Comprehensive Summaries of Uppsala Dissertations
from the Faculty of Social Sciences 129

Posttraumatic Stress Disorder (PTSD) in the General Population

BY

ÖRJAN FRANS

ACTA UNIVERSITATIS UPSALIENSIS
UPPSALA 2003

Dissertation presented at Uppsala University to be publicly examined in Sal IX, Universitetshuset, Uppsala, Friday, October 3, 2003 at 09:15 for the degree of Doctor of Philosophy in Clinical Psychology. The examination will be conducted in Swedish.

Abstract
Frans, Ö. 2003. Posttraumatic Stress Disorder (PTSD) in the General Population. Acta Universitatis Upsaliensis. *Comprehensive Summaries of Uppsala Dissertations from the Faculty of Social Sciences* 129. 66 pp. Uppsala. ISBN 91-554-5697-9

This thesis explored the epidemiology of Posttraumatic Stress Disorder (PTSD) and different aspects of the disorder. Firstly, we investigated the lifetime prevalence of traumatic experiences and PTSD in the general adult population in Sweden and evaluated the impact of different trauma types, trauma frequency, and perceived distress. The results show that traumatic experiences are common and PTSD is not rare; roughly one out of ten traumatic events results in PTSD, with a 5.6% lifetime prevalence. The female/male ratio is 2:1. The risk for PTSD increases considerably with a high trauma-associated emotional impact. The distressing impact of a given trauma appears to be higher in women than in men, indicating an increased vulnerability in women. Secondly, we hypothesized that traffic road accidents (TRA's) are one of the most prevalent types of traumatic events in Swedish society; therefore, we examined the impact of event and response characteristics associated with TRA's on PTSD development. The data demonstrate that of those who had experienced a TRA (n=1074, 58.9%), 6.1% reported lifetime PTSD. TRA's associated with fatal accidents and injury to oneself and related to high distress more than double the risk for PTSD. Thirdly, we compared the relative merits of the DSM-IV's three-factor solution for PTSD symptoms to alternative models. We found that the symptomatology is equally well accounted for using all factor analytic models as yet presented in the literature; the DSM-IV, we found, provides as good a fit to data as other models. Fourthly, we examined the neurofunctional correlates of PTSD symptoms and whether a treatment-induced (serotonin reuptake inhibitor - SSRI) reduction of PTSD symptoms is associated with altered rCBF during symptom provocation. Our results indicate that PTSD symptoms correlates with areas involved in memory, emotion, attention, and motor control and that SSRI treatment normalizes provocation-induced rCBF in these areas.

Keywords: posttraumatic stress disorder, trauma, epidemiology, general population, prevalence, traffic road accidents, DSM-structure, positron emission tomography, regional cerebral blood flow, symptom provocation, selective serotonin reuptake inhibitor

Örjan Frans, Department of Psychology, Box 1225, Uppsala University, SE-75142 Uppsala, Sweden

ISSN 0282-7492
ISBN 91-554-5697-9
urn:nbn:se:uu:diva-3528 (http://urn.kb.se/resolve?urn=urn:nbn:se:uu:diva-3528)

'Hush! no, no – it's the water,' said Lord Peter, with chattering teeth; 'it's up to their waists down there, poor devils. But listen! can't you hear it? Tap, tap, tap – they're mining us – but I don't know where – I can't hear – I can't. Listen, you! There it is again – we must find it – we must stop it …. Listen! Oh, my God! I can't hear – I can't hear anything for the noise of the guns. Can't they stop the guns?'

Lord Peter Wimsey suffering a flashback in Dorothy L. Sayers' '*Whose Body?*' (Hodder and Stoughton: London, 1923/1988, p 132).

To Emma and Joakim

List of Papers

This thesis is based on the following papers, which will be referred to in the text by their Roman numerals.

I. Frans, Ö., Rimmö, P-A., Åberg, L., Fredrikson, M. Trauma exposure and posttraumatic stress disorder in the general population. (in progress)

II. Frans, Ö., Rimmö, P-A., Åberg, L., Fredrikson, M. Traffic road accidents, and posttraumatic stress disorder in the general population. (in progress)

III. Rimmö, P-A., Frans, Ö., Åberg, L., Fredrikson, M. The structure of posttraumatic stress symptoms: A model fitting approach. (manuscript)

IV. Fernandez, M., Pissiota, A., Frans, Ö., von Knorring, L., Fischer, H., Fredrikson, M. (2001) Brain function in a patient with torture related post-traumatic stress disorder before and after fluoxetine treatment:. a positron emission tomography provocation study. *Neuroscience Letters*, 297: 101-104

Repints were made with the kind permission of Elsevier (Paper IV).

Contents

Abbreviations

AGFI	the Adjusted Goodness of Fit index
APA	the American Psychiatric Association
BA	Brodmann's area
CAPS	the Clinician Administered PTSD Scale
CBT	cognitive behavioral therapy
CFA	confirmatory factor analysis
CI/Ci	confidence interval
CIDI	the Composite International Diagnostic Interview
DF/df	degrees of freedom
D4DR	the D4 dopamine receptor gene
DIS	the Diagnostic Interview Schedule
DSM-I	the Diagnostic and Statistical Manual of Mental Disorders, 1st edn.
DSM-II	the Diagnostic and Statistical Manual of Mental Disorders, 2nd edn.
DSM-III	the Diagnostic and Statistical Manual of Mental Disorders, 3rd edn.
DSM-III-R	the Diagnostic and Statistical Manual of Mental Disorders, revised 3rd edn.
DSM-IV	the Diagnostic and Statistical Manual of Mental Disorders, 4th edn
EFA	exploratory factor analysis
$H_2{}^{15}O$	15-oxygen radiolabeled water
ID	identity
ICD-10	International Classification of Diseases and Related Health Problems, 10th edn
IES	the Impact of Event Scale
MMPI-2	the Minnesota Multiphasic Personality Inventory-2
MRI	Magnetic Resonance Imaging
MVA	motor vehicle accident
N/n	number of subjects
PCL/PCLS	the PTSD checklist/scale
PET	Positron Emission Tomography

PTSD	Posttraumatic Stress Disorder
RCBF/rCBF	regional cerebral blood flow
RMSEA	the Root Mean Square Error of Approximation
SCID	the Structured Clinical Interview for DSM-IV Disorders
SD/sd	standard deviation
SSRI(s)	selective serotonin reuptake inhibitor(s)
STAI-S	the Spielberger´s State Anxiety Inventory
TRA	traffic road accident
trbc-MAO	the platelet monoamine oxidase
UCR	the unconditioned response
UCS	the unconditioned stimulus
VAS	visual analogue scale
WAIS-R	the Wechsler Adult Intelligence Scale-Revised
WLS	the weighted least square
WMS	the Wechsler Memory Scale

1. Introduction

1.1 About this thesis

Posttraumatic Stress Disorder (PTSD) is a debilitating anxiety disorder resulting from exposure to trauma. More knowledge is needed on its prevalence and the factors that determine it, as well as on brain mechanisms related to its symptomatology.

This thesis is based on four empirical studies with the general aims of investigating:

1. the prevalence of PTSD and trauma exposure in the general population in Sweden.
2. the impact of traffic road accidents (TRA's) on PTSD development
3. the structure of posttraumatic stress symptoms using a model fitting approach
4. the neurofunctional correlates of PTSD symptoms and the effects of selective serotonin reuptake inhibitor (SSRI) treatment on brain blood flow using positron emission tomography (PET) imaging techniques.

1.2 Historical perspectives on posttraumatic stress disorder

1.2.1 Trauma in the history of psychiatry

It is a common belief that Sigmund Freud was the forefather of the current PTSD nosology. At the end of the 19th century, Sigmund Freud presented the case study of Anna O., who was suffering from hysterical symptoms that appeared to be related to traumatic sexual experiences in her childhood. In fact, Freud noticed an increasing number of women with complaints who reported exposure to sexual events in their childhoods.

Freud's original model of neurosis, the Seduction Theory, was, indeed, a posttraumatic paradigm that emphasized external traumatic events. In 1897, however, he suddenly shifted his paradigmatic focus to intrapsychic fantasy as the central point for traumatic neurosis – the Oedipal Theory. What Freud actually did was to transform his views into the theory that fantasies of childhood sexuality led to neurotic behavior, rather than fully recognizing the probability of childhood sexual abuse – a traumatic event – as the source of the problems (cf. Wilson, 1994; DeMause, 1997; Nemiah, 1998). Freud's shift of paradigm had a great influence on the view of the consequences of traumatic events, as was reflected in both the DSM-I (APA, 1952) and the DSM-II (APA, 1968). In these early DSM versions, classifications of stress response syndromes were described as transient reactive processes – temporary, rather harmless, disturbances. In contrast, present diagnostic systems focus on symptom persistence.

Thus, the origin of trauma theory and research must be sought elsewhere. The first true researcher on traumatic events was probably John Eric Erichsen. In his book *On Railway and Other Injuries of the Nervous System* (Erichsen, 1867), he described the symptoms of patients who had suffered railway accidents, giving special attention to symptoms that occurred days or weeks after the accident, such as memory loss, sleeping problems and nightmares. Erichsen thought that this syndrome, "railway spine," was an effect of chronic myelomeningitic changes in the spinal cord and the brain. Herman Oppenheim was probably the first to use the term "traumatic neurosis" when he, in 1889, described observations made during his work at the Nervenklinik der Charité (Oppenheim, 1889). In his doctoral thesis Eduard Stierlin described his observations of a mining accident and a railway accident and proposed that emotions and fright are the most important etiological factors for the development of a neurosis. Stierlin postulated that emotions lead to lowered resistance within the nervous system and that personal dispositions can cause the development of a neurosis (Stierlin, 1909; 1911); he clearly took into account the victims' individual vulnerabilities.

During Word War I, the effect of combat stress was recognized. Many soldiers suffered from "war neurosis" or "shell shock". This problem was not first regarded as mental illness but rather as physical injury resulting from blasts and noises from bombardment (Ahrenfeldt, 1958). However, by 1917, special centers were established for *mental* treatment of "shell shock". Later that same year, Dr. T. W. Salmon sent his *The Care and Treatment of Mental Diseases and War Neuroses ("Shell Shock") in the British Army* (Salmon, 1917) to the U.S. Surgeon General, and the first principles of America's trauma psychiatry were developed. (As early as the American

Civil War, however, the descriptions of a shell shock-like disorder known as "Da Costa's Syndrome" had been documented).

The use of psychophysiological assessment also began during Word War I. Under bombardment, soldiers experienced severe heart palpitations that produced incapacitating levels of distress, termed "irritable heart syndrome" or "soldiers heart". In one study, Meakins and Wilson (1918) measured heart rate before and after the presentation of an unexpected sulfuric flame and the firing of a gun under the chair where the soldier being tested was seated. Soldiers with "irritable heart syndrome" who were unable to return to duty showed remarkably stronger heart rate responses than did soldiers who were able to return to duty, again addressing the issue of individual vulnerability.

During Word War II, the most frequent symptoms of veterans hospitalized with "operational fatigue" included irritability, difficulty falling asleep, startle reaction, difficulty concentrating, preoccupation with combat experiences, tremor, evidence of sympathetic over-activity and nightmares (Grinker and Spiegel, 1945).

Thus, many of the psychological phenomena in today's PTSD diagnosis have long been recognized and, to some extent, described in disorders such as railway spine, traumatic neurosis, shell shock, irritable heart syndrome, and operational fatigue (Schnurr, 1991; Trimble, 1984).

1.2.2 The history of PTSD symptoms is the history of the "hysteria" construct

Behaviors now being regarded as diagnostic criteria for PTSD, such as "recurrent and intrusive distressing recollections of the event, including images, thoughts, or perceptions" and "illusions, hallucinations, and dissociative flashback episodes" were long regarded as symptoms of hysteria.

The term "hysteria" is derived from the Greek word "hystera," meaning uterus (Veith, 1965). As a construct, hysteria has its beginnings in Egyptian and Greek medicine. Edward Jordan (1569–1632) was probably the first to assume that the etiology of hysteria lay in natural, rather than supernatural, causes (Trimble, 1981). In spite of that, individuals with hysteria were believed to be possessed by demons or the devil himself and were often persecuted or put to death. Society's reaction was to stigmatize the victims; the focus was entirely on the pathologies of the individual, with little if any interest in external traumatic events as possible factors contributing to the symptoms.

The traumatic origins of hysteria were not acknowledged until the 19th century when, in 1853, the physician Robert Carter claimed that the etiology of hysteria included external events (Veith, 1965). In 1890, Charcot's

student Pierre Janet formulated a theory that emphasized the role of dissociation between cognition and affect in the etiology of hysteria (van der Kolk, Weisaeth, and van der Hart, 1996). Traditional psychoanalysis, operating on the Oedipal assumption, however, still refused to see the role of trauma in hysterical symptoms, instead treating actual expressions of traumatic events, especially in childhood, as fantasies (DeMause, 1997; van der Kolk, Waisaeth, and van der Hart, 1996). The impact of traditional psychoanalysis during the 20th century led to society's (including the scientific establishment) reluctance to acknowledge hysterical symptoms as having been caused by traumatic experiences. Until 1980, symptoms currently considered as possible reactions to traumatic events were regarded as being due only to individual pathology and were not seen as environmentally determined.

1.3 The diagnosis of posttraumatic stress disorder

1.3.1 The traumatic stressor – an etiological agent

Since the beginning of the psychiatric establishment, controversy concerning the consequences of traumatic events has existed. This was strongly evident in the first two versions of the DSM. In the DSM-I, for instance, trauma could only lead to "gross stress reactions," which were part of "transient situational personality disorders". Extreme traumatic events were thought to lead only to transient and temporary disturbances and, if the disturbances were chronic, another diagnostic label had to be used. Posttraumatic symptoms, if acknowledged and recognized at all, were regarded as being due to individual endogenous pathology, rather than to exogenous traumatic events. Freud's spirit still had a considerable influence on the diagnostic committee's standpoint and much of the early works of Stierlin, Carter, Janet, and others, was forgotten.

It was not until the beginning of 1980 that the characteristic symptoms of PTSD were formally codified in diagnostic nomenclature (DSM-III, APA, 1980). At the same time, the symptoms connected with the construct of "hysteria" disappeared from the DSM system, and were divided into several other mental disorders, including PTSD (van der Kolk, Pelcovitz, Roth, Mandel, McFarlane, and Herman, 1996).

PTSD is now considered to develop in the aftermath of a traumatic experience if the symptoms persist longer than one month. Shorter reactions to traumatic events should be classified in DSM terms as Acute Stress Disorder or, when milder, as Adjustment Disorder. In the DSM-III, a

traumatic event was described as “a psychologically traumatic event that is generally outside the range of usual human experience”. In the DSM-III-R (APA 1987), the traumatic event also had to be “markedly distressing to almost everyone”. In the DSM-IV (APA 1994), even more emphasis is placed on exposure to the traumatic event, coupled with the individual’s reaction – he or she must respond with “intense fear, helplessness, or horror”. Thus, the DSM-IV takes the individual’s vulnerability into account because a strong emotional response is equally as important as a traumatic event. Thus, PTSD is conceptualized as an interaction between an external event and a subjective response (see Table 1).

Table 1 The diagnostic criteria for trauma prevalence according to the DSM-IV, criterion A.

Criteria	
A.	The person has been exposed to a traumatic event in which both of the following were present:
A1	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.
A2	The person’s response involved intense fear, helplessness, or horror. Note: In children, this may be expressed instead by disorganized or agitated behavior.

1.3.2 The symptoms – a reaction to trauma

With some slight differences, the symptoms have been described from the introduction of the DSM-III, in three different clusters, or criteria: an intrusive and re-experience category (criterion B), an avoidance and numbing category (criterion C), and a hyperarousal category (criterion D) (see Table 2). Note that criterion B and criterion C are specifically connected to an event while criterion D is not.

Table 2 The diagnostic criteria for PTSD symptom prevalence according to the DSM-IV, criteria B–D.

Criteria
B. The traumatic event is persistently re-experienced in one (or more) of the following ways:
B1. Recurrent and intrusive distressing recollections of the event, including images, thoughts, or perceptions. Note: In young children, repetitive play may occur in which themes or aspects of the trauma are expressed.
B2. Recurrent distressing dreams of the event. Note: In children, there may be frightening dreams without recognizable content.
B3. 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). Note: In young children, trauma-specific reenactment may occur.
B4. Intense psychological distress at exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event.
B5. Physiological reactivity on exposure to internal or external cues that symbolize 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:
C1. Efforts to avoid thoughts, feelings, or conversations associated with the trauma
C2. Efforts to avoid activities, places, or people that arouse recollections of the trauma
C3. Inability to recall an important aspect of the trauma
C4. Markedly diminished interest or participation in significant activities
C5. Feeling of detachment or estrangement from others
C6. Restricted range of affect (e.g., unable to have loving feelings)
C7. 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:
D1. Difficulty falling or staying asleep
D2. Irritability or outbursts of anger
D3. Difficulty concentrating
D4. Hypervigilance
D5. Exaggerated startle response

1.3.3 Criteria E and F – validation criteria of the symptoms

The symptoms in criteria B–D must endure at least one month (criterion E) and must be severe enough to cause subjective distress or functional impairment (criterion F).

Table 3 The diagnostic criteria for PTSD symptom prevalence according to the DSM-IV, criteria E–F.

Criteria
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.

Thus, the DSM-IV requires that the person experience either significant distress or that the PTSD symptoms cause marked impairment in an important area of functioning. Criteria E and F can therefore be regarded as measures of the effects of the symptoms described in criteria B–D. These symptoms (criteria B–D), such as loss of interest in social activities and feeling emotionally numb, interfere with communication, trust, emotional intimacy, and responsible assertiveness, and may lead to an emotionally isolated life. Being constantly on guard and easily startled, combined with experiencing terrifying nightmares, prevents the individual from sleeping restfully, which can, in turn, lead to difficulties in maintaining employment. Trauma memories and flashbacks and an ongoing struggle to avoid trauma reminders become obstacles to living a normal life.

1.3.4 A comparison of criteria for a PTSD diagnosis in different versions of the DSM

On the one hand, the demands in the DSM-IV seem less stringent than in previous versions, since it provides considerable latitude in the definition of a traumatic event (as long as it elicits a strong emotional response). On the other hand, neither the DSM-III nor the DSM-III-R demands that both persistent avoidance of stimuli associated with the trauma and numbing of general responsiveness should be present for the diagnosis, while the DSM-IV does. This simultaneity of avoidance and numbing, added to the most current criterion, F (concerning distress or impairment in social, occupational, or other important areas of the individual's functioning),

makes the DSM-IV more arduous. A difference of lesser magnitude is seen in the placement of the symptom of physiologic reactivity; it has been moved from the hyperarousal cluster to the re-experiencing cluster, shifting criterion D6 in the DSM-III-R to criterion B5 in the DSM-IV.

2. Background to the empirical studies

2.1 The epidemiology of posttraumatic stress disorder

Epidemiological research is concerned with three major questions: How common is the disorder? Who is afflicted with it? What causes it? In studies of PTSD epidemiology, the researcher has two challenges. The first is to measure trauma exposure; i.e., to assess trauma experience according to criterion A in the DSM-IV. The second challenge is case identification. The heart of epidemiological studies is case versus control comparisons (here, the definition of a "case" is someone who meets the diagnostic criteria for PTSD). PTSD has a rather complex and diverse symptomatology and can be difficult to detect, requiring the researcher to make comprehensive assessments. Although the syndromes of PTSD are rather distinct and identifiable as described in the DSM-IV (see Table 2), individuals suffering from PTSD can differ in their overall pattern and severity of symptoms and may show differing degrees of impairment.

2.1.1 Trauma prevalence

The most widely studied type of trauma assessed in association with PTSD (i.e., articles indexed in Entrez PubMed, June 2003) is war exposure (1177 articles), especially that experienced by male Vietnam veterans (Vietnam veterans: 629 articles; male Vietnam veterans: 543 articles). Another commonly studied trauma type is the retrospective examination of childhood physical and sexual abuse in adults (sexual abuse: 197 articles; physical abuse: 91 articles). The third most common focus has been on physical and sexual assault, especially with women as victims (physical assault: 86 articles; on women: 80 articles; sexual assault: 141 articles; on women: 133 articles).

The National Comorbidity Survey (Kessler, Sonnega, Bromet, Hughes, and Nelson, 1995), using the DSM-III-R criteria and a modified version of the Diagnostic Interview Schedule (DIS) (measuring an extensive number of psychiatric disorders, not only PTSD), found that 60.7% of men and 51.2%

of women had experienced at least one traumatic event at some point in their lives. The most recent study of a large community sample of younger adults (aged 18–45) in the USA, examining DSM-IV-diagnosed PTSD using the DIS and the Composite International Diagnostic Interview (CIDI), showed a total traumatic event prevalence of 89.6% (Breslau et al. 1998) (see Table 4).

Table 4 The life-time prevalence of trauma and Posttraumatic Stress Disorder (PTSD) in community samples from the general population

Sample features	Exposure to at least one traumatic event %			Prevalence %			Risk of PTSD after exposure to trauma %	Reference
	Male	Female	Total	Male	Female	Total		
USA community sample 2493 persons				0.5	1.3	1.0		Helzer et al. 1987
USA community sample 2985 persons aged 18-95			2.3	0.9	1.7	1.3		Davidson et al. 1991
USA national sample 4.008 women aged 18 -		68.9	68.9		12.3	12.3	17.9	Resnick et al. 1993
USA national sample 5.877 persons aged 15-54	60.7	51.2	55.8	5.0	10.4	7.8		Kessler et al. 1995
USA community sample 2181 persons aged 18-45			89.6			8.3	9.2	Breslau et al. 1998
Germany community sample 3021 persons aged 14-24	25.2	17.7	21.4	1.0	2.2	1.3	7.8	Perkonigg et al. 2000
Sweden national sample 1.824 persons aged 18-70	84.8	77.1	80.8	3.6	7.4	5.6	6.9	Frans et al. 2003

The types of traumas most strongly associated with PTSD and the sociodemographic correlates of PTSD are not fully understood. It has been suggested that certain traumatic events, such as sexual abuse, give rise to PTSD more often than do others and that perceived trauma intensity could

be a prime factor influencing PTSD development (cf. Norris, 1992). There have been reports of gender specificity, with combat experience being most commonly associated with PTSD in men, whereas in women rape and sexual assault carry stronger risks (Kessler, Sonnega, Bromet, Hughes, and Nelson, 1995). Thus, gender differences may, in part, reflect exposure to different trauma types or different exposure rates, or, alternatively, differential effects of the perceived impact of the event.

2.1.2 PTSD prevalence

A number of studies have investigated posttraumatic stress disorder in individuals exposed to different traumatic events. For example, combat, rape, natural disasters, serious motor vehicle accidents, and crime experiences seem to have a strong relation to the subsequent development of PTSD (Acierno, Resnick, Kilpatrick, Saunders, and Best, 1999; Armenian et al., 2000; Blanchard, Hickling, Taylor, Loos, and Gerardi, 1994; Bremner, Southwick, Darnell, and Charney, 1996; Briere and Elliott, 2000; Brewin, Andrews, Rose, and Kirk, 1999; Bryant and Harvey, 1995; Darves-Bornoz, Pierre, Lepine, Degiovanni, and Gaillard, 1998; Foa, Riggs, and Gershuny, 1995; Kato, Asukai, Miyake, Minakawa, and Nishiyama, 1996; Keane et al., 1998; Kilpatrick et al., 1989; Kozaric-Kovacic, Folnegovic-Smalc, Skrinjaric, Szajnberg, and Marusic, 1995; Kozaric-Kovacic, Hercigonja, and Grubisic-Ilic, 2001; Mayou, Bryant, and Ehlers, 2001; McFarlane, Clayer, and Bookless, 1997; Mellman, Randolph, Brawman-Mintzer, Flores, and Milanes, 1992; Pitman, Orr, Forgue, de Jong, and Claiborn, 1987; Taylor, Kuch, Koch, Crockett, and Passey, 1998; Ursano et al., 1999; Valentiner, Foa, Riggs, and Gershuny, 1996).

Studies in the general population, particularly studies with randomly selected subjects, are relatively scarce, with only half a dozen published, the majority reporting prevalence rates in the United States (see Table 4). Helzer, Robins, and McEvoy (1987) and Davidson, Hughes, Blazer, and George (1991), both used DSM-III criteria and the DIS (Robins, Helzer, Croughan, Williams, and Spitzer, 1981) to assess PTSD reported rates of 1.0% and 1.3%, respectively. Leaving that requirement and estimating signs and symptoms of PTSD irrespective of traumatic events Resnick, Kilpatrick, Dansky, Saunders, and Best (1993) reported a DSM-III-R-defined prevalence rate of 12.3% in women. The National Comorbidity Survey (Kessler, Sonnega, Bromet, Hughes, and Nelson, 1995) reported a prevalence rate of 10.4% in women and 5.0% in men. The average number of 7.8% in the Kessler, Sonnega, Bromet, Hughes, and Nelson (1995) study is similar to figures reported by Breslau et al. (1998), who observed an average 8.3% lifetime prevalence and a conditional risk of developing PTSD

after exposure to trauma at roughly 10%. (The two latter studies used the DSM-IV's criteria.)

A recent German study (Perkonigg, Kessler, Storz, and Wittchen, 2000) reported considerably lower lifetime PTSD prevalence rates (1% for men and 2.2% for women) in young Germans (14–24 years old), suggesting a European-American PTSD prevalence mismatch.

To the best of our knowledge, apart from this German study, there exists no other published study on PTSD prevalence in the general population in Europe. Thus, the general aim of the first study was to investigate the prevalence of traumatic experiences and the lifetime prevalence of posttraumatic stress disorder in the general adult population in Sweden.

2.2 Traffic road accidents and posttraumatic stress disorder

A number of case control studies have investigated PTSD in individuals exposed to motor vehicle accidents (MVA's). For example, in survivors of MVA's, PTSD prevalence rates ranging from 10–46% have been noted (Blanchard, Hickling, Taylor, Loos, and Gerardi, 1994; Brom, Kleber, and Hofman, 1993; Mayou, Tyndel, and Bryant, 1997). Nearly all case-control studies have included individuals seeking medical attention after their accidents (cf. Blanchard, Hickling, Taylor, Loos, and Gerardi, 1994). The possibility exists that self-selected samples are not representative of the population at large and that prevalence figures are inflated in self-referred samples. The possibility also exists that event- and response-related factors are distributed unevenly between case-control and general population studies and contribute to outcome differences. For example, confrontation with fatal accidents, the extent of physical injury and perceiving a threat to life may all relate to PTSD development (Green, Lindy, and Grace, 1985; Kilpatrick et al., 1989) and it is likely that these factors are more common in self-selected than random samples. None of the major epidemiological studies in the general population, cited above, have focused specifically on MVA's or TRA's, even though Breslau et al. (1998), for instance, reported an overall MVA prevalence of 67.4%. We hypothesized that TRA's should be one of the most prevalent traumatic events in Swedish society; therefore, the general aim of the second study was to investigate the impact of such events on PTSD development.

2.3 Some methodological issues

2.3.1 PTSD and comorbidity

In clinical cohorts of PTSD patients, up to 80% have at least one additional psychiatric diagnosis. Thus, PTSD, comorbid with other DSM-IV Axis I and Axis II disorders, is actually much more common than "pure" PTSD. The most common comorbid disorders are alcoholism and drug abuse (60–80%), affective disorders (26–65%), personality disorders (40–60%), and other anxiety disorders (30–60%) (Brown, Campbell, Lehman, Grisham, and Mancill, 2001; Friedman, 1990; Jordan, et al., 1991; Kofoed, Friedman, and Peck, 1993; Kulka, et al., 1991; Schnurr, Friedman, and Bernardy, 2002; Spivak, Segal, Laufer, Mester, and Weizman, 2000; Zayfert, Becker, Unger, and Shearer, 2002). In addition, PTSD patients often present with problems of affect regulation, impulsive behavior, inappropriate sexual behavior, and a wide variety of somatic complaints (Andreski, Chilcoat, and Breslau, 1998; Herman, 1992; Shalev, Bleich, and Ursano, 1990; Sharp and Harvey, 2001; Weisberg et al., 2002). Many studies have also described neurobiological abnormalities associated with PTSD (Bremner, 2002; Bremner et al., 1995, 1997; Friedman, 1990; Friedman, Charney, and Deutch, 1995; Gerhards, Yehuda, Shoham, and Hellhammer, 1997; Gurvits et al., 1996; Hull, 2002; Murburg, 1994; Southwick et al., 1997; Stein, Koverola, Hanna, Torchia, and McClarty, 1997; Villarreal et al., 2002; Yehuda, 1998; Yehuda, 2002a).

In the present studies, no data on comorbid disorders will be presented since comorbidity was allowed for – but not assessed –, as "pure" PTSD is probably atypical.

2.3.2 The assessment of trauma exposure in PTSD

To assess trauma prevalence according to the DSM-IV, the measurement tool must cover three degrees of involvement: it must assess direct personal exposure ("it happened to me") and it must also include exposure through witnessing ("I saw it happen to someone else") and vicarious exposure ("I know someone it happened to"). Tools that are used to measure trauma exposure must take these three different forms of exposure modes into account and provide separate items for each type of exposure.

There are several instruments, structured interviews as well as self-administered formats, with acceptable psychometric properties that are useful in assessing PTSD prevalence. Some of these include the CIDI, the Structured Clinical Interview for DSM-IV Disorders (SCID), the Impact of Event Scale (IES), the DIS, the Clinician Administered PTSD Scale (CAPS),

the Minnesota Multiphasic Personality Inventory-2 (MMPI-2), and the PTSD checklist scale (PCL/PCLS). Other measurements have been useful in clinical and research applications exploring different aspects of PTSD, such as the Wechsler Adult Intelligence Scale-Revised (WAIS-R), the Wechsler Memory Scale (WMS), Wisconsin Card Sorting Test, Stroop interference, and different methods of psychophysiological assessment and brain imaging.

2.3.3 The use of questionnaires in PTSD research

Challenging common sense, evidence is accumulating suggesting that more sensitive information is likely to be revealed in questionnaires than in interview settings (cf. Durant and Carey, 2002; Jolly, Wiesner, Wherry, Jolly, and Dykman, 1994; Paivio, 2001; Turner, Lessler, and Gfroerer, 1992). The diagnosis of PTSD is primarily based on self-reports, whether using questionnaires or interviews. In PTSD research, it is necessary to rely on these self-reports of traumatized individuals, although attempts have been made to validate subjective reports with actual trauma occurrence (e.g., comparing them with archival sources such as state records of crime or other sources such as newspapers). None of these studies did report any differences between the objective sources and the self-reported experience nor has evidence suggested that the traumatized state or the symptoms themselves should interfere with memory retrieval of the traumatic event (cf. Schnurr, Friedman, and Bernardy, 2002).

Besides being cost-effective and easy to manage, questionnaires, compared to interviews, have other distinctive advantages. Many (Kessler, Sonnega, Bromet, Hughes, and Nelson, 1995; Resnick, Kilpatrick, Dansky, Saunders, and Best, 1993) have stated that victims can be embarrassed to admit to the trauma experience, as in the case of sexual abuse. Other traumas may be difficult to admit to or to recall. Therefore, Kessler, Sonnega, Bromet, Hughes, and Nelson (1995), in interviewing trauma victims, used a booklet that described the 12 traumatic experiences they were assessing. In questionnaires, different traumatic events can be described in the same way.

As separating frequency from intensity in trauma assessment is vital for an accurate evaluation of criterion A2 (see Table 1); a range of options per traumatic event can be rated on a Likert scale. This method can be used to indicate the number of trauma occurrences and to give a gross estimation of the subject's level of perceived fear and horror per occurrence.

Thus, the use of questionnaires can provide a more effective means of revealing unpleasant experiences than can an interview setting.

The psychometric properties of the measurement tools of trauma exposure may be difficult to establish and, in the case of criterion validity, extremely difficult. Construct validity (i.e., the event in the questionnaire seems

reasonable) and concurrent validity (i.e., there is a correlation to other, similar scales) are the validity values that must suffice. Test-retest reliability is the correct stability method but internal consistency (e.g., alpha) is not applicable to traumatic event measures because the experience of one event does not necessarily imply the experience of another. In Table 5, the most frequently used scales for trauma assessment are listed.

Table 5 Descriptions of self report measures of trauma exposure

Scale	Number of event items	Data provided for prevalence assessment	Data provided for impact assessment	Stability (test-retest)	Reference
Traumatic Stress Schedule	10	yes	yes	0.88	Norris 1990
Traumatic Events Questionnaire	11	yes	yes	0.91	Vrana & Lauterbach 1994
Trauma History Questionnaire	24	yes	no	0.54 - 0 .92	Mueser et al. 2001
Stressful Life Events Screening Questionnaire	20	yes	yes	0.73	Goodman et al. 1998

In symptom measures, on the other hand, it is important to establish both internal consistency and stability over time. Criterion validity is often presented in terms of the scale's correlation with other symptom measures but most important is to show the scale's ability to correctly classify individuals into diagnostic groups. The degree of the scale's sensitivity (the proportion of cases correctly classified) and its specificity (the proportion of non-cases correctly classified) are the most crucial figures when judging its quality. In Table 6, the most frequently used scales for PTSD symptoms are listed.

Table 6 Descriptions of some self-report measures of symptoms associated with PTSD

Scale	Number of items	Stability (test-retest)	Consistency (alpha)	Sensitivity	Specificity	Reference
PTSD - I	20	0.95	0.92	0.89	0.94	Watson et al. 1991
Trauma Symptom Checklist-40, TSC-40	40	no data	0.90 - 0.92	no data	no data	Elliott & Briere 1992
Harvard Trauma Questionnaire, HTQ	30	0.92	0.96	0.78	0.65	Mollica et al. 1992
MMPI-PTSD (PK)	46	0.94	0.95	0.79 - 0.83	0.71 - 0.79	Lyons & Keane 1992 Dutton et al. 1994
Penn Inventory	26	0.96	0.94	0.89 - 0.90	0.55 - 0.62	Hammarberg 1992 Scragg et al. 2001
PTSD Checklist PCL/PCLS	17	0.96	0.94	0.78 - 0.94	0.86	Weathers et al. 1993 Blanchard et al 1996 Ventureyra et al. 2002
PTSD Symptom Scale PSS-SR (self-report)	17	0.80	0.85 - 0.91	0.80 - 0.90	0.84 - 0.96	Foa et al. 1993 Wohlfarth et al. 2003
Impact of Event Scale - Revised / IES-R	22	0.89 - 0.94	0.84 - 0.91	0.93 - 1.00	0.78 - 0.84	Horowitz et al. 1979 Marmar et al. 1996 Wohlfarth et al. 2003

Although there are a great number of measurement tools, none is perfect, and we have to accept less-than-perfect assessments. However, of vital importance is the evaluation of each tool through a standard psychometric procedure, with special emphasis on sensitivity and specificity.

2.3.4 Symptomatology

There has been a debate over whether descriptions of symptoms are best-accomplished using categorical or dimensional models (cf. Costa and McCrea, 1990). For example, in the area of personality disorders, there is empirical support from a wealth of data that individuals vary in dimensions rather than categories. The same could be claimed for PTSD. For example, fulfilling 95% rather than 100% of the criteria for a diagnosis would not render that individual a PTSD diagnosis, yet such a "sub-clinical" disorder might cause prominent stress, compromised well being, and malfunctioning.

It might also be argued that PTSD is not a unitary phenomenon but is composed of a spectrum of symptoms. Certain symptoms might tend to cluster together, while others might be relatively independent. Whether such clustering represents the same, similar or different disorders might be debated. However, it seems vital to find models that may group certain clusters of symptoms together in order to improve diagnostic capability. For example, it might be argued that if certain symptoms consistently cluster together, the number of questions used to define such symptom groups could be narrowed and hence the diagnostic system could be simplified.

One possible way to perform such reductions involves factor analytic techniques. There have been two factor analyses reported in the literature on symptom clustering in PTSD: Foa, Riggs, and Gershuny (1995) reported a three-factor solution and Taylor, Kuch, Koch, Crockett and Passey (1998) reported a two-factor solution. Neither of these solutions corresponds to what is suggested in the DSM-IV, using one arousal, one avoidance/numbing, and one re-experiencing factor. Foa, Riggs and Gershuny (1995), for example, grouped different individual symptoms under different higher order factors than does the DSM-IV, while Taylor, Kuch, Koch, Crockett and Passey (1998) found only one intrusion and one arousal factor.

The factor analyses made by both these research teams used data from specially selected samples. It seems therefore of importance to compare these models to each other using data from the general population to determine which one fits the data the best. (A random population sample would also improve generalizability.)

Thus, the aim of the third study was to use confirmatory factor analysis in order to establish which model provides the best fit to the empirical data collected through postal surveys in a random sample from the general population and in a random community sample in Sweden.

2.4 Neuroimaging findings in posttraumatic stress disorder

Neuroimaging techniques provide tools to investigate both structural and functional brain abnormalities in PTSD but the results are far from uniform. The central findings of neuroimaging studies are presented in Table 7.

Table 7 Central findings of neuroimaging studies (previously presented in Hull (2002)).

Finding	Replicability a)
Decreased hippocampal volume	+++ b)
Increased amygdala activity	+++ b)
Decreased Broca's area (left inferior cortex) activity	+ b)
Hemispheric lateralisation	+++ b)
Decreased anterior cingulate cortex activation	++ b)
Decreased *N* -acetyl aspartate in medial temporal regions	+
Activation in visual cortex	+ b)

a) Replicability was rated as follows: (+)two, (++)three and (+++) four or more studies.
b) Inconsistent findings.

Neuroimaging studies have especially focused on two major brain structures – the hippocampus and the amygdala.

The most replicated structural finding is hippocampal volume reduction using Magnetic Resonance Imaging (MRI) (cf. Bremner et al., 1995, 1997; Gurvits et al., 1996: Stein, Koverola, Hanna, Torchia, and McClarty, 1997).

The amygdala is regarded as the central structure in the emotional network of the brain (cf. Angrilli et al., 1996; Dager, Layton, and Richards, 1996; Davis, Gendelman, Tischler, and Gendelman, 1982; LeDoux, 1996) and, therefore, a great amount of effort has been put into investigating activity in the amygdala, especially during symptom provocation. However, neuroimaging studies of regional cerebral blood flow (rCBF) in PTSD have not invariably demonstrated an increased rCBF in the amygdala during symptom provocation. For example, Bremner et al. (1999a) and Shin et al. (1999) did not report amygdalar activation in response to sexual abuse reminders, while Rauch et al. (1996) and Shin et al. (1997) both reported a right-sided amygdalar activation in patients with PTSD resulting from war and combat experiences. Liberzon et al. (1999), who compared combat sounds to white noise, reported activation in the left amygdaloid region. But when comparing combat slides combined with combat sounds to neutral slides paired with music, Bremner et al. (1999b) did not observe increased activity in the amygdala. Pissiota et al. (2002) observed right-amygdalar activation during auditory trauma reminders and found that individual differences in rCBF were highly correlated with fear experience. In addition, Rauch et al. (2000) reported exaggerated automatic amygdalar responses to masked fearful human faces in PTSD subjects and Semple et al. (2000) observed increased right-amygdala rCBF in PTSD patients during a performance task, suggesting a generally heightened sensitivity to aversive stimuli and demanding tasks in PTSD.

The failure to demonstrate unambiguous results of amygdalar activation may be due to its involvement in encoding the emotional significance of an

event but not necessarily in the recall of the event per se (Cahill et al., 1996). Also, individuals traumatized by sexual abuse may react with shame rather than fear and, because shame does not seem to activate the amygdala, this may be part of the explanation for the inconsistency.

Alterations have been observed in the motor (Bremner et al., 1999b; Rauch et al., 1996) and parietal cortices, particularly the retrosplenial area (Bremner et al., 1999b; Fischer, Wik, and Fredrikson, 1996), and in visual association cortex (Bremner et al., 1999b). Increased rCBF has been demonstrated in other limbic and paralimbic regions and both decreased and increased rCBF have been observed in the temporal and prefrontal cortices after symptom provocation. For example, in the anterior cingulate cortex, rCBF has been reported to both increase (Liberzon et al. 1999; Rauch et al. 1996; Shin et al. 1997) and decrease (Bremner et al. 1999b; Shin et al. 1997, 1999) as a function of trauma exposure. Decreased rCBF has been observed in Broca's area when viewing an aversive videotape (Fischer, Wik, and Fredrikson, 1996), combat pictures (Shin et al., 1997) or listening to traumatic scripts (Rauch et al. 1996). Thus, affected brain territories and the direction of change are not always consistent across studies. Future investigations must broaden the selected trauma populations and incorporate a wider spectrum of trauma, using comparable study designs and imaging techniques in order to establish generalizability.

In addition, studies on the treatment of PTSD indicate that both cognitive behavioral therapy (CBT) (cf. Chemtob, Novaco, Hamada, and Gross, 1997; Foa, Hearst-Ikeda, and Perry 1995) and pharmacological therapy (cf. Frank, Kosten, Giller, and Dan, 1988; Katz et al., 1994–95) could alleviate symptoms. For example, selective serotonin reuptake inhibitors (SSRI's) (van der Kolk et al., 1994), exposure therapy (cf. Marks, Lovell, Noshirvani, Livanou, and Thrasher, 1998; Zlotnick et al., 1997), and eye movement desensitization and reprocessing (cf. Carlson, Chemtob, Rusnak, Hedlund, and Muraoka, 1998; Marcus, Marquis, and Sakai, 1997) have all been reported to reduce symptoms in patients with PTSD. The neurobiological mechanisms through which those treatments work are not well understood. In obsessive compulsive disorder and social phobia, it has been reported that both SSRI-preparations and CBT alleviate symptoms by reducing synaptic activity in areas that initially seem to have an increased neural activity. Schwartz, Stoessel, Baxter, Martin, and Phelps (1996) reported that increased glucose metabolic rates in the nucleus caudate were reduced both by SSRI and exposure paired with response prevention. Likewise, an initially heightened amygdala activity during symptom provocation (Tillfors et al., 2001) in individuals diagnosed with social phobia was reduced both by SSRI and CBT (Furmark et al., 2002).

Due to the paucity of neuroimaging data and because the most commonly utilized treatment for PTSD involves SSRI's, the aim of the fourth study was to examine the neurofunctional correlates of PTSD symptoms in a patient suffering from combat-related PTSD and to evaluate the effect of a specific SSRI (Fluoxetine) on rCBF during symptom provocation before and after treatment.

Thus, the specific scientific aims of the empirical studies were

- to investigate trauma and PTSD prevalence as related to gender, age, education, ethnicity, and place of residence (Study I)
- to evaluate the conditional risk for PTSD in relation to different traumatic events and perceived emotional impact (Study I)
- to investigate the impact of event and response characteristics associated with traffic road accidents on PTSD development (Study II)
- to test whether previously presented alternative models of the PTSD symptom structure fit the data equally well as the criteria described in the DSM-IV (Study III)
- to examine the neurofunctional correlates of PTSD symptoms in a patient suffering from combat-related PTSD (Study IV)
- to elucidate whether a treatment-induced reduction of PTSD symptoms is associated with altered rCBF during symptom provocation (Study IV).

3. The empirical studies

3.1 General aspects of the method in Studies I, II, and III

3.1.1 Samples

The sample, used in all three studies, consisted of 3,000 subjects (1,500 men and 1,500 women); aged 18–70 years, randomly selected from the general population in Sweden by use of a population-based registry (the Sema Group). A questionnaire, described below, was mailed to each subject, together with a separate ID-sheet, two stamped return envelopes, and an explanatory letter, in which the aim of the study was described and participant anonymity was guaranteed. To secure anonymity, subjects were asked to return the questionnaire and the ID-sheet in separate envelopes. A reminder was mailed to non-responders after three weeks. After six weeks, questionnaires and stamped return envelopes were again sent out to non-responders, followed by another reminder after another two weeks. Respondents were asked to reveal their names and addresses, should they be willing to be contacted in the future. Those 157 who did so received the questionnaire six months after the initial assessment, in order to evaluate test-retest reliability. In addition, they also filled out the PTSD checklist (PCL) (Blanchard, Jones-Alexander, Buckley, and Forneris, 1996; Weathers, Litz, Herman, Huska, and Keane, 1993), which is a questionnaire used in diagnosing PTSD that has been validated against the CAPS (Blake et al., 1990). Thus, questionnaire answers from the second cohort were used to study the test-retest reliability and validity of the questionnaire (i.e., sensitivity and specificity). Seventy-five individuals (2.5%) returned their ID-sheets but refused to participate in the study. Eight subjects (0.26%) were considered by their relatives to be too ill to participate. Sixty-six individuals (2.2%) could not be reached by mail and their questionnaires were returned undelivered. The replies from five respondents (0.16%) were impossible to interpret, and 1,022 subjects (34%) did not respond at all. Thus, a total of

1,824 individuals (60.8%) were qualified for analyses (863 men, 961 women; mean age = 42.99; SD = 14.85).

The second sample, used only in study III, was treated identically except that TRA-related questions were not included (see 3.3.2). This sample consisted of 1,000 men and 1,000 women aged 18–70 years, randomly selected from a Swedish population-based registry incorporating the greater Stockholm area (Enator). Interpretable questionnaires were obtained from 1,207 individuals (60.4%).

3.1.2 Questionnaire design and diagnostic procedure

The questionnaire contained two different sections. The first descriptive section evaluated the following sociodemographic variables: gender, age, place of residence (city, urban vs. countryside, rural), educational level (low, medium, and high, corresponding to 1–9 years of elementary school, high school or trade school, and university or university college training, respectively) and immigration (whether the respondent was domestic- or foreign-born).

The second section was diagnostic. The diagnostic procedure followed the DSM-IV. First, to fulfill criterion A, the person had to admit that s/he had experienced, witnessed, or been confronted with an event involving actual or threatened death or serious injury, or a threat to the physical integrity of him-/herself or others. In addition, the person's response had to be characterized as "intense fear, helplessness, or horror". Thereafter followed true/false (yes or no) questions using all DSM-IV items for criteria B–D. Criterion B was met if at least one symptom of re-experiencing the traumatic event was present, as indexed by five types of questions. The first type included questions on "intrusive images, thoughts or perceptions". The second re-experience question inquired whether the individual had had frightening dreams of the trauma. A third question pertained to whether there were feelings as if the traumatic event were recurring. The fourth concerned whether psychological distress in similar situations was present. Finally, we inquired whether physiological reactions to trauma-related cues occurred. Three or more symptoms had to be consistently confirmed to fulfill the avoidance/numbing criterion, criterion C. The first set of questions concerned the avoidance of thoughts, feelings, or conversations associated with the traumatic event. To gauge the second symptom, participants were asked if efforts were made to avoid activities, places, or people that aroused recollection of the trauma. The third symptom examined was an inability to recall an important aspect of the trauma, and the fourth was a loss of interest in participation in significant activities. The fifth and sixth sets of questions affirmed feelings of detachment from others and restricted affect or

numbness, respectively. Finally, subjects were asked if they had a sense of a foreshortened future.

Criterion D was fulfilled if at least two symptoms of increased arousal were reported. Questions on the following areas were asked: difficulty in falling or staying asleep, outbursts of anger or irritability, difficulty concentrating, and hypervigilance. Finally, subjects were asked to state if they had an exaggerated startle response.

In order to fulfill criterion E, disturbance duration had to be more than one month.

Criterion F was met if the subject reported that he or she had experienced marked distress or functional impairment in at least one of three life domains (personal, social, or professional life).

Thus, the questionnaire separated the assessment of event prevalence and PTSD symptoms, instead of instituting a method that required the subject to note the connection between a given traumatic event and PTSD symptoms, as in the DIS, used in The Epidemiologic Catchment Area research project (Helzer, Robins, and McEvoy, 1987). The DIS has been criticized because the traumatic event and PTSD are not independently assessed but instead the events that induce the symptoms of PTSD are required to be subjectively perceived as being related to the traumatic event that predated the symptoms. The alternatives for answers on the questionnaire were ‘yes’ or ‘no,’ appropriate response choices since the categorical definitions of symptoms in DSM-IV calls for a categorical assessment arrangement, verifying the presence or absence of the events or symptoms.

3.1.3 Trauma event assessment

To evaluate trauma experiences, seven different traumatic events were assessed using true/false alternatives. If the true alternative was endorsed, questions then followed on experienced trauma intensity, rated on a ten-point scale ranging from ‘no distress’ (1) to ‘maximum distress’ (10). The following traumatic events were rated: robbery, physical assault, sexual assault (including any type of unwanted sexual activity), sudden unexpected death of a loved one (tragic death), war experience, and TRA’s. A blank space for “other traumas” was supplied and to be rated accordingly. All individuals who reported an “other trauma” also reported at least one other traumatic event. Thus, the variable “other traumas” was used when estimating trauma frequency and experienced trauma intensity but is not reported separately.

3.1.4 Psychometric properties

The six-month test-retest reliability of the questionnaire was 0.86 (n=157). Using the PCL (Weathers, Litz, Herman, Huska, and Keane, 1993) as a reference, the sensitivity of the questionnaire was estimated at 100% (19 of 18) and the specificity at 99% (136 of 137) for the DSM-IV's criteria B–D (n=155); diagnosis using the questionnaire resulted in one false positive and one false negative. The PCL has been correlated with the CAPS, one of the most valid instruments for assessing PTSD, with an overall correlation of 0.93 (Blanchard, Jones-Alexander, Buckley, and Forneris, 1996). Thus, the psychometric properties of the questionnaire were deemed satisfactory (cf. Mueser et al., 2001; cf. Ventureyra, Yao, Cottraux, Note, and De Mey-Guillard, 2002).

3.1.5 Attrition analysis

Approximately six months after the last reminder, 50 non-responders, matched to the original sample with respect to sex, age, and place of residence (urban or rural), were selected from the group of 1,022 non-responders, to be interviewed in a telephone survey (25 men, 25 women; mean age = 40.3; SD = 16.3; range 18–70 years). If a subject refused (n=8) or was unreachable by telephone, another matched subject was chosen from the list of non-responders. Those selected were first asked whether they were willing to answer some brief questions from the questionnaire. Those who responded positively were then asked whether they had suffered any traumatic event. If they had, they were asked whether they had found it too difficult to answer the questionnaire due to being impaired or severely troubled when reminded of the trauma. If the answer was "yes" to this last question, we investigated if criterion F was fulfilled by asking if they experienced significant distress or impairment in social, occupational, or other important areas of daily functioning. Thus, the proxy marker for the diagnosis involved trauma experience, admitting to severe distress, and functional impairment. The attrition analysis resulted in an estimated PTSD prevalence (6.0%) at the same level as the epidemiological study, suggesting that the sample was representative of the population at large.

3.1.6 Some methodological weaknesses of the studies

To obtain a lifetime trauma history in PTSD epidemiological research is, indeed, a challenge in many respects. In the overall trauma assessment, we did not ask the subject to state the chronological order of the events; in case of multiple traumatic events, they were requested to rate only the emotional impact of the traumatic events. Therefore, we can not evaluate the effect of

trauma order in developing PTSD (e.g., if the first or the most recent event causes the development of PTSD or if the trauma order has any effect at all or if there are cumulative effects).

3.2 Study I

Trauma exposure and posttraumatic stress disorder in the general population

3.2.1 Aims and background

The first aim of Study I was to investigate the prevalence of lifetime traumatic experiences and posttraumatic stress disorder in the general adult population of Sweden. The second aim was to evaluate the impact of different trauma types, trauma frequency, and perceived distress on gender differences in PTSD by using logistic regression analysis techniques to statistically control for various contributing factors, in order to disentangle their relative independent contribution. The third aim was to assess the conditional risk for developing PTSD; i.e., overall risk and risk given the trauma exposure. We also related the conditional risk for PTSD to trauma intensity and frequency. The fourth aim was to evaluate whether PTSD was more common among domestic- or foreign-born individuals, and if urban versus rural differences exist.

3.2.2 Method

The method for data collection, including sample and assessment method, was identical in Study I, Study II, and Study III, as stated above. Contingency tables were analyzed using χ^2-tests. To describe the association between variables, estimates of odds ratios (OR's) and logistic regression analysis were used. Student's *t*-tests and analyses of variance were used to compare group means. Tests were performed in StatView 5.0 for Macintosh (Abacus Concepts, 1996) and in the Statistical Analysis Software (SAS) 6.08 for PC (SAS Institute, 1990). All statistical tests were adapted for unequal variances and hence degree of freedom was adapted for unequal variances and therefore varies.

3.2.3 Main results

A total of 102 subjects (3.6% of the men, 7.4% of the women, 5.6% overall), met the criteria for posttraumatic stress disorder (see Table 8).

Table 8 Sociodemographic and descriptive characteristics of subjects with and without lifetime PTSD.

Characteristics	PTSD - lifetime %	CIs	n	No PTSD n	χ^2 (df)
Gender					
men	3.6	2.4 - 4.8	31	832	12.4 (1)*
women	7.4	5.7 - 9.1	71	890	
Age					
18-34	6.1	4.1 - 8.1	35	540	3.1 (2)
35-54	6.2	4.5 - 7.9	50	762	
55-70	3.9	2.1 - 5.7	17	418	
Educational level [a)]					
Low	4.5	2.8 - 6.2	26	547	2.6 (2)
Medium	5.7	4.1 - 7.3	44	724	
High	6.8	4.5 - 9.1	32	438	
Ethnicity					
Swedish born	4.6	3.6 - 5.6	75	1537	23.7 (1)**
Foreign born	12.9	8.4 - 17.4	27	183	
Residence					
Urban	6.0	4.7 - 7.3	80	1260	1.1 (1)
Rural	4.7	2.8 - 6.6	22	449	

** p<.05; ** p<.01; *** p<.001; **** p<.0001*

a) Low: grades 1-9 or elementary school; Medium: high school, trade school or technical education below university level; High: university or university college

CI = Confidence Interval

Neither age nor educational level had any impact on PTSD prevalence, whereas gender and ethnicity had. Those born abroad had an almost threefold increased risk of PTSD (see Table 8). The percentage of the foreign-born subjects reporting PTSD was 13.7% (13 of 95) for men and 12.2% (14 of 115) for women (χ^2 (1) <1; n.s.). Among the Swedish-born, the comparative percentages were 2.3% (18 of 766) for men and 6.7% (57 of 846) for women ($\chi^2(1) = 16.5$; $P < .0001$). The OR and CI associated with ethnicity was 3.02 (1.90–4.82); $P < .0001$.

Traumatic experiences were highly common, with 80.8% of the sample having experienced at least one traumatic event (see Table 9). More men than women had experienced trauma. An increased prevalence of trauma exposure was also associated with a young age, a high educational level, and with being born abroad.

Table 9 Sociodemographic and descriptive characteristics of subjects who reported at least one specific traumatic event [a)].

Characteristics	Trauma-prevalence %	CIs	n	No trauma n	χ^2 (df)
Gender					
men	84.8	82.4 - 87.2	732	131	16.9 (1)***
women	77.1	74.4 - 79.8	741	220	
Age					
18-34	83.0	79.9 - 86.1	477	98	18.2 (2)***
35-54	83.0	80.4 - 85.6	674	138	
55-70	73.7	69.6 - 77.8	320	114	
Educational level [b)]					
Low	73.1	69.5 - 76.7	419	154	34.9 (2)***
Medium	83.2	80.6 - 85.8	639	129	
High	86.6	83.5 - 89.7	407	63	
Ethnicity					
Swedish born	80.1	78.2 - 82.0	1291	321	4.1 (1)*
Foreign born	86.2	81.5 - 90.9	181	29	
Residence					
Urban	81.3	79.2 - 83.4	1084	251	<1 (1)
Rural	79.6	76.0 - 83.2	375	96	

** p<.05; ** p<.01; *** p<.001; **** p<.0001*

a) including robbery, physical assault, sexual assault, tragic death, war, traffic accident, and other disaster or hazard

b) Low: grades 1-9 or elementary school; Medium: high school, trade school or technical education below university level; High: university or university college

CI = Confidence Interval

The trauma most commonly experienced was TRA's (59%), whereas the least commonly encountered was sexual assault (5.8%). Most traumatic events were experienced more frequently by men than women: robbery: 14.8% vs. 10.9%, (χ^2(1) 5.9; $P < .05$); physical assault 59.2% vs. 37.7% (χ^2(1) 83.7; $P < .001$); traffic accidents: 68.3% vs. 50.5% (χ^2(1) 59.2; $P < .001$). The exception was sexual assault, where the reverse was true, with 10% for women and 1.2% for men (χ^2(1) 63.2; $P < .001$). Multiple traumas were reported by 77.9% (570 of 732) of the men and 69.6% (516 of 741) of the women (χ^2(1) = 12.5; $P < .001$). Women reported greater distress to all events compared to men ($3.24 < t < 11.34$; $.05 > P > .0001$). The average reported mean (±SD) distress of those who had experienced trauma was 6.1 (±2.20) for men and 7.8 (±1.99) for women (t (1452) = 15.96; $P < .0001$). Multiple traumatic experiences were associated with higher mean distress ratings in both men and women (6.0 vs. 5.6; $P < .05$ and 7.8 vs. 7.2; $P < .0001$).

Those born abroad more frequently reported experiences of robbery, physical assault, tragic death, and war. Distress ratings were higher for robbery, physical assault, war, and TRA's ($3.57 < t < 5.0$; $.001 > P > .0001$), with no difference for sexual assault and tragic deaths ($1 < t < 1.51$; n.s.).

The conditional probability of PTSD given at least one trauma was 6.9% (CI = 5.6–8.2). The conditional risk of PTSD was not influenced by age ($\chi^2(2) = 1.7$; n.s.) or education ($\chi^2(1) < 1$) but it was by ethnicity and gender, with 14.9% of the foreign-born reporting with PTSD as compared to 5.8% of the domestic-born individuals ($\chi^2(1) = 19.0$; $P < .001$), and 4.2% of men (CI = 2.7–5.7) as compared to 9.6% of women (CI = 7.5–11.7), ($\chi^2(1) = 15.5$; $P < .0001$) reporting with PTSD. Multiple- as compared to single-trauma experiences resulted in a higher conditional risk of 8.5% vs. 2.6% ($\chi^2(1)$ 14.4; $P < .0001$); in men 5.1% (29 of 570) vs. 1.2% (2 of 162) ($\chi^2(1) = 3.7$; $P = .06$); and in women 12.2% (63 of 516) vs. 3.6% (8 of 225) ($\chi^2(1) = 12.6$; $P < .001$).

A logistic regression analysis with gender and ethnicity as covariates demonstrated that all events except TRA's independently contributed to the prediction of a PTSD diagnosis. Gender made an independent contribution when accounting for trauma type but the increased risk for a PTSD diagnosis in those born abroad was explained by trauma type (see Table 10). Trauma type independently explained about 20% of the variance, while gender fell short of 2%.

Table 10 Results from logistic regression predicting a diagnosis of posttraumatic stress disorder from different trauma types.

Types	estimate	Odds ratio	95% CIs	p	% variance explained (cum.)
Covariates					
Gender	0.79	2.20	1.33 - 3.64	**	2.0
Ethnicity	0.40	1.49	0.80 - 2.79	n.s	4.8
Significant Predictors					
Robbery	0.84	2.31	1.40 - 3.80	***	
Physical Assault	0.99	2.68	1.55 - 4.65	***	
Sexual Assault	1.61	5.02	2.87 - 8.77	****	- 21.5
Tragic Death	0.65	1.92	1.22 - 3.01	**	
War	0.79	2.21	1.08 - 4.52	*	
Traffic Accident	-0.05	0.95	0.60 - 1.51	n.s.	

* p<.05; ** p<.01; *** p<.001; **** p<.0001
CI = Confidence Interval

Because men, when compared to women, reported an increased trauma frequency, while women had higher distress ratings, we entered average intensity and frequency as well as gender and ethnicity as factors in a logistic regression analysis. Both trauma intensity and frequency made independent contributions to the diagnosis, while gender and ethnicity were accounted for. Perceived distress and trauma frequency explained roughly 10 times more of the variance than ethnicity and gender did (see Table 11).

Table 11 Results from logistic regression predicting a diagnosis of posttraumatic stress disorder from trauma intensity and trauma frequency respectively.

Types	estimate	Odds ratio	95% CIs	p	% variance explained (cum.)
Covariates					
Gender	0.41	1.50	0.92 - 2.51	n.s.	2.0
Ethnicity	0.23	1.26	0.72 - 2.20	n.s.	2.9
Significant Predictors					
Trauma intensity	0.48	1.61	1.37 - 1.90	****	12.1
Trauma frequency	0.57	1.67	1.48 - 1.87	****	26.2

* p<.05; ** p<.01; *** p<.001; **** p<.0001
CI = Confidence Interval

We also investigated the relation between perceived distress, gender, trauma frequency, and ethnicity. First, we excluded perceived distress as a predictor from the logistic regression analysis. The result showed that gender (OR = 3.06; CI = 1.92–4.87; $P < .0001$) and trauma frequency (OR = 1.79; CI = 1.60–2.00; $P < .0001$) both were significant predictors of PTSD, whereas the effect of ethnicity was not significant. We then excluded trauma frequency as a predictor and found that ethnicity (OR = 2.30; CI = 1.41–3.75; $P < .001$) and perceived distress (OR = 1.55; CI = 1.35–1.78; $P < .0001$) were both significant predictors, whereas gender was not.

Multiple traumatic experiences were associated with higher mean distress ratings, both in men and women (6.0 vs. 5.6; $P < .05$ and 7.8 vs. 7.2; $P < .0001$). As is evident from Figure 1, distress ratings of six or seven did not increase the risk for PTSD, while ratings of eight and above did. The pattern was similar for men and women. However, when the proportion of men and women giving distress ratings of up to five were compared to those giving ratings of five or higher, it became evident that women were

underrepresented in the low distress area and over-represented in the high distress area.

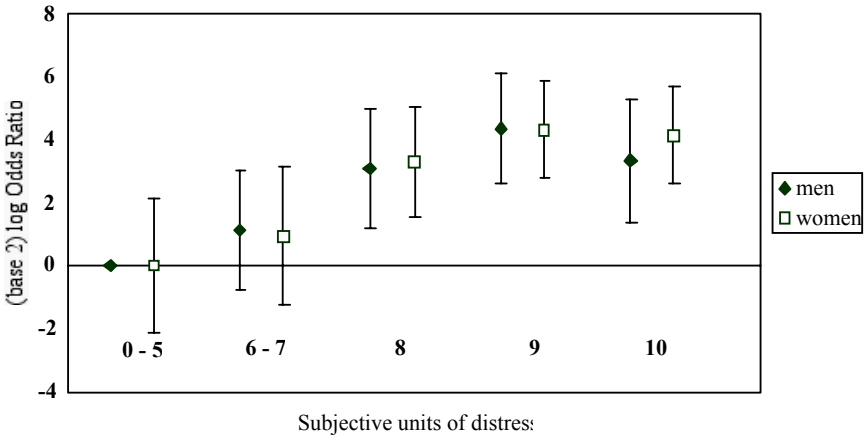

Figure 1 Odds ratios and 95% confidence interval for a diagnosis of PTSD plotted against subjective units of distress with 0–5 in men as a reference rating.

3.2.4 Conclusions

Traumatic events are commonly experienced in the general population but most exposures do not lead to posttraumatic stress disorder. The highest PTSD risk was associated with sexual and physical assault, robbery, and multiple trauma experiences and the lowest with TRA's. Women reported PTSD more often then men. Controlling for trauma type did not account for gender differences, while controlling for experienced distress did. An increased frequency of traumatic events and those with a highly distressing impact are associated with an increased risk. Thus, the conditional probability for PTSD varied as a function of trauma type, frequency, and impact of the event, with increased rates associated with prevalent trauma exposure and higher perceived distress. The latter accounted for the gender effect, suggesting that gender differences in PTSD in part represent a generally greater vulnerability to stress in women. The increased risk of PTSD associated with being foreign-born as compared to domestic-born was accounted for both by the fact that certain trauma types were more common among the foreign-born and also by the higher rate of experienced event-related distress in those born abroad.

3.3 Study II

Traffic road accidents and posttraumatic stress disorder in the general population

3.3.1 Aim and background

The aim of Study II was to relate PTSD lifetime prevalence to event- and response-related factors associated with TRA's in a random sample from the general population. Specifically, we studied whether perceived distress, number of accidents, degree of physical injury and material damage, as well as type of involvement (e.g., being a driver or a passenger vs. being unprotected (walking/cycling) vs. being a bystander) affect PTSD prevalence rates.

3.3.2 Method

The method for data collection, including sample and assessment method, was identical in Study II to that in Studies I and III as previously described. In addition, questions relevant for event- and response-related factors in TRA's included the following yes/no items: "Were you a victim of the accident as a driver of a motor vehicle, a passenger, a pedestrian, a cyclist, or a bystander? (Choose one). Were you physically injured? Was the accident a fatal one? Were other people physically injured? Was there material damage only?"

Contingency tables were analyzed using χ^2-tests. OR's and logistic regression were used to tease out the association between variables. Student's *t*-tests were also calculated to compare group means. Tests were performed in the SAS 6.08 for PC.

3.3.3 Main results

As reported in Study I, of the 102 cases (5.6%) diagnosed with PTSD, 31 (3.6%) were men and 71 (7.4%) were women. Of those involved in any TRA (N = 1,074), 65 individuals (6.1%) (42 women and 23 men) reported the presence of PTSD. Besides a gender (covariate) effect, the experience of robbery, physical and sexual assault, as well as war and tragic deaths but not TRA´s, were associated with an increased risk for a PTSD diagnosis. An increased number of accidents and enhanced perceived distress was related to higher PTSD prevalence when accounting for gender used as a covariate. Female sex contributed significantly to the prediction of a PTSD diagnosis (see Table 12).

Table 12 Results from logistic regression predicting a diagnosis of posttraumatic stress disorder from event and response related traffic road accident related variables in accident victims (N= 1074 and 65 PTSD cases).

Types	estimate	Odds ratio[a]	95% CIs	p
Covariates				
Gender	0.76	2.13	1.21 - 3.74	**
Significant Predictors				
Number of Accidents	0.28	1.33	1.03 - 1.71	*
Perceived Distress	0.16	1.18	1.06 - 1.30	**

* p<.05; ** p<.01; *** p<.001; **** p<.0001
CI = Confidence Interval
[a] Odds ratiosÕ represent relative risk of PTSD prevalence per SD change independent of other variables in the model.

Thus, high-perceived distress after accident involvement and frequent TRA's predicted a PTSD diagnosis. Logistic regression demonstrated that accidents with maximum or near maximum distress ratings but not high accident frequency were associated with PTSD when controlling for robbery experiences, sexual and physical assault, war, and tragic death. High distress accidents were more likely to involve fatalities and injury to the respondent but not to others and were associated with a PTSD prevalence rate of 14%. Type of involvement, such as being in a car (driver or passenger), being unprotected (pedestrian or bicyclist), or being a bystander, did not have differential effects on perceived trauma impact.

3.3.4 Conclusions

Fourteen percent of those who had experienced a severe TRA had a diagnosis of PTSD, in contrast to less than 5% of those who had experienced less severe accidents. Thus, in a random general population sample, severe TRA's associated with fatal outcomes and injury to oneself more than double the PTSD risk, when controlling for exposure to other traumatic events.

3.4 Study III

The structure of posttraumatic stress symptoms: A model fitting approach

3.4.1 Aim and background

Because the DSM is by far the most prevalent diagnostic system in use and, as such, was the basis of our questionnaire, we compared the relative merits of the DSM-IV's three-factor solution to alternative models using the same item but grouping them differently (Foa, Riggs, and Gershuny, 1995; Taylor, Kuch, Koch, Crockett, and Passey, 1998). Thus, the aim of Study III was to compare the DSM-IV's diagnostic criteria with the Foa, Riggs, and Gershuny (1995) three-factor model, as well as the two-factor model advocated by Taylor, Kuch, Koch, Crockett, and Passey (1998) (see Figure 2) by means of a confirmatory factor analysis (CFA) using LISREL 8.50 (Jöreskog and Sörbom, 1993). More specifically, our aim was to explore the feasibility of each model on two data sets obtained in two relatively large independent samples, using the group facility of LISREL.

3.4.2 Method

The method for data collection, including the first sample (sample 1) and assessment method, was identical in Study III as previously described, but in Study III we added data from sample 2 (see *3.1.1)*.

The presence of PTSD symptoms were rated in two samples of 3,000 (sample 1) and 2,000 (sample 2) randomly selected men and women in Sweden aged 18 to 70 years. Interpretable questionnaires were obtained from 1,824 and 1,207 subjects, respectively. The PTSD prevalence in sample 1 was 5.6%, as presented earlier, and 5.5% in sample 2.

CFA was used to investigate the model fit of three different measurement models, on both data sets. CFA is a technique that is quite different from exploratory factor analysis (EFA). In EFA, one aim is to reduce the number of measurement variables to extract a relatively small number of latent factors that reflect a particular construct. In principle, any of the measurement variables submitted to EFA may contribute to the variance in a particular factor. In contrast, in CFA, one has a particular model of interest, supposed to reflect the construct, which is tested. Here, a particular set of measurement variables is a priori hypothesized to indicate a certain latent factor. Data from the two different studies were first prepared with PRELIS 2 to obtain the correlation (tetrachoric) and asymptotic covariance matrices as suggested by Jöreskog and Sörbom (1993). These matrices were used in the subsequent confirmatory factor analysis using LISREL 8.50. The

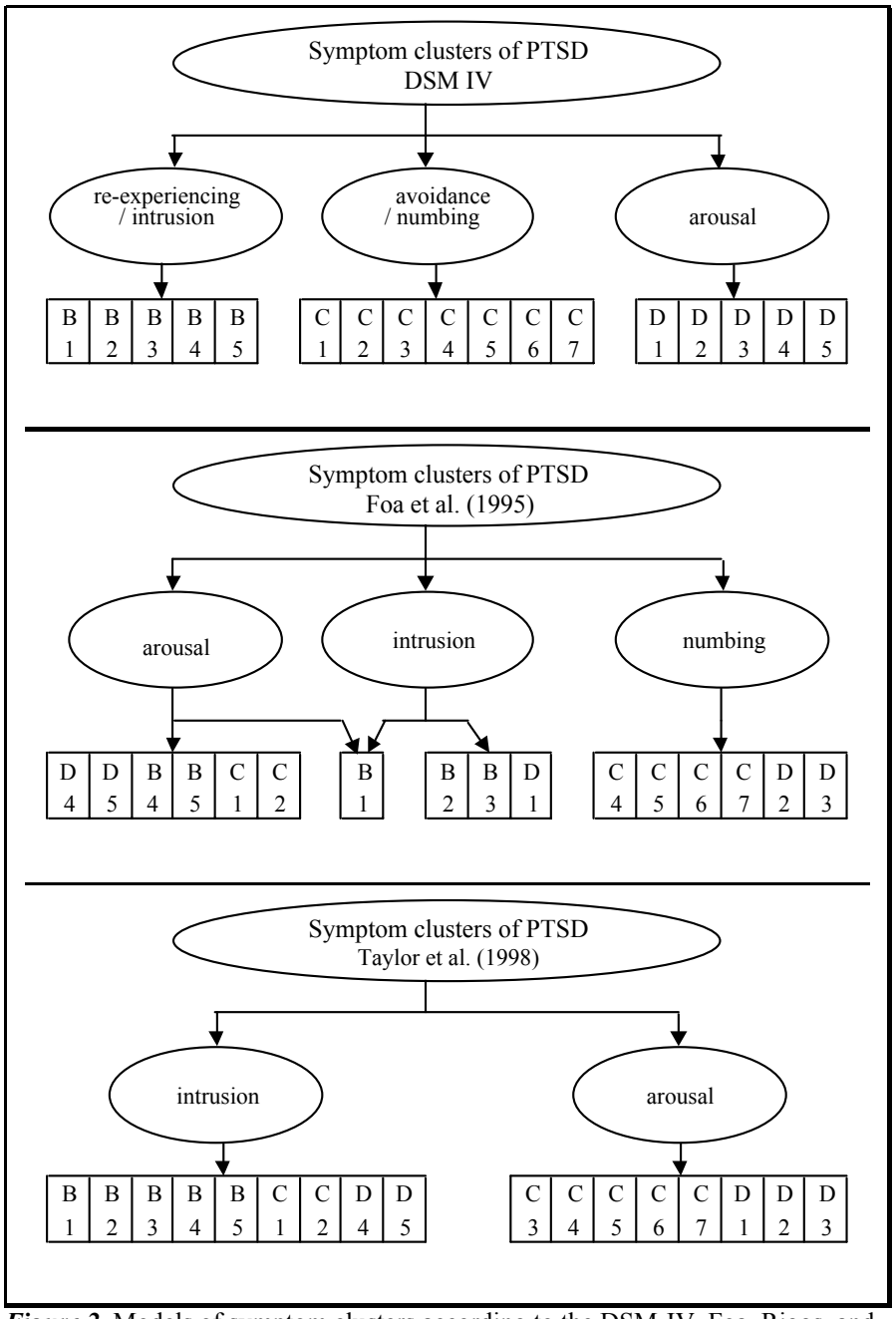

Figure 2 Models of symptom clusters according to the DSM-IV, Foa, Riggs, and Gershuny (1995) and Taylor, Kuch, Koch, Crockett, and Passey (1998).

estimation method was weighted least squares. The data from each individual sample were first submitted to establish the model fit in the

respective samples, after which the overall fit of each model (i.e., using both data sets) was established (cf. Jöreskog and Sörbom, 1993). In the analysis using the individual samples, each factor loading, measurement error, and correlation was estimated.

How well a particular model fits the data is expressed as a discrepancy between the original correlation matrix and the correlation matrix dependent on that particular model. In the subsequent analyses on both samples, the factor correlation and individual loading were set to be invariant, whereas errors of the measurement variables were set free to vary between samples. This provided an overall model test for the average discrepancy between the model-dependent matrix and the data obtained from several samples, while controlling for the deviance obtained in a single sample. Simply put, this is established by subtracting the χ^2-value (with the appropriate df.) obtained in each sub-sample from the χ^2-value (and df.) obtained in the group comparison. This provides a measure of the discrepancy in overall model fit (i.e., smaller is better). A great number of possible fit indices can be obtained from LISREL 8.50. An exact fit of a model is indicated when the p-value for χ^2 is above a certain p-level (i.e., $P > .05$). However, a model can be useful even though it does not meet this criterion (e.g., Browne and Cudeck, 1993). Browne and Cudeck (1993) suggest a measure of the approximate fit: the Root Mean Square Error of Approximation (RMSEA). In comparison with χ^2, the RMSEA takes into account both sampling error and errors in the model (cf. MacCallum, Browne, and Sugawara, 1996). An approximate fit is indicated based on the RMSEA, such that a RMSEA below 0.05 indicates a model with a close fit, whereas a fair fit is indicated within 0.06–0.08. A RMSEA within 0.09–0.10 indicates a poor fit and, finally, when RMSEA is over 0.10, model fit is not indicated (cf. Browne and Cudeck, 1993).

We also include the Adjusted Goodness of Fit Index (AGFI) as a measure of fit relative to no model at all (Jöreskog, 1993). The χ^2, RMSEA, and AGFI, were applied on single samples, whereas when both samples were included we used only the χ^2 and RMSEA.

3.4.3 Main results

Because the models are so diverse (i.e., not nested), it was not possible to compare the models by formal statistical criteria. Hence, the analyses were designed to investigate how well each model fits data obtained from the two independent samples. None of the three models had an exact fit with respect to any of the two samples. However, all three models met an approximate fit criterion (see Table 13). The AGFI was 0.99 for all models.

Table 13 Model fit indices for all models

		Model		
		DSM-IV	Foa et al.	Taylor et al.
χ^2	Sample			
	1	271.54	255.38	288.34
	2	285.38	259.42	331.65
	both	597.95	569.43	673.15
P	1	< 0.001	< 0.001	< 0.001
	2	< 0.001	< 0.001	< 0.001
	both	< 0.001	< 0.001	< 0.001
df	1	116	100	118
	2	116	100	118
	both	252	236	254
RMSEA	1	0.027	0.029	0.028
(CI)		(0.023 - 0.031)	(0.025 - 0.034)	(0.024 - 0.032)
	2	0.035	0.036	0.039
		(0.030 - 0.040)	(0.031 - 0.042)	(0.034 - 0.044)
	both	0.030	0.031	0.033
		(0.027 - 0.033)	(0.027 - 0.034)	(0.030 - 0.036)

CI = = 90% Confidence Interval for RMSEA

In the overall model test we evaluated the overall fit of each model including both samples. Again, all models had an approximate fit with no apparent superiority for any model. Point estimates and confidence intervals were almost identical. Thus, even though the three different models group the separate items quite differently, we could not differentiate between them.

3.4.4 Conclusions

The structure of the PTSD symptom profile was equally well accounted for using two- and three-factor models, suggesting that individual differences in symptom structure are an important modulating factor. Individuals with some symptom constellation might show a good fit to one but not another model, whereas the reverse might be true for other symptom constellations.

3.5 Study IV

Brain function in a patient with torture-related posttraumatic stress disorder before and after Fluoxetine treatment: A positron emission tomography provocation study

3.5.1 Aim and background

The aim of this case report was to describe the effect of the SSRI Fluoxetine on brain and behavioral reactions to symptom provocation in a patient with torture and war-related PTSD by using $H_2{}^{15}O$ PET measurements of rCBF during auditory baseline and symptom provocation. The patient was diagnosed with PTSD according to DSM-IV criteria.

3.5.2 Method

During PET scanning, the subject was exposed twice to the provocation (war sounds) and the baseline tapes (simple sounds) before and after treatment. To reduce within-session order effects, an ABBA design was used, with A being baseline and B provocation. Subjective ratings of anxiety were performed using all 20 items (range 1±4) from the Spielberger's State Anxiety Inventory, STAI-S (Spielberger, Gorusch, and Lushene, 1983). Heart rate was also recorded. The wish to flee was rated using a 0–100 visual analogue scale (VAS). The outpatient was treated with Fluoxetine, starting with 20 mg daily. The dosage was increased until a significant clinical effect was obtained, with an important reduction of symptoms. The maximum dose was 50 mg. The duration of the treatment until the second PET examination, when the patient showed a marked improvement, was six months. The PCL (Weathers, Litz, Herman, Huska, and Keane, 1993) was administered each month before and after treatment.

3.5.3 Main results

The PTSD symptoms measured by the PCL scores were reduced as a function of pharmacotherapy. Provoked subjective and physiological anxiety measures to war- and torture-related sounds, including the wish to flee, were reduced by at least 50%. Thus, subjective distress was significantly reduced. A cluster involving the insula (Brodmann's area; BA15), prefrontal (BA10), orbitofrontal (BA11), and inferior temporal cortices (BA47) reflected relative decreased perfusion as a function of provocation compared to base before and was normalized after treatment with the SSRI. The cluster with initially increased activity in the cerebellum, supplementary motor cortex

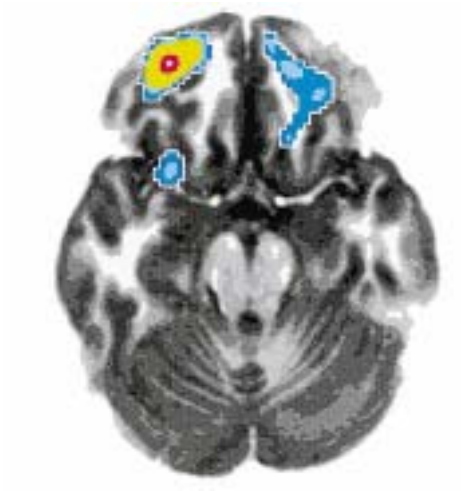

Figure 3 Transversal PET-image, superimposed on a magnetic resonance reference image, showing significant relative increases in the regional cerebral blood flow response to war and torture reminders as compared to resting base as a function of treatment with a selective serotonin re-uptake inhibitor (Fontex). All z-scores are above 2.6 corrected for multiple comparisons.

(BA6), precuneus (BA7), and parietal cortex (BA39, 40) decreased as a function of treatment (see Figure 3). We also found a negative correlation between heart rate alteration and frontal rCBF changes.

3.5.4 Conclusions

The PET-study showed that rCBF was altered in areas involved in emotional processing as well as motor preparation, initiation, and execution. Thus, activity in areas of relevance for emotion, memory, and attention were altered by pharmacotherapy with an SSRI.

In conclusion, this case study suggests that symptom provocation in PTSD alters neural activity in brain territories involved in memory, emotion, and attention, as well as motor control. Pharmacotherapy with an SSRI normalized this brain pattern.

3.6 Discussion of the individual studies

3.6.1 Study I

Of the 80.8% who had experienced a traumatic event in the present sample, 5.6% presented with PTSD, giving a conditional risk (i.e., risk given a trauma experience) of 6.9%. Similar to most previous studies, we observed a gender effect, with more women than men presenting with a PTSD diagnosis; however, trauma event type, exposure rate and perceived intensity were more important than gender in determining PTSD. This conclusion is substantiated by the fact that when gender, ethnicity, trauma intensity ratings and trauma frequency were entered into a logistic regression analysis, the effects of ethnicity and gender were accounted for. The increased risk in women is due to the fact that more women than men give higher distress ratings, and not to the fact that PTSD risk increases at a lower distress level for women than men.

3.6.2 Study II

The most important event-related risk factor for developing PTSD in the aftermath of a TRA seems to be the severity of the accident. More severe events, with physical injury to oneself, and accidents involving fatalities, result in higher perceived distress that most likely facilitates the development of PTSD. First, the strongest response-related predictor of a PTSD diagnosis from the logistic regression analysis was perceived subjective distress. Second, the effect of accident frequency was accounted for when accident severity and other trauma types were entered into the analysis. Third, when assessed in isolation from distress ratings, neither involvement type (i.e. being a passenger or driver vs. being a pedestrian or cyclist vs. being a bystander) nor damage extent (i.e. injury to oneself or others, fatal accidents, or material damage only) makes a significant contribution to the prediction of the presence of a PTSD diagnosis. Generally, this is consistent with a huge amount of literature demonstrating that the development of PTSD following other traumatic events than TRA's is strongly related to the subjective impact of the event (cf. Norris, 1992). It also emphasizes the original focus in the DSM-IV on the importance of the traumatic event as being a producer of a strong subjective emotional response.

3.6.3 Study III

All three models tested were equally good fits to the data. The reason that we could not separate the three models probably does not reflect the fact that we included a general population sample. For example, Buckley, Blanchard, and Hickling (1998) studied patients using the original model of Taylor, Kuch, Koch, Crockett, and Passey (1998) in their data and obtained a poorer fit (RMSEA = .078) than we did with the same model in the present data set (RMSEA = .028–033). In all likelihood, this difference in approximate fit does not represent differences in sample size because RMSEA is claimed to be independent of sample size. Instead, it might suggest that the constellation of symptoms and their grouping in individuals with PTSD is, to a certain degree, idiosyncratic, and that no single system based on factor analytic approaches is likely to fit a group with distinct individual differences. This hypothesis also accounts for the fact that the results from the factor analyses performed by Foa, Riggs, and Gershuny (1995), and Taylor, Kuch, Koch, Crockett, and Passey (1998) were markedly different. Again, it seems possible that this is due to the impact of individual differences in symptom clustering. For example, Buckley, Blanchard, and Hickling (1998) studied survivors of motor vehicle accidents; Taylor, Kuch, Koch, Crockett, and Passey (1998) included not only individuals traumatized by motor vehicle accidents but also by war zone trauma, and Foa, Riggs, and Gershuny (1995) analyzed data from female rape victims and female victims of nonsexual assault. It is not unlikely that Taylor, Kuch, Koch, Crockett, and Passey (1998) tested their data with a more restricted variability than Foa, Riggs, and Gershuny (1995) did. Should this be the case, this might reduce the numbers of factors observed, compared to the model of Foa, Riggs, and Gershuny (1995). It is also possible that other statistical approaches based on individuals, like discriminant analysis, rather than those rooted in variables, like factor analysis, could provide means to resolve some of those issues. This could be tested; for example, by providing evidence-based determined subgroups of PTSD and estimating specificity to test whether different symptom grouping models fit certain subgroups of patients but not others.

Some symptoms may reflect different brain mechanisms than others. The cardinal symptom in veterans with combat experience, for example, is fear, which is associated with amygdalar activation (Pissiota et al., 2002; Rauch et al., 2000), whereas in rape victims, shame and guilt are predominant and are associated with activity in other brain regions (Shin et al., 1999).

Thus, there are possible biological correlates to differences in the symptom structure of PTSD.

3.6.4 Study IV

Before the pharmacotherapy was induced and during symptom provocation, rCBF was altered in areas involved in emotional processing as well as motor preparation, initiation, and execution. RCBF decreased in the orbitofrontal and prefrontal cortices during anxiety provocation. This has been associated with a loss of emotional control (Fredrikson, Fischer, and Wik, 1997; Rauch et al., 2000) and failure to extinguish fear conditioning (Morgan and LeDoux, 1999). Because loss of emotional control is a PTSD hallmark, and fear conditioning is a likely etiological mechanism in PTSD (Pitman, Orr, Shalev, Metzger, and Mellman, 1999), we speculate that the normalized rCBF in the orbitofrontal and prefrontal cortices after SSRI treatment reflect extinction of fear and possibly increased emotional control. The negative correlation between heart rate and frontal rCBF may indicate a role for the orbitofrontal, prefrontal, and cingulate cortices in the regulation of psychophysiological process during symptom provocation.

Alterations in the left frontal cortex (BA47) seem related to the emotional processing of negative affect (Sprengelmeyer, Rauch, Eysel, and Przuntek, 1998) and may form part of an evaluative system taxed by the experience of PTSD. Because the prefrontal and anterior/medial cingulate cortices are heavily interconnected with the limbic system (particularly the amygdala), it is possible that SSRI preparations act by normalizing activity in this cortical-limbic loop. A reduction in the patient's flight tendencies and altered activity in his/her motor system may reflect this.

The insula cortex is involved in autonomic control (Fredrikson, Furmark, Olsson, Fischer, Andersson, and Langstrom, 1998) and activated areas in the parietal cortex are part of the dorsal object recognition pathway supporting visuospatial memory involvement. The absence of activation in the anterior cingulate gyrus may be associated with the inability of people with PTSD to extinguish fear and the increased activation of the posterior cingulate gyrus may relate to its role in the emotional processing of distressing material (Fischer, Wik, and Fredrikson, 1996). Thus, this case study suggests that symptom provocation in PTSD alters neural activity in brain territories involved in memory, emotion, and attention, as well as motor control. Treatment with an SSRI normalized this brain pattern. Yet, randomized controlled trials are needed to confirm these observations, especially since Levin, Lazrove, and van der Kolk (1999), reporting a case study on the effect of EMDR, described neural alterations in areas other than those observed here.

3.7 Overall discussion

According to our studies, 80.8% of the general population of Sweden has experienced a traumatic event sometime in life. With that figure in mind, the prevalence rates of PTSD at 5.6% and with a conditional risk (i.e., PTSD when exposed to a trauma) of 6.9% are relatively low; 93% that experience at least one trauma do not develop PTSD. This raises two fundamental questions: 1) What, in addition to trauma, increases the risk of developing PTSD? 2) What are the causes of PTSD and how can we identify individuals at risk?

The most commonly experienced trauma type is TRA's, but this type of trauma carries with it a relatively small risk of developing PTSD. (Trauma as a result of the more rarely occurring assault – in particular sexual assault – carries with it a far higher risk of developing PTSD.) Rather, the most important event-related risk factor for developing PTSD in the aftermath of a TRA seems to be the severity of the accident. Thus, the frequency in a given population of a specific type of trauma does not seem to be a crucial factor in determining whether or not the victim will develop PTSD. Instead, the severity of the incident, determined in terms of subjective distress, can indicate an increased risk for developing PTSD. TRA's with a minor subjective impact do not carry an increased PTSD risk but major and severe accidents invoking high subjective distress do. This implies that injured but surviving victims of TRA's involving the death of others should be carefully monitored for the development of PTSD.

Victims of sexual and physical assault, with an increased frequency of other experienced traumatic events and with highly distressful reactions, are at the greatest risk of developing PTSD. Trauma type (independent of frequency and intensity), trauma frequency and intensity (independent of trauma type) explained the greatest amount of variance, suggesting that trauma type, exposure rate, and perceived intensity are important in determining the risk for developing PTSD.

The increased risk for women developing PTSD was related to the fact that women reported higher distress levels than men, and not to the fact that they develop PTSD at lower distress levels. This seems important because if there is a vulnerability factor, with women being more apt to develop PTSD after trauma, the mechanism seems mediated by increased distress levels. It is not possible to state why this is the case, only to speculate. If it is due to a preexisting vulnerability for illness, the development of PTSD should be more common in women given a trauma that "objectively" is similar to both sexes. This was the case for tragic death, where the sex ratio remained the same. Distress ratings may reflect the victim's feelings of helplessness or fear and, in this respect, women and men might experience seemingly

similar events differently. Perhaps we should acknowledge that vulnerability does not exist purely in the neuroendocrine system or the hypothalamic-pituitary-adrenal axis, but also in the 'cognitive', emotional domain, reflecting ways of regarding life, which may possibly lead to the higher distress ratings of women.

With respect to gender differences, it has been argued both against (Yehuda, 2002b) and in favor of (Breslau, 2002) women having a greater vulnerability toward developing PTSD. Yehuda (2002b) suggested that gender differences in PTSD prevalence reflect "different degrees of actual threat and physical injury," while Breslau (2002) replied that PTSD is more common in women "even when the type of traumatic event is controlled for". The present data support an increased vulnerability in women as compared to men because gender made a significant contribution to predicting PTSD, even when the impact of the traumatic event(s) was statistically controlled for using logistic regression analysis. In fact, the risk doubling for PTSD in women was similar using both unadjusted risk estimates and estimates adjusted for trauma type, suggesting that exposure to certain trauma types does not account for the gender effect. Using a different method to control for trauma event type, Breslau, Chilcoat, Kessler, Peterson and Lucia (1999) drew a similar conclusion.

Thus, it has been tentatively suggested that gender-related factors, particularly those associated with a high level of subjective distress, is one mechanism through which gender differences in PTSD may emerge. Both in men and women, the increased risk of developing PTSD occurred at distress ratings of eight or higher. The increased risk in women is due to the fact that more women than men gave higher distress ratings, and not to the fact that the risk for PTSD increases at a lower distress level for women than men. Thus, the increased vulnerability to PTSD in women may reflect a generally increased vulnerability to emotional stress and the ability to form emotional memories (Fujita, Diener, and Sandvik, 1991; Seidlitz and Diener, 1998). The latter process seems to engage different neural networks in men and women (Canli, Desmond, Zhao, and Gabrieli, 2002), suggesting possible gender-specific neurobiological underpinnings of PTSD.

It has been argued that PTSD is an example of fear conditioning, where the traumatic event is the unconditioned stimulus (UCS) and the reaction to the event the unconditioned response (UCR) and PTSD the conditioned response elicited by trauma reminders serving as conditioned stimuli. Thus, in terms of conditioning theory, men encounter UCS more often, while in women the UCR (distress) is enhanced. PTSD has been linked to a greater conditionability (Orr et al., 2000) and, if women displayed enhanced conditionability compared to men, it might qualify as a possible gender-specific mechanism. Experimental studies have not demonstrated this

(Fredrikson, Hugdahl, and Ohman, 1976), however, suggesting that gender differences in PTSD do not mirror gender differences in fear conditioning. However, it should be noted that in experimental studies on human fear conditioning, the impact of the UCS is individually determined. This would act to reduce or abolish gender differences, allowing women to choose a degraded UCS, when compared to men. In naturally occurring traumas this is not the case, so the hypothesis remains that an enhanced UCR in women serves to induce PTSD more frequently in women than in men.

A related question on individual differences, both in men and women, is why only some, not all, traumatic encounters lead to PTSD. Of course, factors related to trauma type and perceived intensity are most likely important. But neurobiological determinants might be operative as well (Hageman, Andersen, and Jorgensen, 2001). For example, Hettema, Annas, Neale, Kendler, and Fredrikson (2003) have recently demonstrated that fear conditioning is moderately heritable. Specifically, the serotonin promotor and possibly dopamine D4 receptor genes and trombocyte monoaminooxidase activity are involved in the encoding and extinction of human fear conditioning (Garpenstrand, Annas, Ekblom, Oreland, and Fredrikson, 2001). Therefore, we propose that genetic factors associated with conditionability may partly explain individual differences in exhibiting PTSD in the aftermath of trauma, and specifically that individual differences in dopaminergic and serotonergic neurotransmission may relate to differences in the risk of experiencing PTSD. This mechanism may substantiate the observation that PTSD, in part, seems genetically determined (Stein, Jang, Taylor, Vernon, and Livesley, 2002). The hypothesis is not proven but easily tested, and it remains an open question whether serotonergic and dopaminergic mechanisms relate to gender differences in PTSD.

The issue of symptom profiles in PTSD is not consistent and models differ markedly even though the body of research comparing different diagnostic systems is scarce. Studies might benefit from using more data-driven and exploratory classification methods, for example to delineate subtypes of patients having certain symptom profiles or certain clusters of symptom aggregation as well as identifying individuals with sub-clinical PTSD. Ideally, diagnostic systems could be validated not only using subjective, self-reported data, as in the present studies, but also using other techniques, such as behavioral and brain imaging approaches.

Emotionally salient situations seem to be encoded vividly and are probably recalled better than less salient events (Christiansson, 1992). Furthermore, studies using longitudinal designs (Shalev et al., 1998) report that increased and endurable distress at the time of the trauma is predictive of the subsequent development of PTSD. Thus, memory bias is unlikely to

be solely accountable for the association between traumatic distress and the presence of PTSD. Therefore, it seems important to study prognostic and predictive factors for PTSD development in the aftermath of traumatic events. For example, Bryant and Harvey (1995) have reported that both certain coping styles and personality characteristics predict the development of PTSD. A related question pertains to whether it is possible to use event-related factors in trauma survivors to predict who will benefit most from the treatment of Acute Stress Disorder to prevent the development of chronic PTSD (Bryant, Sackville, Dang, Moulds, and Guthrie, 1999; Harvey and Bryant, 2000).

Thus, there are certain promising leads for identifying individuals at risk and, in keeping with the DSM-IV (or the ICD-10, for that matter) definition of PTSD, the dominant causative agent seems to be trauma impact.

4. Conclusions

- Traumatic experiences are common in the Swedish population and PTSD is not uncommon; roughly one out of ten traumatic events results in PTSD, giving a 5.6% lifetime prevalence. The female/male sex ratio is 2:1.
- The risk for PTSD increases considerably with a high trauma-associated emotional impact.
- Severe but not minor TRA's increase the risk of developing PTSD.
- The distressing impact of a given trauma appears to be higher in women than in men. This may represent an increased vulnerability in women, in part accounting for gender differences.
- The PTSD symptomatology is equally well accounted for using all factor analytic models as yet presented in the literature; the DSM-IV does not provide a better fit to data than other models.
- The anxiolytic effect of SSRI's on PTSD symptoms could be mediated by prefrontal and paralimbic cortices. Data suggest that SSRI treatment normalize provocation-induced rCBF alterations in areas involved in memory, emotion, attention, and motor-control.

5. References

Abacus Concepts. (1996). *StatView 5.0*, Abacus Concepts, Inc., Berkeley, CA.

Acierno, R., Resnick, H., Kilpatrick, D.G., Saunders, B., & Best, C.L. (1999). Risk factors for rape, physical assault, and posttraumatic stress disorder in women: examination of differential multivariate relationships. *Journal of Anxiety Disorders, 13*, 541–563.

Ahrenfeldt, R.H. (1958). *Psychiatry in the British army in the Second World War*. New York: Columbia University Press.

American Psychiatric Association. (1952). *Diagnostic and statistical manual of mental disorders, 1st edn. (DSM-I)*. Washington, DC: American Psychiatric Association.

American Psychiatric Association. (1968). *Diagnostic and statistical manual of mental disorders, 2nd edn. (DSM-II)*. Washington, DC: American Psychiatric Association.

American Psychiatric Association. (1980). *Diagnostic and statistical manual of mental disorders, 3rd edn. (DSM-III)*. Washington, DC: American Psychiatric Association.

American Psychiatric Association. (1987). *Diagnostic and statistical manual of mental disorders, revised 3rd edn. (DSM-III-R)*. Washington, DC: American Psychiatric Association.

American Psychiatric Association. (1994). *Diagnostic and statistical manual of mental disorder, 4th edn. (DSM-IV)*. Washington, DC: American Psychiatric Association.

Andreski, P., Chilcoat, H., & Breslau, N. (1998). Post-traumatic stress disorder and somatization symptoms: a prospective study. *Psychiatry Research, 15,* 131–138.

Angrilli, A., Mauri, A., Palomba, D., Flor, H., Birbaumer, N., Sartori, G., & di Paola, F. (1996). Startle reflex and emotion modulation impairment after a right amygdala lesion. *Brain, 119*, 1991–2000.

Armenian, H.K., Morikawa, M., Melkonian, A.K., Hovanesian, A.P., Haroutunian, N., Saigh, P.A., Akiskal, K., & Akiskal, H.S. (2000). Loss as a determinant of PTSD in a cohort of adult survivors of the 1988 earthquake in Armenia: implications for policy. *Acta Psychiatrica Scandinavica, 102*, 58–64.

Blake, D., Weathers, F., Nagy, D., Kaloupek, G., Klauminzer, D., Charney, D., & Keane, T. (1990). *Clinician-Administered PTSD Scale (CAPS)*. Boston MA: National Center for Post-Traumatic Stress Disorder, Behavioral Science Division Boston-VA.

Blanchard, E.B., Hickling, E.J., Taylor, A.E., Loos, W.R., & Gerardi, R.J. (1994). Psychological morbidity associated with motor vehicle accidents. *Behaviour Research and Therapy, 32*, 283–290.

Blanchard, E.B., Jones-Alexander, J., Buckley, T.C., & Forneris, C.A. (1996). Psychometric properties of the PTSD Checklist (PCL). *Behaviour Research and Therapy, 34*, 669–673

Bremner JD. (2002). Neuroimaging Studies in Post-traumatic Stress Disorder. *Current Psychiatry Reports, 4*, 254–263.

Bremner, J.D., Narayan, M., Staib, L.H., Southwick, S.M., McGlashan, T., & Charney, D.S. (1999a). Neural correlates of memories of childhood sexual abuse in women with and without post traumatic stress disorder. *American Journal of Psychiatry, 156*, 1787–1795.

Bremner, J.D., Randall, P., Scott, T.M., Bronen, R.A., Seibyl, J.P., Southwick, S.M., Delaney, R.C., McCarthy, G., Charney, D.S., & Innis, R.B. (1995). MRI-based measurement of hippocampal volume in patients with combat-related posttraumatic stress disorder. *American Journal of Psychiatry, 152*, 973–981.

Bremner, J.D., Randall, P., Vermetten ,E., Staib, L., Bronen, R.A., Mazure, C., Capelli, S., McCarthy, G., Innis, R.B., & Charney, D.S. (1997). Magnetic resonance imaging-based measurement of hippocampal volume in posttraumatic stress disorder related to childhood physical and sexual abuse--a preliminary report. *Biological Psychiatry, 41*, 23–32.

Bremner, J.D., Southwick, S.M., Darnell, A., & Charney, D.S. (1996). Chronic PTSD in Vietnam combat veterans: course of illness and substance abuse. *American Journal of Psychiatry, 153*, 369–375

Bremner, J.D., Staib, L.H., Kaloupek, D., Southwick, S.M., Soufer, R., & Charney, D.S. (1999b). Neural correlates of exposure to traumatic pictures and sound in Vietnam combat veterans with and without post traumatic stress disorder: A positron emission tomography study. *Biological Psychiatry, 45*, 806–816

Breslau N. (2002). Post-traumatic stress disorder. *New England Journal of Medicine, 346,* 1495–1498.

Breslau N., Chilcoat H.D., Kessler R.C., Peterson E.L.& Lucia V.C. (1999). Vulnerability to assaultive violence: Further specification of the gender difference in post-traumatic stress disorder. *Psychological Medicine; 29*, 813–821.

Breslau, N., Kessler, R.C., Chilcoat, H.D., Schultz, L.R., Davis, G.C., & Andreski, P. (1998). Trauma and posttraumatic stress disorder in the community: the 1996 Detroit Area Survey of Trauma. *Archives of General Psychiatry; 55*, 626–632

Briere, J. & Elliott, D. (2000). Prevalence, characteristics, and long-term sequelae of natural disaster exposure in the general population. *Journal of Traumatic Stress, 13*, 661–679

Brewin, C.R., Andrews, B., Rose, S., & Kirk, M. (1999). Acute stress disorder and posttraumatic stress disorder in victims of violent crime. *American Journal of Psychiatry, 156*, 360–366

Brom, D., Kleber, R.J., & Hofman, M.C. (1993). Victims of traffic accidents: incidence and prevention of post-traumatic stress disorder. *Journal of Clinical Psychology, 49,* 131–140.

Brown, T.A., Campbell, L.A., Lehman, C.L., Grisham, J.R., & Mancill R.B. (2001). Current and lifetime comorbidity of the DSM-IV anxiety and mood disorders in a large clinical sample. *Journal of Abnormal Psychology, 110*, 585–599

Browne, M.W. & Cudeck, R. (1993). Alternative ways of assessing model fit. In K.A Bollen & J.S. Long (Eds.) *Testing structural equation models*. Newbury Park, CA: SAGE Publications.

Bryant, R.A. & Harvey, A.G. (1995). Psychological impairment following motor vehicle accidents. *Australian Journal of Public Health, 19*, 185–188.

Bryant, R.A. & Harvey, A.G. (1995). Avoidant coping style and post-traumatic stress following motor vehicle accidents. *Behaviour Research and Therapy, 33*, 631–635.

Bryant, R.A., Sackville, T., Dang, S.T., Moulds, M., & Guthrie, R. (1999). Treating acute stress disorder: An evaluation of cognitive behavior therapy and supportive counseling techniques. *American Journal of Psychiatry, 156*, 1780–1786.

Buckley, T.C., Blanchard, E.B., & Hickling, E.J. (1998). A confirmatory factor analysis of posttraumatic stress symptoms. *Behaviour Research and Therapy, 36*, 1091–1099.

Cahill, L., Haier, R.J., Fallon, J., Alkire, M.T., Tang, C., Keator, D., Wu, J., McGaugh, J.L. (1996). Amygdala activity at encoding correlated with long-term, free recall of emotional information. *Proceedings of the National Academy of Sciences of the United States of America., 93*, 8016–8021.

Canli, T., Desmond, J.E., Zhao, Z., & Gabrieli, J.D. (2002). Sex differences in the neural basis of emotional memories. *Proceedings of the National Academy of Sciences of the United States of America., 99*, 10789–10794.

Carlson, J.G., Chemtob, C.M., Rusnak, K., Hedlund, N.L., Muraoka, M.Y. (1998). Eye movement desensitization and reprocessing (EDMR) treatment for combat-related posttraumatic stress disorder. *Journal of Traumatic Stress, 11*, 3–24.

Chemtob, C.M., Novaco, R.W., Hamada, R.S., & Gross, D.M. (1997). Cognitive-behavioral treatment for severe anger in posttraumatic stress disorder. *Journal of Consulting and Clinical Psychology, 65*, 184–189.

Christianson, S-A. (Ed.). (1992). *The handbook of emotion and memory: Research and theory*. Hillsdale, NJ, Lawrence Erlbaum Associates.

Costa, P.T., & McCrea, R.R. (1990). Personality disorders and the five factor models of personality. *Journal of Personality Disorders, 4*, 362–371.

Dager, S.R., Layton, M., & Richards, T. (1996). Neuroimaging Findings in Anxiety Disorders. *Seminars in Clinical Neuropsychiatry, 1*, 48–60.

Darves-Bornoz, J.M., Pierre, F., Lepine, J.P., Degiovanni, A., & Gaillard, P. (1998). Screening for psychologically traumatized rape victims. *European Journal of Obstetrics, Gynecology, and Reproductive Biology, 77*, 71–75.

Davis, M., Gendelman, D.S., Tischler, M.D., & Gendelman, P.M. (1982). A primary acoustic startle circuit: lesion and stimulation studies. *Journal of Neuroscience, 2*, 791–805.

Davidson, J.R., Hughes, D., Blazer, D.G., & George, L.K. (1991). Post-traumatic stress disorder in the community: an epidemiological study. *Psychological Medicine, 21*, 713–721.

DeMause, L. (1997). The psychogenic theory of history. *Journal of Psychohistory*, 25, 112–183.

Durant, L.E. & Carey, M.P. (2002). Reliability of retrospective self-reports of sexual and nonsexual health behaviors among women. *Journal of Sex & Marital Therapy, 28*, 331–338.

Dutton, M.A., Hohnecker, L.C., Halle, P.M., & Burghardt, K.J. (1994). Traumatic responses among battered women who kill. *Journal of Traumatic Stress, 7,* 549–564.

Elliott, D.M., & Briere, J. (1992). Sexual abuse trauma among professional women: validating the Trauma Symptom Checklist-40 (TSC-40). *Child Abuse and Neglect, 16*, 391–398.

Erichsen, J.E. (1866). *On railway and other injuries of the nervous system*. London: Walton and Moberly; Philadelphia: H.C. Lea, 1867.

Fischer, H., Wik, G., & Fredrikson, M. (1996). Functional neuroanatomy of robbery re-experience: Affective memories studied with PET. *Neuroreport, 7*, 2081–2086.

Foa, E.B., Hearst-Ikeda, D., & Perry, K.J. (1995). Evaluation of a brief cognitive-behavioral program for the prevention of chronic PTSD in recent assault victims. *Journal of Consulting and Clinical Psychology, 63*, 948–955.

Foa, E., Riggs, D., Dancu, C., & Rothbaum, B. (1993). Reliability and validity of a brief intrument for assessing post-traumatic stress disorder. *Journal of Traumatic Stress, 6*, 459–474.

Foa, E.B., Riggs, D.S., & Gershuny, B.S. (1995). Arousal, numbing, and intrusion: symptom structure of PTSD following assault. *American Journal of Psychiatry, 152*, 116–120.

Frank, J.B., Kosten, T.R., Giller, E.L. Jr, & Dan, E. (1988). A randomized clinical trial of phenelzine and imipramine for posttraumatic stress disorder. *American Journal of Psychiatry, 145*, 1289–1291.

Fredrikson, M., Fischer, H., & Wik, G. (1997). Cerebral blood flow during anxiety provocation. *Journal of Clinical Psychiatry, 58*, 16–21.

Fredrikson, M., Furmark, T., Olsson, M.T., Fischer, H., Andersson, J. & Langstrom, B. (1998). Functional neuroanatomical correlates of electrodermal activity: a positron emission tomographic study. *Psychophysiology., 35*, 179–185.

Fredrikson, M., Hugdahl, K., & Ohman, A. (1976). Electrodermal conditioning to potentially phobic stimuli in male and female subjects. *Biological Psychiatry, 4*, 305–314.

Friedman, M.J. (1990). Interrelationships between biological mechanisms and pharmacotherapy of posttraumatic stress disorder. In M.E. Wolf & D.A. Mosnaim (Eds.). *Posttraumatic Stress Disorder: Etiology, Phenomenology, and Treatment*, Washington, DC: American Psychiatric Press.

Friedman, M.J., Charney, D.S. & Deutch, A.Y. (1995). *Neurobiology and Clinical Consequences of Stress: From Normal Adaptation to PTSD*. New York: Raven Press.

Fujita F., Diener E. & Sandvik E. (1991). Gender differences in negative affect and well-being: the case for emotional intensity. *Journal of Personality and Social Psychology*., *61*, 427–434.

Furmark, T., Tillfors, M., Marteinsdottir, I., Fischer, H., Pissiota, A., Langstrom, B., & Fredrikson, M. (2002). Common changes in cerebral blood flow in patients with social phobia treated with citalopram or cognitive-behavioral therapy. *Archives of General Psychiatry, 59*, 425–433.

Garpenstrand, H., Annas, P., Ekblom, J., Oreland, L., & Fredrikson, M. (2001). Human fear conditioning is related to dopaminergic and serotonergic biological markers. *Behavioral Neuroscience, 115*, 358–364.

Gerhards, F., Yehuda, R., Shoham, M., & Hellhammer, D.H. (1997). Abnormal cerebral laterality in posttraumatic stress disorder. *Annals of the New York Academy of Sciences, 21*, 482–485.

Goodman, L.A., Corcoran, C., Turne,r K., Yuan, N., & Green, B.L. (1998). Assessing traumatic event exposure: general issues and preliminary findings for the Stressful Life Events Screening Questionnaire. *Journal of Traumatic Stress, 11*, 521–542.

Green, B.L., Lindy, J.D., & Grace, M.C. (1985). Posttraumatic stress disorder. Toward DSM-IV. *Journal of Nervous and Mental Disease, 173*, 406–411.

Grinker, R.R., & Spiegel, J.P. (1945). *Men Under Stress*. Blakiston, Philadelphia.

Gurvits, T.V., Shenton, M.E., Hokama, H., Ohta, H., Lasko, N.B., Gilbertson, M.W., Orr, S.P., Kikinis, R., Jolesz, F.A., McCarley, R.W., & Pitman, R.K. (1996). Magnetic resonance imaging study of hippocampal volume in chronic, combat-related posttraumatic stress disorder. *Biological Psychiatry, 40*, 1091–1099.

Hageman, I., Andersen, H.S., & Jorgensen, M.B. (2001). Post-traumatic stress disorder: a review of psychobiology and pharmacotherapy. *Acta Psychiatrica Scandinavica, 104*, 411–422.

Hammarberg, M. (1992). Penn Inventory for Posttraumatic Stress Disorder: Psychometric properties. *Psychological Assessment, 4*, 67–76.

Harvey, A.G. & Bryant, R.A. (2000). Two-year prospective evaluation of the relationship between acute stress disorder and posttraumatic stress disorder following mild traumatic brain injury. *American Journal of Psychiatry, 157*, 626–628.

Helzer, J.E., Robins, L.N., & McEvoy, L. (1987). Post-traumatic stress disorder in the general population. Findings of the epidemiologic catchment area survey. *New England Journal of Medicine, 317*, 1630–1634

Herman, J.L. (1992). *Trauma and Recovery*. New York: Basic Books.

Hettema, J.M., Annas, P., Neale, M.C., Kendler, K.S., & Fredrikson, M. (2003). A twin study of the genetics of fear conditioning. *Archives of General Psychiatry, 60*, 702–708

Horowitz, M., Wilner, N., & Alvarez, W. (1979). Impact of Event Scale: a measure of subjective stress. *Psychosomatic Medicine, 41*, 209–218

Hull, A.M. (2002). Neuroimaging findings in post-traumatic stress disorder: Systematic review. *British Journal of Psychiatry; 181*, 102–110.

Jolly, J.B., Wiesner, D.C., Wherry, J.N., Jolly, J.M., & Dykman, R.A. (1994). Gender and the comparison of self and observer ratings of anxiety and depression in adolescents. *Journal of the American Academy of Child and Adolescent Psychiatry, 33*, 1284–1288.

Jordan, B.K., Schlenger, W.E., Hough, R., Kulka, R.A., Weiss, D., Fairbank, J.A., & Marmar, C.R. (1991). Lifetime and current prevalence of specific psychiatric disorders among Vietnam veterans and controls. *Archives of General Psychiatry, 48*, 207–215.

Jöreskog, K.G. & Sörbom, D. (1993). *LISREL®8: Structural equation modelling with the SIMPLIS™ command language*. Hillsdale, NJ: Lawrence Erlbaum Associates, Inc.

Jöreskog, K.G. (1993). Testing Structural Equation Models. In K.A. Bollen, & J.S. Long (Eds.), *Testing structural equation models*. Newbury Park, CA: SAGE Publications.

Kato, H., Asukai, N., Miyake, Y., Minakawa, K., & Nishiyama, A. (1996). Post-traumatic symptoms among younger and elderly evacuees in the early stages following the 1995 Hanshin-Awaji earthquake in Japan. *Acta Psychiatrica Scandinavica, 96*, 477–481.

Katz, R.J., Lott, M.H., Arbus, P., Crocq, L., Herlobsen, P., Lingjaerde, O., Lopez, G., Loughrey, G.C., MacFarlane, D.J., McIvor, R., et al. (1994–95). Pharmacotherapy of post-traumatic stress disorder with a novel psychotropic. *Anxiety, 1*, 169–174.

Keane, T.M., Kolb, L.C., Kaloupek, D.G., Orr, S.P., Blanchard, E.B., Thomas, R.G., Hsieh, F.Y., & Lavori, P.W. (1998). Utility of psychophysiological measurement in the diagnosis of posttraumatic stress disorder: results from a Department of Veterans Affairs Cooperative Study. *Journal of Consulting and Clinical Psychology, 66*, 914–923

Kessler, R.C., Sonnega, A., Bromet, E., Hughes, M., Nelson ,C.B. (1995). Posttraumatic stress disorder in the National Comorbidity Survey. *Archives of General Psychiatry, 52*, 1048–1060

Kilpatrick, D.G., Saunders, B., Amick-McMullan, A.E., Best, C.L., Veronen, L.J., & Resnick, H. (1989). Victim and crime factors associated with the development of posttraumatic stress disorder. *Behaviour Therapy, 20*, 199–214.

Kofoed, L, Friedman, M.J. & Peck, R. (1993). Alcoholism and drug abuse in patients with PTSD. *Psychiatric Quarterly, 64*, 151–171

Kozaric-Kovacic, D., Folnegovic-Smalc, V., Skrinjaric, J., Szajnberg, N.M.,& Marusic, A. (1995). Rape, torture, and traumatization of Bosnian and Croatian women: psychological sequelae. *American Journal of Orthopsychiatry, 65*, 428–433.

Kozaric-Kovacic, D., Hercigonja, D.K., & Grubisic-Ilic, M. (2001). Posttraumatic stress disorder and depression in soldiers with combat experiences. *Croatian Medical Journal, 42*, 165–170.

Kulka, R. A., Schlenger, W.E., Fairbank, J. A., Hough, R.L., Jordan, B.K., Marmar, C.R., & Weiss, D.S. (1991). Assessment of posttraumatic stress disorder in the community: prospects and pitfalls from recent studies of Vietnam veterans. *Psychological Assessment, 3*, 547–560.

LeDoux, J. (1996). *The emotional brain: The mysterious underpinnings of emotional life.* New York; Simon and Schuster.

Levin, P., Lazrove, S., & van der Kolk, B. (1999). What psychological testing and neuroimaging tell us about the treatment of Posttraumatic Stress Disorder by Eye Movement Desensitization and Reprocessing. *Journal of Anxiety Disorders, 13,* 159–172.

Liberzon, I., Taylor, S.F., Amdur, R., Jung, T.D., Chamberlain, K.R., Minoshima, S., Koeppe, R.A., & Fig, L.M. (1999). Brain activation in PTSD in response to trauma-related stimuli. *Biological Psychiatry, 45*, 817–826.

Lyons, J., & Keane, T. (1992). Keane PTSD Scale: MMPI and MMPI-2 update. *Journal of Traumatic Stress, 5*, 111–117.

MacCallum, R.C., Browne, M,Q. & Sugawara, H.M. (1996). Power analysis and determination of sample size for covariance structure modeling. *Psychological Methods, 1*, 130–149.

Marcus, S.V., Marquis, P., & Sakai, C. (1997). Controlled study of treatment of PTSD using EMDR in an HMO setting. *Psychotherapy, 343*, 307–315.

Marks, I., Lovell, K., Noshirvani, H., Livanou, M., & Thrasher, S. (1998). Treatment of posttraumatic stress disorder by exposure and/or cognitive restructuring: a controlled study. *Archives of General Psychiatry, 55*, 317–325.

Marmar, C.R., Weiss, D.S., Metzler, T.J., Ronfeldt, H.M., & Foreman C. (1996). Stress responses of emergency services personnel to the Loma Prieta earthquake Interstate 880 freeway collapse and control traumatic incidents. *Journal of Traumatic Stress, 9*, 63-85.

Mayou, R., Bryant, B., & Ehlers, A. (2001). Prediction of psychological outcomes one year after a motor vehicle accident. *American Journal of Psychiatry, 158*, 1231–1238.

Mayou, R., Tyndel, S., & Bryant, B. (1997). Long-term outcome of motor vehicle accident injury. *Psychosomatic Medicine, 59*, 578–584.

McFarlane, A.C., Clayer, J.R., & Bookless, C.L. (1997). Psychiatric morbidity following a natural disaster: an Australian bushfire. *Social Psychiatry and Psychiatric Epidemiology, 32*, 261–268

Meakins, J.C., & Wilson, R.M. (1918). The effect of certain sensory stimulation on respiratory and heart rate in cases of so-called 'irritable heart'. *Heart, 1*, 17–22

Mellman, T.A., Randolph, C.A., Brawman-Mintzer, O., Flores, L.P., & Milanes, F.J. (1992). Phenomenology and course of psychiatric disorders associated with combat-related posttraumatic stress disorder. *American Journal of Psychiatry, 149*, 1568–1574.

Mollica, R.F., Caspi-Yavin, Y., Bollini, P., Truong, T., Tor, S., & Lavelle, J. (1992), The Harvard Trauma Questionnaire. Validating a cross-cultural instrument for measuring torture, trauma, and posttraumatic stress disorder in Indochinese refugees. *The Journal of Nervous and Mental Disease, 180*, 111–116.

Morgan, M.A. & LeDoux, J.E. (1999). Contribution of ventrolateral prefrontal cortex to the acquisition and extinction of conditioned fear in rats. *Neurobiology of Learning and Memory, 72*, 244–251.

Mueser, K.T., Salyers, M.P., Rosenberg, S.D., Ford, J.D., Fox, L., & Carty, P. (2001). Psychometric evaluation of trauma and posttraumatic stress disorder assessments in persons with severe mental illness. *Psychological Assessment, 13*, 110–117.

Murburg, M.M. (1994). *Catecholamine Function in Post-Traumatic Stress Disorder: Emerging Concepts*. Washington, DC: American Psychiatric Press.

Nemiah, J.C. (1998).Early concepts of trauma, dissociation, and the unconscious: Their history and current implications. In J.D. Bremner & C. Marmar (Eds.), *Trauma, Memory and Dissociation* (pp. 1–18), Washington DC American Psychiatric Press.

Norris, F. (1990). Screening for traumatic stress: A scale for use in the general population. *Journal of Applied Social Psychology, 20*, 1704–1718.

Norris, F.H. (1992). Epidemiology of trauma: frequency and impact of different potentially traumatic events on different demographic groups. *Journal of Consulting and Clinical Psychology, 60*, 409–418.

Orr, S.P., Metzger, L.J., Lasko, N.B., Peri, T., Macklin, M.L., & Pitman, R.K. (2000). De novo conditioning in trauma-exposed individuals with and without post traumatic stress disorder. *Journal of Abnormal Psychology, 109*, 290–298.

Oppenheim, H. (1889). *Die traumatischen Nervosen; nach den in der Nervenklinik der Charité in den letzten 5 Jahren gesammelten Beobachtungen [Traumatic neuroses; collected observations from the last five years in the Nervenklinik der Charité]*. Berlin: Hirschwald.

Paivio, S.C. (2001). Stability of retrospective self-reports of child abuse and neglect before and after therapy for child abuse issues. *Child Abuse & Neglect, 25*, 1053–1068.

Perkonigg, A., Kessler, R.C., Storz, S., & Wittchen, H-U. (2000). Traumatic events and post-traumatic stress disorder in the community: Prevalence, risk factors and comorbidity. *Acta Psychiatrica Scandinavica, 101*, 46–59.

Pissiota, A., Frans, O., Fernandez, M., Von Knorring, L., Fischer, H., & Fredrikson, M. (2002). Neurofunctional correlates of posttraumatic stress disorder: a PET symptom provocation study. *European Archives of Psychiatry and Clinical Neuroscience, 252*, 68–75.

Pitman, R.K., Orr, S.P., Forgue, D.F., de Jong, J.B., & Claiborn, J.M. (1987). Psychophysiologic assessment of posttraumatic stress disorder imagery in Vietnam combat veterans. *Archives of General Psychiatry, 44*, 970–975.

Pitman, R.K., Orr, S.P., Shalev, A.Y., Metzger, L.J., & Mellman, T.A. (1999). Psychophysiological alterations in post traumatic stress disorder. *Seminars in Clinical Neuropsychiatry, 4*, 234–241.

Rauch, S.L., van der Kolk, B.A., Fisler, R.E., Alpert, N.M., Orr, S.P., Savage, C.R., Fischman, A.J., Jenike, M.A., & Pitman, R.K. (1996). A symptom provocation study of posttraumatic stress disorder using positron emission tomography and script-driven imagery. *Archives of General Psychiatry, 53*, 380–387

Rauch, S.L., Whalen, P.J., Shin, L.M., McInerney, S.C., Macklin, M.L., Lasko, N.B., Orr, S.P., & Pitman, R.K. (2000). Exaggerated amygdala response to masked facial stimuli in post traumatic stress disorder: a functional MRI study. *Biological Psychiatry, 47*, 769–776.

Resnick, H.S., Kilpatrick, D.G., Dansky, B.S., Saunders, B.E., & Best, C.L. (1993). Prevalence of civilian trauma and posttraumatic stress disorder in a representative national sample of women. *Journal of Consulting and Clinical Psychology, 61*, 984–991

Robins, L.N., Helzer, J.E., Croughan, J.L., Williams, J.B.W., & Spitzer, R.L. (1981). *NIMH diagnostic interview schedule. Version III*. Rockville, Md: NIMH, Public Health Service.

Salmon, T.W. (1917). *The care and treatment of mental diseases and war neuroses ("shell shock") in the British army*. New York: War Work Committee of the National Committee for Mental Hygiene.

SAS Institute. (1990). *SAS Procedures Guide, version 6.08*. SAS Institute, Cary, NC.

Schnurr, P.P. (1991). PTSD and combat-related psychiatric symptoms in older veterans. *PTSD Research Quarterly. 2*, 1.

Schnurr, P.P., Friedman, M.J., & Bernardy, N.C. (2002). Research on posttraumatic stress disorder: Epidemiology, pathophysiology, and assessment. *Journal of Clinical Psychology, 58*, 877–889.

Schwartz, J.M., Stoessel, P.W., Baxter, L.R. Jr., Martin, K.M., & Phelps, M.E. (1996). Systematic changes in cerebral glucose metabolic rate after successful behavior modification treatment of obsessive-compulsive disorder. *Archives of General Psychiatry, 53*, 109–113.

Scragg, P., Grey, N., Lee, D., Young, K., & Turner, S. (2001). A brief report on the Penn Inventory for posttraumatic stress disorder. *Journal of Traumatic Stress, 14*, 605–611.

Seidlitz, L., & Diener, E. (1998). Sex differences in the recall of affective experiences. *Journal of Personality and Social Psychology, 74*, 262–271.

Semple, W.E., Goyer, P.F., McCormick, R., Donovan, B., Muzic, R.F. Jr., Rugle, L., McCutcheon, K., Lewis, C., Liebling, D., Kowaliw, S., Vapenik, K., Semple, M.A., Flener, C.R., & Schulz, S.C. (2000). Higher brain blood flow at amygdala and lower frontal cortex blood flow in PTSD patients with comorbid cocaine and alcohol abuse compared with normals. *Psychiatry, 63*, 65–74.

Shalev, A., Bleich, A., & Ursano, R.J. (1990). Posttraumatic stress disorder: somatic comorbidity and effort tolerance. *Psychosomatics, 31*, 197–203.

Shalev, A.Y., Freedman, S., Peri, T., Brandes, D., Sahar, T., Orr, S.P., & Pitman, R.K. (1998). Prospective study of posttraumatic stress disorder and depression following trauma. *American Journal of Psychiatry; 155*, 630–637.

Sharp, T.J., & Harvey, A.G. (2001). Chronic pain and posttraumatic stress disorder: mutual maintenance? *Clinical Psychology Review, 21*, 857–877.

Shin, L.M., Kosslyn, S.M., McNally, R.J., Alpert, N.M., Thompson, W.L., Rauch, S.L., Macklin, M.L., & Pitman, R.K. (1997). Visual imagery and perception in post traumatic stress disorder. A positron emission tomographic investigation. *Archives of General Psychiatry, 54*, 233–241.

Shin, L.M., McNally, R.J., Kosslyn, S.M., Thompson, W.L., Rauch, S.L., Alpert, N.M., Metzger, L.J., Lasko, N.B., Orr, S.P., & Pitman, R.K. (1999). Regional cerebral blood flow during script-driven imagery in childhood sexual abuse-related PTSD: A PET investigation. *American Journal of Psychiatry, 156*, 575–584.

Southwick, S.M., Krystal, J.H., Bremner, J.D., Morgan, C.A. 3rd, Nicolaou, A.L., Nagy, L.M., Johnson, D.R., Heninger, G.R., & Charney, D.S. (1997). Noradrenergic and serotonergic function in posttraumatic stress disorder. *Archives of General Psychiatry, 54*, 749–758.

Spielberger, C.D., Gorusch, R.L., & Lushene, R. (1983). *Manual for the State-Trait Anxiety (STAI Form Y)*, Consulting Psychologist Press, Palo Alto, CA.

Spivak, B., Segal, M., Laufer, N., Mester, R., & Weizman, A. (2000). Lifetime psychiatric comorbidity rate in Israeli non-help-seeking patients with combat-related post-traumatic stress disorder. *Journal of Affective Disorders, 57*, 185–188.

Sprengelmeyer, R., Rauch, M., Eysel, U.T., & Przuntek, H. (1998). Neutral structures associated with recognition of facial expression of basic emotions. *Proceedings of the Royal Society of London. Series B: Biological Sciences, 265*, 1927–1931.

Stein, M.B., Jang, K.L., Taylo,r S., Vernon, P.A., & Livesley, W.J. (2002). Genetic and environmental influences on trauma exposure and posttraumatic stress disorder symptoms: a twin study. *American Journal of Psychiatry, 159,* 1675–1681

Stein, M.B., Koverola, C., Hanna, C., Torchia, M.G., McClarty, B. (1997). Hippocampal volume in women victimized by childhood sexual abuse. *Psychological Medicine 27*, 951–959.

Stierlin, E. (1909). *Über psychoneuropathische Folgezustände bei den Überlebenden der Katastrophe von Courrières am 10. Marz 1906*. Doctoral dissertation, University of Zürich.

Stierlin, E. (1911). Nervöse und psychische Störungen nach Katastrophen. [Nervous and psychic disturbances after catastrophes]. *Deutsches Medizinisches Wochenschrift, 37*, 2028–2035.

Taylor, S., Kuch, K., Koch, W.J., Crockett, D.J., & Passey, G. (1998). The structure of posttraumatic stress symptoms. *Journal of Abnormal Psychology, 107*, 154–160.

Tillfors, M., Furmark, T., Marteinsdottir, I., Fischer, H., Pissiota, A., Langstrom, B., & Fredrikson, M. (2001). Cerebral blood flow in subjects with social phobia during stressful speaking tasks: a PET study. *American Journal of Psychiatry, 158*, 1220–1226.

Trimble, M., R. (1981). *Post-traumatic neurosis: From railway spine to the whiplash.* Chichester, England: John Wiley & Sons.

Trimble, M., R. (1984). *Post-traumatic Neurosis: From Railway Spine To Whiplash*. Wiley, New York.

Turner, C.F., Lessler, J.T., & Gfroerer, J.C. (Eds.).(1992). *Survey measurement of drug use: Methodological studies*. Washington, DC; U.S. Government Printing Office.

Ursano, R.J., Fullerton, C.S., Epstein, R.S., Crowley, B., Kao, T.C., Vance, K., Craig, K.J., Dougall, A.L., & Baum, A. (1999). Acute and chronic posttraumatic stress disorder in motor vehicle accident victims. *American Journal of Psychiatry, 156*, 589–595.

Valentiner, D.P., Foa, E.B., Riggs, D.S., & Gershuny, B.S. (1996). Coping strategies and posttraumatic stress disorder in female victims of sexual and nonsexual assault. *Journal of Abnormal Psychology, 105*, 455–458.

van der Kolk, B.A., Dreyfuss, D., Michaels, M., Shera, D., Berkowitz, R., Fisler, R., & Saxe, G. (1994). Fluoxetine in posttraumatic stress disorder. *Journal of Clinical Psychiatry, 55*, 517–522.

van der Kolk, B.A, Pelcovitz, D., Roth, S., Mandel, F.S., McFarlane, A., & Herman, J.L. (1996). Dissociation, somatization, and affect dysregulation: The complexity of adaptation to trauma. *American Journal of Psychiatry, 153*, 83–93.

van der Kolk, B.A., Weisaeth, L., & van der Hart, O. (1996). History of trauma in psychiatry. In B.A. van der Kolk, A.C. McFarlane, & L. Weisaeth (Eds.), *Traumatic stress. The effects of overwhelming experience on mind, body, and society*. NY: Guilford Press.

Veith, I. (1965). *Hysteria: The history of a disease*. Chicago: University of Chicago Press.

Ventureyra, V.A., Yao, S.N., Cottraux, J., Note, I., & De Mey-Guillard, C. (2002). The validation of the Posttraumatic Stress Disorder Checklist Scale in posttraumatic stress disorder and nonclinical subjects. *Psychotherapy and Psychosomatics, 71*, 47–53.

Villarreal, G., Hamilton, D.A., Petropoulos, H., Driscoll, I., Rowland, L.M., Griego, J.A., Kodituwakku, P.W., Hart, B.L., Escalona, R., & Brooks, W.M. (2002). Reduced hippocampal volume and total white matter volume in posttraumatic stress disorder. *Biological Psychiatry, 15*, 119–125.

Vrana, S., & Lauterbach, D. (1994). Prevalence of traumatic events and post-traumatic psychological symptoms in a nonclinical sample of college students. *Journal of Traumatic Stress, 7,* 289–302.

Watson, C.G., Juba, M.P., Manifold, V., Kucala, T., & Anderson, P.E. (1991). The PTSD interview: rationale, description, reliability, and concurrent validity of a DSM-III-based technique. *Journal of Clinical Psychology, 47*, 179–188.

Weathers, F.W., Litz, B.T., Herman, D.S., Huska, J.A., & Keane, T.M. (1993). *The PTSD checklist: reliability, validity & diagnostic utility*. Paper presented at the Annual Meeting of the International Society for Traumatic Stress Studies, San Antonio TX.

Weisberg, R.B., Bruce, S.E., Machan, J.T., Kessler, R.C., Culpepper, L., & Keller, M.B. (2002). Nonpsychiatric illness among primary care patients with trauma histories and posttraumatic stress disorder. *Psychiatric services: a journal of the American Psychiatric Association., 53*, 848–854.

Wilson, J.P. (1994). The historical evolution of PTSD diagnostic criteria: from Freud to DSM-IV. *Journal of Traumatic Stress, 7*, 681–698.

Wohlfarth, T.D., van den Brink, W., Winkel, F.W., & ter Smitten, M. (2003) Screening for Posttraumatic Stress Disorder: an evaluation of two self-report scales among crime victims. *Psychological Assessment, 15*, 101–109.

Yehuda, R. (1998). Psychoneuroendocrinology of post-traumatic stress disorder. *Psychiatric Clinics of North America, 21*, 359–379.

Yehuda, R. (2002a). Current status of cortisol findings in post-traumatic stress disorder. *Psychiatric Clinics of North America, 25*, 341–368.

Yehuda R. (2002b) Post-traumatic stress disorder. *New England Journal of Medicine*, *346*, 108–114.

Zayfert, C., Becker, C.B., Unger, D.L., & Shearer, D.K.. (2002). Comorbid anxiety disorders in civilians seeking treatment for posttraumatic stress disorder. *Journal of Traumatic Stress, 15*, 31–38.

Zlotnick, C., Shea, T.M., Rosen, K., Simpson, E., Mulrenin, K., Begin, A., & Pearlstein, T. (1997). An affect-management group for women with posttraumatic stress disorder and histories of childhood sexual abuse. *Journal of Traumatic Stress, 10*, 425–436.

Acknowledgements

Many people have supported me throughout the years and the completion of this thesis would not have been possible without their help and encouragement. I can not thank all, but there are some I would especially like to thank.

First and mostly, Mats Fredrikson, my scientific coach and supervisor, for his enthusiastic inspiration, incredible support and warm friendship over the years.

My colleague and dear friend Anna Pissiota, for her tremendous collaboration, especially during the studies on PTSD patients (sometimes with some tears but often with a great lot of laughs).

My colleague and co-author Per-Arne Rimmö for his pleasant collaboration and invaluable data analyses, and for his excellent discussions and a fine friendship.

My co-authors Manuel Fernandez and Lars Åberg for being excellent colleagues.

Carina Karlsson and Tomas Furmark for their never failing help and support.

Berit Scott for valuable and profound comments on a preliminary version of this thesis.

Amanda Hicks, for proofreading the manuscript in a quick and excellent way.

The personnel of the Uppsala Imanet AB (former Uppsala University PET Centre), for providing a stimulating working environment.

All of my friends and colleagues at the Department of Psychology, Uppsala University, for making this department such a fantastic place to work. Especially I would like to express my sincere gratitude to Ann-Margret Rydell and Åke Pålshammar, for helping and supporting me in every possible way, both in ups and downs.

This thesis was supported by grants from the L F (Länsförsäkringar) Research Foundation and the Swedish Council for Research in Humanities and Social Sciences. I would also like to thank the Non-graduated Researchers Fund at Uppsala University for its financial support.

Acta Universitatis Upsaliensis

Comprehensive Summaries of Uppsala Dissertations from the Faculty of Social Sciences
Editor: The Dean of the Faculty of Social Sciences

A doctoral dissertation from the Faculty of Social Sciences, Uppsala University, is either a monograph or, as in this case, a summary of a number of papers. A few copies of the complete dissertation are kept at major Swedish research libraries, while the summary alone is distributed internationally through the series *Comprehensive Summaries of Uppsala Dissertations from the Faculty of Social Sciences.* (Prior to July 1985, the series was published under the title "Abstracts of Uppsala Dissertations from the Faculty of Social Sciences".)

Distributor:
Uppsala University Library,
Box 510, SE-751 20 Uppsala, Sweden
www.uu.se, acta@ub.uu.se

ISSN 0282-7492
ISBN 91-554-5697-9