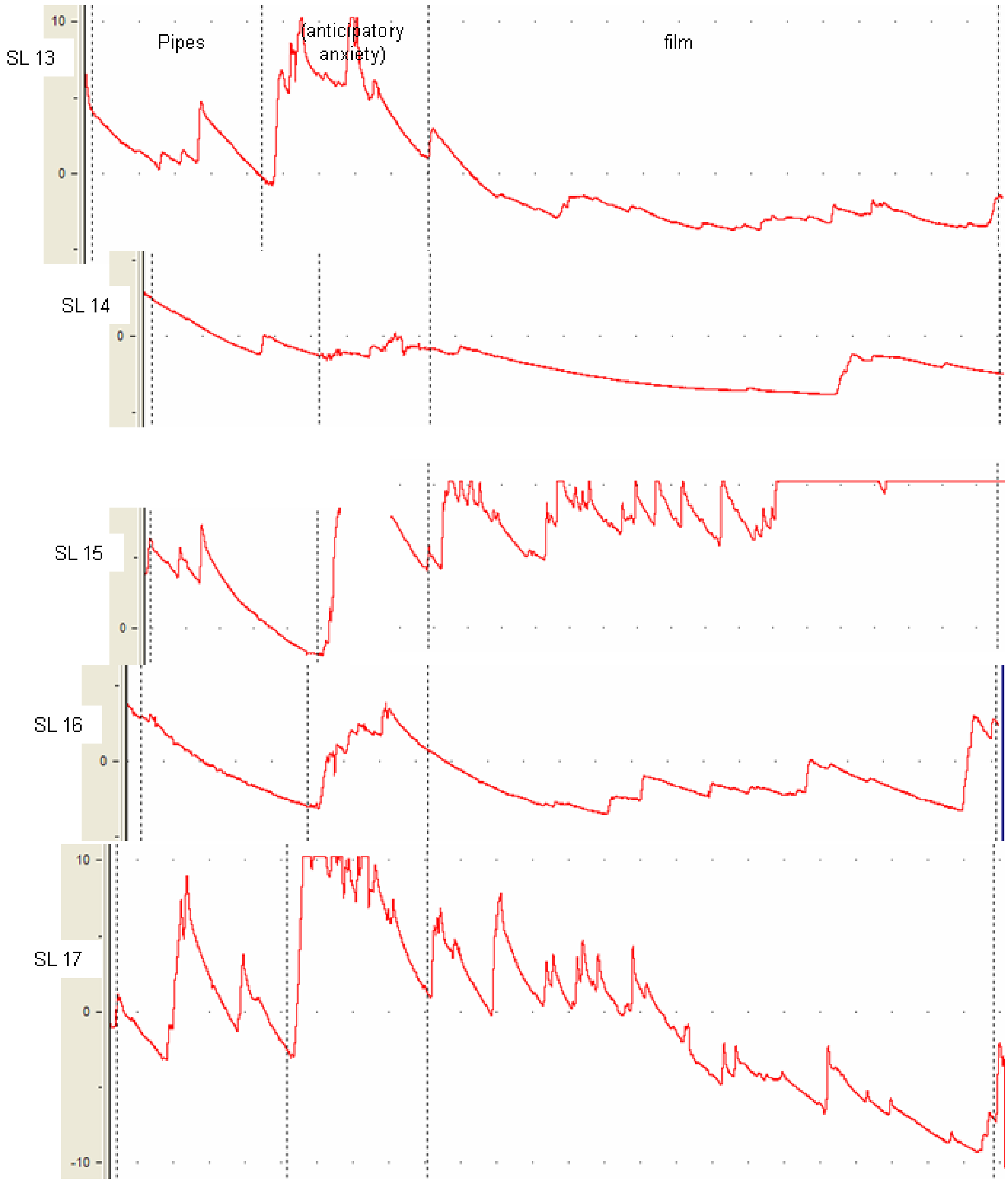

Pipes
film1
film2
SH 17
SH 18
0
SH 19
0
SH 20
0
10
SH 21
0

Appendix 17 Chart recordings (Silence of the Lambs)

(SL# refers to participant ID number)




Pipes
(anticipatory anxiety)
film
SL 5
SL 6
SL 7
SL 8
SL 9
SL 10
SL 11
SL 12
10
0


SL 13
Pipes
(anticipatory anxiety)
film
10
0
SL 14
0
SL 15
0
SL 16
0
SL 17
10
0
-10

Appendix 18 Methodological issues in determining the 2D:4D

1. Use of a scanner to capture images of palmar surface of the hand

A scanner was used in order to attract visitors in the science centre to participate in the research study reported in Chapter 3 and Chapter 7 as it enhanced the novelty value and hands-on approach in a way similar to the interactive exhibits in the Science Centre. It was also used for the general student sample for this study. However, 34% of the scans turned out to be unusable, for a variety of reasons.

Where participants' hands were hot, fogging of the colder glass of the scanner bed with condensation obscured the palmar creases. Similarly, if participants did not, or were not able to, place their hands flat on the glass, shadowing around the palmar crease obscured the lines of the crease. This was particularly a problem in older participants, with arthritic hands that could not be placed flat on the scanner bed. Also a problem with older hands was the changed, vertical nature of creases evident in "old" skin, which obscured any horizontal creases at the finger joints.

Another problem, particularly in the Science Centre sample, with predominantly married participants, was due to the wearing of rings on the left fourth digit. Although rings could often be moved up the finger, away from the palm, in many cases, where a ring had obviously been worn for many years, the palmar crease had been completely rubbed away and was no longer visible on the scanned image! This explains the lower percentage of usable left compared to right hand calculated digit ratios.

Finally, while the method seems simple, identification of a basal crease, particularly on index fingers (second digit), can be problematic. In many individuals, there is an incomplete crease extending only halfway across the base of the digit. It is therefore difficult to decide which is the true basal crease and this is particularly so on a scanned image rather than *in vivo*. If a crease was shorter and did not reach the midline, then the basal crease was at a higher level, therefore shortening the length of the second digit measurement.

Though some of these difficulties were specifically due to the use of scanned images for this study, others, to do with the changed shape and texture of elderly hands, the wearing of rings in a married sample and difficulties in determining a true basal crease in second digits, have not been previously commented upon in the literature.

2. Determination of digit ratio

Although convenient to use with scanned images, the AutoMetric software has one shortcoming which does not allow for repeatabilities to be tested. The size of the imported images can be magnified or reduced, but cannot be precisely controlled. While this facilitates viewing of an image at any scale appropriate to conducting the necessary measurements, the values assigned to each digit measure are arbitrary, in that they do not reflect the actual (*in vivo*) length of the digit; the output from the program is a calculated 2D:4D ratio, not a measurement of the length of each digit. For this reason, repeatability of this method can not be assessed.

However, a smaller sample of data (n=68) collected from a student population for another study in progress, using both scanned images and *in vivo* measurements of the digits, afforded the opportunity to assess different methods and therefore repeatability of the measurements used to establish the 2D:4D. In addition, the scanned images were presented on screen at their original size using Photoshop, and the calipers used to measure the image on the PC monitor. Digits (*in vivo*) and the scanned images in

Photoshop were all measured twice in order to establish the reliability of these measurements.

3. Repeatability of digit ratio measures

Model III univariate analysis of variance (ANOVA) tests were used to calculate the repeatabilities, r1, of the measurements made of digit length (where r1 = (groups MS - error MS)/(groups MS +errorMS); Zar, 1984; MS = mean squares). A repeated measures ANOVA was used to calculate the ratio, F, between groups MS (that is, the differences between individuals) and error MS (the measurement error).

For the *in vivo* measurements (all n=68), repeatabilities were high and the variance of between-subject measures was significantly greater than the variance of the repeated measures (left 2nd digit: $r_1 = 0.992$, $F = 15326$, $p < 0.001$; left 4th digit: $r_1 = 0.994$, $F = 13594$, $p < 0.001$; right 2nd digit: $r_1 = 0.993$, $F = 16900$, $p < 0.001$; right 4th digit: $r_1 = 0.993$, $F= 15808$, $p < 0.001$).

For the measurements of the full scale scanned images using calipers, similar high repeatabilities and significantly greater variance of between-subject than repeated measures was also found (left 2nd digit: $r_1 = 0.995$, $F = 14816$, $p < 0.001$; left 4th digit: $r_1 = 0.996$, $F = 12878$, $p < 0.001$; right 2nd digit: $r_1 = 0.994$, $F = 17207$, $p < 0.001$; right 4th digit: $r_1 = 0.995$, $F= 16706$, $p < 0.001$).

These findings suggest that both sets of measurements were showing real differences in finger length between subjects. In order to compare the two sorts of measurement, the two readings in each case were averaged and then the same repeatability calculations performed using the average *in vivo* measure and the average caliper measure of the scanned image. Repeatabilities were similarly high for the 4th digits (left 4th digit: $r_1 =$

0.960, $F = 13274$, $p < 0.001$; right 4th digit: $r_1 = 0.947$, $F= 16261$, $p < 0.001$), but though still high, were less so for 2nd digits (left 2nd digit: $r_1 = 0.888$, $F = 15300$, $p < 0.001$; right 2nd digit: $r_1 = 0.993$, $F = 17323$, $p < 0.001$). When conducting *in vivo* measurements, with the calipers, it was quite easy to see the "half" creases on second digits and judge whether they did or did not form the basal crease; these results suggest that there was more variability in measurements of the second digits as these "half" creases were less clear in scanned images, despite the good resolution achieved in Photoshop compared to the AutoMetric program.

The high repeatabilities in two alternate methods suggest that reliability of measures by the same investigator using the AutoMetric program would also be high. However, due to the output of the latter being in the form of a calculated 2D:4D, there is no way to directly test the compatibility of results from this method with those from the caliper measurements of digits or scans. Pearson correlations between calculated 2D:4D were all significantly positively correlated at the $p < 0.001$ level, but coefficients were higher between the AutoMetric and caliper measures of the scanned image (right 2D:4D $\rho = 0.931$; left 2D:4D $\rho = 0.913$) which measured the same, static image than coefficients between the AutoMetric output and *in vivo* caliper measures (right 2D:4D $\rho = 0.858$; left 2D:4D $\rho = 0.775$) and between caliper measures of the scanned and *in vivo* hands (right 2D:4D $\rho = 0.849$; left 2D:4D $\rho = 0.766$). When paired samples t-tests were performed, the mean 2D:4D was significantly lower using the AutoMetric program compared to both the measured scans and *in vivo* measures, and significantly lower for measured scans than for *in vivo* scans (all $p < 0.001$, except left 2D:4D AutoMetric vs Photoshop where $p = 0.053$).

This is consistent with the problems in identifying where the basal crease lies on the second digit; if a more distal crease is not clearly visible on the lowest resolution AutoMetric image, or slightly better resolution Photoshop image, then the reduction in length of the second digit reduces the calculated second to fourth digit ratio. The preferred method is measuring *in vivo*, as it possible to determine every crease by close inspection, the only problem remaining being a judgment of when the "half" crease is sufficient to become the basal crease. While these results suggest that in the first study reported in Chapter 7 the absolute 2D:4D ratios may be an underestimate of true, *in vivo*, digit ratio, and therefore not to be compared with other 2D:4D values in the literature, for the purposes of the study here the scanned images are likely to be reliable and internally consistent.

Appendix 19 Characteristics of second GSC sample

This sample consisted of 227 individuals recruited over an Easter bank holiday weekend. Males formed 43.2% (n=98) of the sample and females 56.8% (n=129).

There were very different distributions of left handedness in men and women. Overall the prevalence of left handedness in the sample was 11.9%, a percentage not apparently different from expected values. This disguised a highly significant difference in prevalence between males and females: males 18.4% prevalence (n=18/98); females 7.0% prevalence (n=9/129); $\chi^2(1,N=227)=6.895$, p=.009. The prevalence in males was far greater and the prevalence in females far lower than expected. There are no obvious reasons as to why this should be the case.

In addition, there was no sexual dimorphism in the 2D:4D, an uncommon, but not unreported phenomenon; Hönekopp et al (2006) failed to find sexual dimorphism in 2D:4D in one of their two student samples. The table below shows the results for independent t-tests; none of these approached significance.

	sex	*N*	*mean*	*std dev*	*t*	*df*	*p*
L 2D:4D	male	98	.9887	.03640	-.128	225	.898
	female	129	.9893	.03437			
R 2D:4D	male	98	.9872	.03119	-.595	210.803	.552
	female	129	.9897	.03174			
mean 2D:4D	male	98	.9878	.03065	-.384	225	.701
	female	129	.9894	.02996			

Since reasons for these unexpected findings were not apparent, it was considered that any hypothesis testing with this unusual sample could be unreliable and there were concerns about generalising from this sample. Further analysis was not therefore performed.

Appendix 20 Methodological difficulties in Christman & colleagues' studies of strong vs mixed handers

The approach of Christman and colleagues is not to consider left and right handers; instead the thrust of their research is to consider differences between strong and mixed handers. This has immediate methodological consequences. Tabulated below is a body of Christman and colleague's work according to the criteria used for cut-off points to demarcate left from right handers. It is apparent that no consistent cut off point is used, sometimes in two experiments within one paper and although sometimes a median split value is indicated as a criterion, it is remarkable in how many studies the median value is reported as 80 (exactly). These studies use the LQ score derived from the EHI (Oldfield, 1971); the disadvantages of so doing have been discussed in Chapter 2 above and this resultant inherent confounding of strength with direction of handedness is not acknowledged. Indeed it is not the case that mixed handers (defined by any value of an LQ score) show some left handed use as claimed directly in some studies (see comments following table below).

It is also unclear how strong left handers should be treated (by any criterion used – for example, commonly, a negative value of the median value). Propper & Christman (2004a) cite evidence that only 2% of the population are strong left handers (Propper & Christman, 2004b). There is a methodological dilemma in how they should be treated: if they are eliminated from studies then we remain unsure of how variables of interest relate to strong left handedness; if they are combined with strong right handers then their influence will be swamped by effects due to strong right handedness; if combined with mixed handers, this runs counter to the treatment of strong right handers and again effects will be swamped by the greater number of mixed handers in a sample. Using mixed and strong handedness thus essentially ignores any differences there may be between left and right handers, but simplifies recruitment.

Table showing criteria used in Christman's studies of mixed/strong handers: unless specifically mentioned that the sample is exclusively right handed (for writing) the presence of left handers is inferred.

Study	*criteria*	*justification*	**LH ers?**
(Propper et al., 1998)	(all RHers) ≥70 = RH < 70 = mixed	none given	none in sample
(Christman, 2001)			
Expts 1/2	for writing: n=32 RH		n=32 LH
(Christman & Propper, 2001)			
Expt 1	≥70 = RH < 70 = mixed	none given	included in mixed
Expt 2	(all RHers) ≥70 = RH < 70 = mixed	none given	none in sample
(Christman & Garvey, 2003)	n=20: all RH for writing		
(Christman, 2004)	≥ 85 =strong RH < 85 = mixed	median in sample = 82.5	included in mixed
(Niebauer et al., 2004)			
Study 1	LQ scores used without classification: differentiated on familial handedness measure		10% of sample = LH
	one of these groups eliminated “left handers”	< 0 (all negative scores)	
	additional analysis used n=20 scoring +100 and 20 of the “most mixed handed”	no criteria given for selection of “most mixed handed”	
Study 2	LQ scores used		7% of sample = LH
(Christman et al., 2004)			
Expt 1	≥ 80 = strong RH < 75 = mixed	median = 80 in sample	included in mixed
Expt 2	all ≥75 = strong RH	unclear if selected or fortuitous	

(Propper et al., 2004)	≥80 and ≤-80 = strong between +80 and -80 = mixed	a median split	included with SRH
	NOTE: unclear where borderline is: where are +/- 80 scored?		
(Propper & Christman, 2004a)			
Expt 1	≥ 75 = strong RH 45 – 70 mixed	none given	≤ 40? ?only RHers in sample
Expt 2	≥ 75 = strong RH -70 to +70 = mixed	none given	< -75? ?only RHers in sample
(Jasper & Christman, 2005)	-75 to +75 = mixed all others = strong	70-80 provides approx median split on previous data	< -75: included with strong RHers
(Propper et al., 2005)*			
Expt 1	≥ 85 =strong -80 to +80 = mixed	median EHI score for sample	no one scored <-80 implies included in mixed
Expt 2	≥ 85 =strong -85 to +85 = mixed		<-85: n=1 eliminated from study
(Christman et al., 2006) **			
Expt 1	≥80 = strong RH ≤75 = mixed	median of sample = 80	-90: n=1 eliminated from study
Expt 2	≥80 = strong RH ≤75 = mixed	median of sample = 80	≤ -75: n=6 eliminated from study

* Propper et al (2005) state: "In essence, *mixed-handedness* refers to any pattern of hand use that involves some level of both left- and right-hand use, and *strong right-handedness* refers to virtually exclusive use of the right hand" p 752 (their italics). Clearly this statement is logically invalid; as the discussion of measurement of handedness in Ch2 has shown, someone answering "usually" right handed to all items will score +50 on a LQ score. They demonstrate no preferential use of the left hand yet on the criteria used above will be classified as mixed handers.

** Christman et al (2006) make this same invalid statement.

Appendix 21 Pilot studies to determine stimuli for Stroop tasks

1. Film related words

In order to determine which words should comprise a set of film-related words for the Stroop task, a list of items (e.g. railway, cooker) or sounds (e.g. barking) which were salient features of the film excerpt and with neither intrinsic positive or negative associations, other than from their salience to the film, was prepared. These criteria excluded items such as “gun” and sounds such as “screaming”. A total of 22 words were selected and arranged alphabetically for piloting. Eleven individuals (7 undergraduate and 4 postgraduate students) were asked to watch the film excerpt and attend to it for a later task. At the end of the film they were presented with the list of 22 words and asked to rate whether they remembered each of them from the film using a Likert scale from 1 (definitely no) to 5 (definitely yes).

Scores from all participants were summed for each word; results are presented in the table below.

Scores used to derive film-related words for the Stroop task

Word	*Score*	*Word*	*Score*	*Word*	*Score*
barking	51	**darkness**	**55**	*pit*	*52*
basement	**55**	dog	37	**railway**	**55**
bat	18	**doors**	**54**	*reaching*	*53*
bathtub	49	fireplace	17	scarf	33
clingfilm	29	*goggles*	*52*	sewing	39
coat	45	map	46	**shouts**	**55**
cooker	*53*	*moth*	*52*	stairs	48
				thread	47

Four words received the maximum score of 55 (basement, darkness, railway, shouts) and one a score of 54 (doors) so these words were used (emboldened in table). The five next most highly scored words (cooker, reaching, moth, pit, goggles; italicised in table) were used as distracters in the Stroop word-recognition test.

2. Non-word stimuli

A second pilot study using 41 volunteer psychology undergraduates was carried out to compile the novel, non-word Stroop task. Twenty recognisable items were selected (from webdings, wingdings and normal text symbols: fonts within MS Word). Each item was presented in a cluster of five (equivalent to the baseline clusters of OOOOO's) on a list; participants were asked to rate each item type on a five point scale ranging from -2 (very negative) to +2 (very positive).

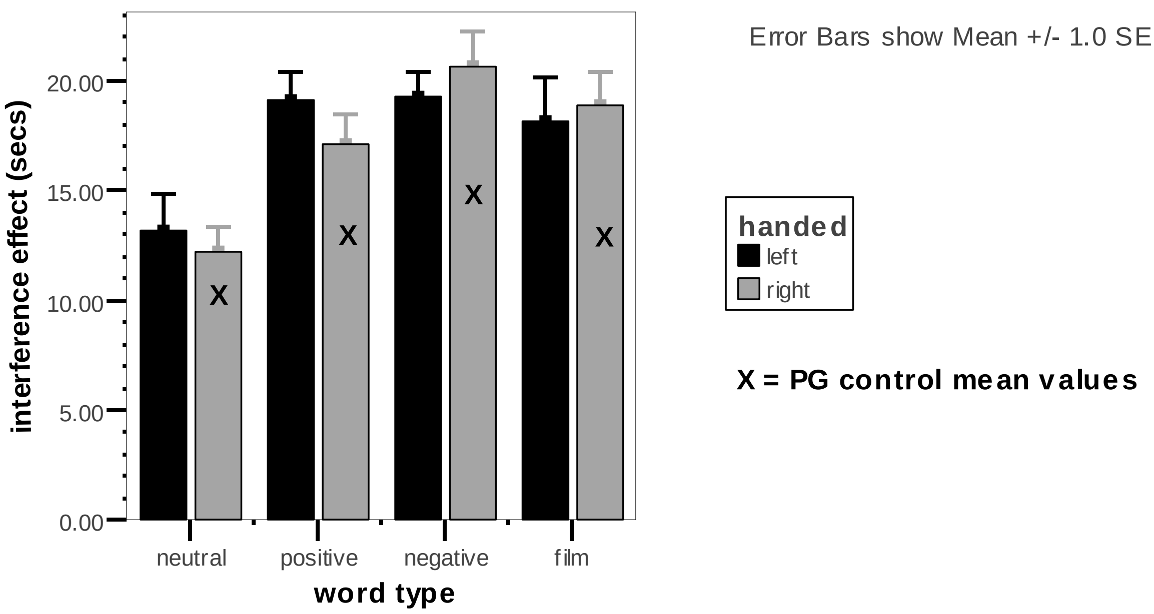
Based on these scores, the items selected for positive and negative sets were those which had the mode score in the desired direction, and, in rank order, had the highest sum and mean scores; those selected for the neutral set had the lowest sum and mean scores (that is, nearest to zero). With respect to the choices for positive items, of the two black on white smileys, the one with the larger smile had a greater score, so only this one was used and the other discarded; similarly, while the two "note" items had similar scores, the single note scored slightly higher and was selected for use. Scores were checked for possible sex differences using independent t-tests for each item; significant differences were found for two items not selected for use (flash and parcel) and for two that matched selection criteria: the alien was rated lower by females than males and this approached significance (mean scores -1.2 and -0.85 respectively, $t_{(36)}$ = 1.994, p=0.54) but the lower male mean score did not alter the selection criteria described above. The flag was rated significantly more positively by females (mean score 0.52 compared to 0.08 for males, $t_{(33.317)} = -2.573$, p=0.015), but was still sufficiently near the neutral score of 0 to be retained in comparison to other items.

The non-word Stroop task cards were then prepared as for the word cards using the following items: neutral (🚘🚘🚘🚘🚘, 🚍🚍🚍🚍🚍, 🚲🚲🚲🚲🚲, 🎳🎳🎳🎳🎳, 🏳🏳🏳🏳🏳), positive (☼☼☼☼☼, 🕊🕊🕊🕊🕊, ☺☺☺☺☺, ♥♥♥♥♥, ♪♪♪♪♪) and negative (🗡🗡🗡🗡🗡, 👽👽👽👽👽, ☔☔☔☔☔, 💣💣💣💣💣, ☠☠☠☠☠). Clusters were created in font size 20 (though some were reduced for more consistent sizing: 🏳 ☼ ☺ 🗡 👽 to 16 and 💣 🕊 🎳 to 18) and character spacing adjusted (condensed/enlarged) where necessary to minimise blank space between each of the five items forming a string. A set of practice stimuli, incorporating six lines of non-words, was constructed using five items from those not already used that were the next most neutral (❄ ☯ 🔔 🛠 sizing at 16 and 🚖 sizing at 18). All sets of non-word cards are at Appendix 6.

Appendix 22 The Stroop paradigm: intended control protocol - problems with this comparison group

The 4x2 (word type over baseline x handedness) repeated measures ANOVA showed a highly significant main effect for type of word [$F_{(2.625,133.887)}$=18.933, p<.001] but no between subjects main effect of handedness [$F_{(1,51)}$=.008, p=.931] and no interaction [$F_{(2.625,133.887)}$=1.092, p=350]. Independent sample t-tests showed no significant differences between right and left handers for film [$t_{(51)}$= -.245, p=.807] or negative words [$t_{(51)}$= -.707, p=.483]. However, Figure 22.1 shows that absolute levels of interference appear high. This runs counter to the hypothesis that it is exposure to the fearful film that is responsible for generating an interference effect on the Stroop paradigm.

Figure 22.1 Interference effects on the word based Stroop for the Control protocol, also showing mean values for comparison sample of right handed postgraduate students



However, while running this study it was felt that the students recruited to the control protocol were of lower ability and/or were less motivated than the other samples. The left handers were still voluntarily responding to appeals to take part in this study, and by this stage of recruitment, were almost entirely recruited outwith the psychology undergraduate subject pool. The right handers who comprised the control group (more females than males) were mainly recruited at the end of a semester where there had been few other studies available to the subject pool; in order to meet course requirements, they were forced to participate to gain credits rather than by a positive choice to take part in this particular study.

A one-way ANOVA was performed on results on the AVLT (a standard test of memory, reported in Chapter 5 above) for the female right handers across the three experimental protocols (standard, reversed and control) to test the hypothesis that the control group performed worse on this test (due either to poorer ability or to "not bothering" to try very hard in remembering the word list presented in the AVLT). These results are presented in Table 22.1.

Table 22.1 Results of one-way ANOVA comparing female right handers across experimental protocols and significant differences between standard/reversed protocols and the control protocol

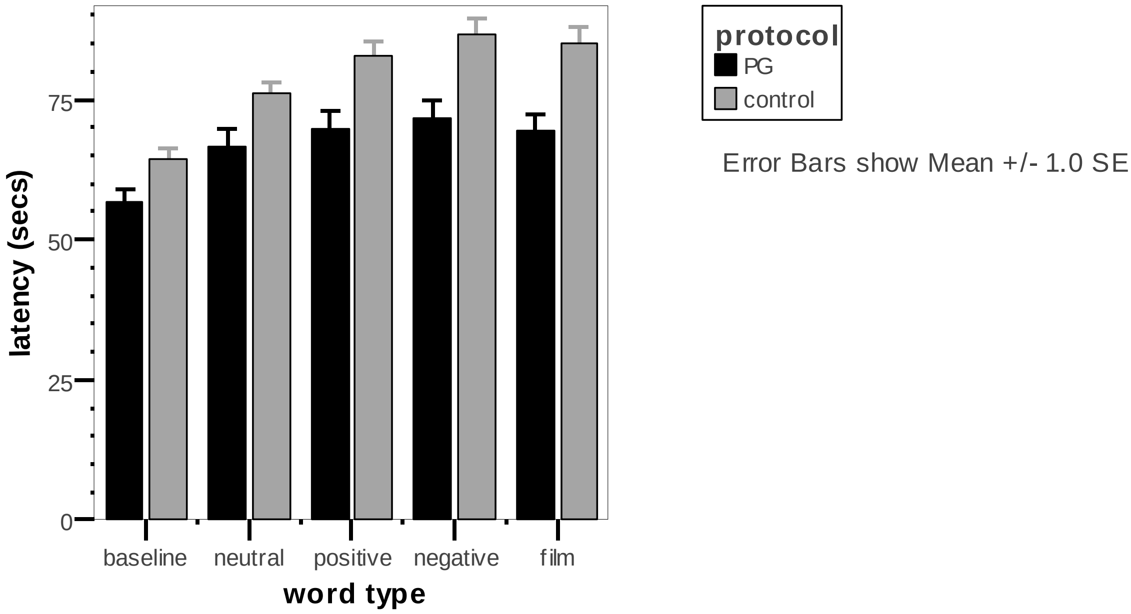
AVLT	One way ANOVA			Multiple Comparisons		
Dependent Variables	df	F	p	LSD		p
recall 1	2,58	3.094	0.053	control	standard	0.016
recall 2	2,58	2.700	0.076	control	reversed	0.024
recall 3	2,58	3.013	0.057	control	standard	0.017
recall 4 (delayed)	2,58	3.545	0.035	control	standard	0.035
					reversed	0.021
total learned in 3 attempts	2,58	3.093	0.053	control	standard	0.024
					reversed	0.067
n forgotten after delay	2,58	2.979	0.059	control	reversed	0.023

For all recall attempts on the AVLT, values of F were at or around significance (across the three protocols); planned comparison *a priori* t-tests (using Fisher's Least Significant Difference test for comparisons between three groups) showed significant differences existed between the control and either one or both of the other protocols for each variable comprising the AVLT. These results suggest that the ability, or motivation, or both of the participants comprising the control protocol was significantly lower than for the other two protocols and this may have influenced performance on the Stroop tasks which required effort in order to colour name words as quickly as possible.

As a second check that this may have been the case, a sample (n=15) of right handed female postgraduate students (PG group) was tested on the word Stroop task in isolation and without prior knowledge of the purpose of the experiment. Their performance on the word Stroop task was compared to that of the female right handers in the control protocol group using A 4x2 (word type x group) repeated measures ANOVA showed a main effect of word type [$F_{(2.553,97.005)}$=22.071, p<.001, a significant word type by group interaction [$F_{(2.553,97.005)}$=4.023, p=.014] and a significant between subjects effect of group [$F_{(1,38)}$=5.662, p=.022]. The PG group performed with significantly less interference effects than the female right handers in control protocol group; these values are indicated on Figure 22.1 above.

A 5x2 (word type by group) repeated measures ANOVA carried out for response latency also showed highly significant main effects of word type [$F_{(2.581,98.092)}$=87.946, p<.001] and group [$F_{(1,38)}$=10.477, p=.003], with significantly reduced response latencies in the PG group than in the control protocol, and a highly significant interaction [$F_{(2.581,98.092)}$=4.709, p=.006] (see Figure 22.2).

Figure 22.2 Comparison of latency effects between control protocol and PG control group:



These apparent difficulties with the control group compromise the intended control for watching the film, preventing definitive support in relating findings from the standard and reversed protocols to the film; however, the differences in patterns of interference and response latency in the latter two protocols suggest that watching the film may be responsible for the effect.

Appendix 23 Ethics approvals

The following letters confirming ethical approval follow:

Chapter 3.1: Approval by Department of Psychology Ethics Committee combined with approval for Chapter 7:

Chapter 3.2: Experimental studies included ethical approval for completion of the PDS reported in this section of Chapter 3 –see Chapter 5.2 & Chapter 6 below.

Chapter 4: Ethical approval in respect of the pooled samples comprising this study was obtained as follows:

Aberdeen: Grampian COREC - letter
London: Ethical approval was obtained by Prof. Chris Brewin for their project
Melbourne: Ethical approval was obtained by Dr David Forbes for their project
Dundee: Tayside COREC - letter

Chapter 5.1: Approval by Department of Psychology Ethics Committee

Chapter 5.2 & Chapter 6: Approval by Department of Psychology Ethics Committee

Chapter 3.1 & Chapter 7: Approval by Department of Psychology Ethics Committee

Carolyn Choudhary

From:	James Anderson
Sent:	02 December 2005 10:10
To:	Carolyn Choudhary
Subject:	RE: Ethics approval

February 1, 2005

Carolyn,

This is to inform you that your research proposal entitled:

"Left/mixed handedness as a risk factor for PTSD: in utero testosterone as a possible contributing factor in left/mixed handedness"

has been approved by the departmental Ethics Committee.

No concerns were raised during the review process.

Jim Anderson
Chair, Psychology Ethics Committee

Chapter 4: Ethical approval in respect of the pooled samples comprising this study was obtained as follows:

Aberdeen: Grampian COREC - letter
London: Ethical approval was obtained by Prof Chris Brewin for their project
Melbourne: Ethical approval was obtained by Dr David Forbes for their project
Dundee: Tayside COREC - letter

NHS Grampian

Grampian Local Research Ethics Committee (1)
Summerfield House
2 Eday Road
Aberdeen
AB15 6RE

Telephone: 01224 558503
Facsimile: 01224 558609

22 June 2006

Ms Carolyn J Choudhary
PhD Research Student
University of Stirling
Department of Psychology
STIRLING
FK9 4LA

Dear Ms Choudhary

Full title of study: **An investigation of whether the existing finding of excess left/mixed handedness in male combat veterans with PTSD extends to civilian populations with PTSD and to women.**

REC reference number: **06/S0801/64**

Thank you for your letter of 8 June 2006, responding to the Committee's request for further information on the above research and submitting revised documentation.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised.

Conditions of approval

The favourable opinion is given provided that you comply with the conditions set out. You are advised to study the conditions carefully, in particular:

Condition 1: Annual Progress Report

Under the Central Office of Research Ethics Committees (COREC) regulations NHS Research Ethics Committees are required to monitor research with a favourable opinion. This is to take the form of an annual progress report which should be submitted to the Grampian Research Ethics Committee 12 months after the date on which the favourable opinion was given. Annual reports should be submitted thereafter until the end of the study.

Points to note:

- The first annual progress report should give the commencement date for the study. This is normally assumed to be the date on which any of the procedures in the protocol are initiated. Should the study not commence within 12 months of approval a written explanation must be provided in the 1st annual progress report.
- Progress reports should be in the format prescribed on the COREC website (www.corec.org.uk/applicants/apply/progress.htm).
- Progress reports must be signed by the Principal Investigator/Chief Investigator.
- Failure to submit a progress report could lead to a suspension of the favourable ethical opinion for the study.
- Please note the Annual Progress Report is a short 3 page form which is extremely easy to complete.

Condition 2: Notification of Study Completion/Termination

Under the Central Office of Research Ethics Committees (COREC) regulations researchers are required to notify the Ethics Committee from which they obtained approval of the conclusion or early termination of a project and to submit a Completion/Termination of Study Report. Researchers should follow the instructions on the COREC website (www.corec.org.uk/applicants/apply/endofproject.htm).

Points to note:

- For most studies the end of a project will be the date of the last visit of the last participant or the completion of any follow-up monitoring and data collection described in the protocol.
- Final analysis of the data and report writing is normally considered to occur after formal declaration of the end of the project.
- A Final Report should be sent to the GREC within 12 months of the end of the project.
- The summary of the final report may be enclosed with the end of study declaration, or sent to the REC subsequently.
- There is no standard format for final reports. As a minimum we should receive details of the end date and information on whether the project achieved its objectives, the main findings and arrangements for publication or dissemination of research, including any feedback to participants.
- Please note the Completion/Termination of Study Report need only be a summary document and should, therefore, be easy to prepare.

06/S0801/64 Page 3

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Application	1	9 May 2006
Investigator CV		9 May 2006
Protocol	1	
Covering Letter		
Covering Letter		8 June 2006
Letter from Sponsor		21 April 2005
Questionnaire: Validated Questionnaire		
Letter of invitation to participant	2	8 June 2006
GP/Consultant Information Sheets	1	19 August 2005
Participant Information Sheet	1	8 June 2006
Participant Consent Form	2	8 June 2006
Response to Request for Further Information		8 June 2006
Laterality Form 6	1	8 June 2006
Statement of indemnity arrangements		21 April 2005
Summary CV for supervisor		20 January 2006

Research governance approval

The study should not commence at any NHS site until the local Principal Investigator has obtained final research governance approval from the R&D Department for the relevant NHS care organisation.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

06/S0801/64	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project

Yours sincerely

Carol Bain

pp **Dr Melvin Morrison**
Chair

Enclosures: Standard approval conditions

Tayside Committee on Medical Research Ethics B
Level 9
Ninewells Hospital & Medical School
DUNDEE
DD1 9SY
Telephone Number: 01382 632701
Fax Number: 01382 496207
www.nhstayside.scot.nhs.uk

NHS
Tayside

Ms Carolyn J Choudhary
PhD Research Student
Department of Psychology
University of Stirling
STIRLING
FK9 4LA

Date	17 November 2006
Your Ref	
Our Ref	FB/06/S1402/87
Enquiries to	Miss Fiona Bain
Extension	32701
Direct Line	01382 632701
Email	fionabain@nhs.net

Dear Ms Choudhary

Full title of study: **An investigation of whether the existing finding of excess left/mixed handedness in male combat veterans with PTSD extends to civilian populations with PTSD and to women.**

REC reference number: **06/S1402/87**

Thank you for your letter of 16 November 2006, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Administrator.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised.

Ethical review of research sites

The favourable opinion applies to the research sites listed on the attached form.

Conditions of approval

The favourable opinion is given provided that you comply with the conditions set out in the attached document. You are advised to study the conditions carefully.

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	Version	Date
Application		15 September 2006
Investigator CV		15 September 2006
Investigator CV	Supervisor CV - Professor Ronan O'Carroll	28 August 2006
Protocol	1	
Covering Letter		15 September 2006
Letter from Sponsor		17 August 2006
Questionnaire	3	08 June 2006

POSITIVE ABOUT DISABLED PEOPLE

Document	Version	Date
Letter of invitation to participant	2	30 October 2006
GP/Consultant Information Sheets	GP Letter - 1	08 August 2006
Participant Information Sheet: Participant Information Sheet	2	30 October 2006
Participant Information Sheet: Internal Students/Staff	2D4D - 1	24 January 2005
Participant Information Sheet: Glasgow Science Centre	GSC2	03 April 2006
Participant Consent Form	1	08 August 2006
Response to Request for Further Information		09 November 2006
Response to Request for Further Information		16 November 2006
Patient Reminder Letter	3	16 November 2006

Research governance approval

The study should not commence at any NHS site until the local Principal Investigator has obtained final research governance approval from the R&D Department for the relevant NHS care organisation.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

06/S1402/87	Please quote this number on all correspondence

Yours sincerely

for **Chair**

Enclosures: Standard approval conditions
Site approval form

Copy to: Department of Psychology, University of Stirling
NHS Tayside R&D Department

Continued

Chapter 5.1: Approval by Department of Psychology Ethics Committee

Re: Choudhary Physiology study Page 1 of 1

Carolyn Choudhary

From: James Anderson
Sent: 19 March 2007 10:50
To: Carolyn Choudhary
Cc: Ronan O'Carroll; Hazel O'Donnell
Subject: Re: Choudhary Physiology study

Carolyn,

This is to inform you that your proposal entitled:

"Do men and women differ in physiological reactions to a film?"

has been approved by the departmental Ethics Committee.

Jim Anderson
Chair, Psychology Ethics Committee

09/12/2008

Chapter 5.2 & Chapter 6: Approval by Department of Psychology Ethics Committee

Carolyn Choudhary

From: James Anderson
Sent: 07 February 2005 16:38
To: Carolyn Choudhary
Cc: Ronan O'Carroll; Claire Wilson {Psych}
Subject: RE: Ethics application

Carolyn,

This is to inform you that your proposal entitled:

"Left/mixed handedness as a risk factor for PTSD and relevance in processing emotional material: the Stroop task"

has been approved by the departmental Ethics Committee.

No concerns were raised by the reviewers.

Jim Anderson
Chair, Psychology Ethics Committee

From: Carolyn Choudhary
Sent: Wednesday, February 2, 2005 11:30 AM
To: James Anderson
Subject: Ethics application

<<File: ETHICS application- Stroop.DOC>><<File: PSS10.DOC>><<File: lateralityform2.DOC>><<File: FILMFORMv2.DOC>><<File: PDS+text.pdf>><<File: CONSENT Stroop.DOC>><<File: INFO Stroop.DOC>><<File: DEBRIEF Stroop.DOC>>
Hi Jim

I have attached an Ethics Application plus supporting forms; I have still not resolved the problem with ProCite/Word so still can't produce the references used, so apalogies for this.

Regards
Carolyn

Carolyn J Choudhary
PhD Research Student
Department of Psychology
University of Stirling, UK
Visit my web page
Email: cjc2@stir.ac.uk
Phone: 01786 466853

Carolyn Choudhary

From: James Anderson
Sent: 22 September 2005 13:24
To: Carolyn Choudhary
Subject: RE: Ethics application: revision for follow up study

Carolyn,

That seems fine.

Jim

From: Carolyn Choudhary
Sent: Thursday, September 22, 2005 11:46 AM
To: James Anderson
Cc: Ronan O'Carroll
Subject: RE: Ethics application: revision for follow up study

Hi Jim

Thanks for this. Will spell out PTSD in the info sheet – this is a helpful point.

I note the comment re the violent nature of the film; this excerpt is tense and suspenseful but until the two characters fire guns at each other in the last seconds, I would maintain there is no violence. The last part of the excerpt is in darkness (the male character has switched out the lights in the basement) with the female character seen only through his night vision goggles. In the last seconds there is an incredibly brief (1-2 frames only) image of the male character with gunshot wounds to his chest as the window behind him is smashed (by the gunfire) letting in the light. Hence the question (21) about the wounds sustained: this is so briefly presented, but are people seeing it, and if so which participants see it…? Does it relate to self-reported levels of fear experienced? Other than this, I can't see any other questions in the Film MCQ that suggest the film is violent – unless I'm missing something?

Obviously, I don't know from whom the comment originated, but perhaps this will reassure that the film isn't violent: if there are further concerns please let me know.

Regards
Carolyn

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-----Original Message-----
From: James Anderson
Sent: 22 September 2005 09:48
To: Carolyn Choudhary
Subject: RE: Ethics application: revision for follow up study

Sorry, Carolyn,

Was in too much of a hurry before leaving last week. Just got back.

Here are the comments:

"Approve but note that the film is said in the ethics application to be rated 18 'although not pornographic or violent in nature' when clearly from the memory questionnaire it is violent. Also in the information sheet it might be better to spell out what PTSD stands for."

Jim

From: Carolyn Choudhary
Sent: Monday, September 19, 2005 12:14 PM
To: James Anderson
Subject: RE: Ethics application: revision for follow up study

Hi Jim

Thanks for this – but I think the promised pasted in comments are missing? If you have them, I would be grateful for them!

Regards
Carolyn

Carolyn J Choudhary
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Phone: 01786 466853

-----Original Message-----
From: James Anderson
Sent: 15 September 2005 09:04
To: Carolyn Choudhary
Subject: RE: Ethics application: revision for follow up study

Carolyn,

This is to inform you that your proposal entitled:

"Left/mixed handedness as a risk factor for PTSD and relevance in processing emotional material: the Stroop task (replication)"

has been approved by the departmental Ethics Committee.

Below I'm pasting in a couple of comments that you might want to take on board before proceeding.

Jim Anderson
Chair, Psychology Ethics Committee

From: Carolyn Choudhary
Sent: Tuesday, September 13, 2005 10:19 AM
To: James Anderson
Cc: Ronan O'Carroll
Subject: Ethics application: revision for follow up study

<<File: ETHICS application- Reversed Stroop + scan.DOC>><<File: INFO Stroop v3.DOC>><<File: CONSENT Stroop v2.DOC>><<File: CONSENT Stroop II.DOC>><<File: DEBRIEF Stroop R.DOC>><<File: DEBRIEF Stroop IIv2.DOC>><<File: PSS10.DOC>><<File: lateralityform3 change hands.DOC>><<File: FILMFORMv2.DOC>><<File: PDS+text.pdf>><<File: AVLT A.DOC>><<File: film recognition memory test.DOC>>
Hi Jim

I have attached an ethics application, with slight revisions to a previously approved study, to run as a follow up. There are no significant changes to the original study.

I would appreciate an expedited reply if possible, so that I can start running the revised study back to back with the previous study, from as soon as possible next week.

Many thanks
Carolyn

Carolyn J Choudhary
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Phone: 01786 466853

Carolyn Choudhary

From: James Anderson
Sent: 23 April 2006 15:49
To: Carolyn Choudhary
Subject: RE: Ethics Application

Carolyn,

This is to inform you that the proposal entitled:

"Additional control condition for Stroop Experiments"

has been approved by the departmental Ethics Committee.

Jim Anderson
Chair, Psychology Ethics Committee

From: Carolyn Choudhary
Sent: Sunday, April 23, 2006 11:21 AM
To: James Anderson
Subject: RE: Ethics Application

<<File: BPSEthicsForm control x-o.doc>>
Hi Jim
Here is the attachment!!!
Regards
Carolyn

Carolyn J Choudhary
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From: James Anderson
Sent: Sat 22/04/2006 10:07
To: Carolyn Choudhary
Subject: RE: Ethics Application

Carolyn,

No attachment....

Jim

From: Carolyn Choudhary
Sent: Thursday, April 20, 2006 22:23 PM
To: James Anderson
Cc: Ronan O'Carroll
Subject: Ethics Application

Hi Jim

I have attached an application in respect of a short, additional control condition I need to run. I would be grateful for an early reply if possible.

Many thanks
Carolyn

Carolyn J Choudhary
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Appendix 24 removed from digital copy of thesis for copyright reasons