Sequelae of traumatic stress: psychopathology, cortisol, and attentional function in the aftermath of a disaster

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Chapter 7

General conclusions and discussion
7.1 Overview

This thesis focused on important and yet unresolved topics related to psychopathology following a major disaster. The following research questions - posed in the Introduction (Chapter 1) – were addressed:

• How many survivors suffer from mental disorders, and which specific mental disorders are prominent?
• How long do survivors suffer from – or are at risk of development of – these potential mental disorders?
• Are there particular risk factors for chronic mental disorders among survivors?
• Do survivors with post-trauma mental disorders differ from survivors without mental disorders in their level of the stress-hormone cortisol?
• What is the burden of symptoms of PTSD and depression on attentional function in the short- and long-term?

In this final chapter first the main results answering the questions above will be summarized. Second, strengths and limitations of the studies will be presented. Study findings will be discussed and finally clinical implications will be presented, along with suggestions for further research. With the exception of the systematic review, studies in this thesis were based on the Enschede in-depth cohort, a unique and relatively large sample of trauma survivors, as they all experienced the same disaster and were followed from 2-3 weeks till 4 years post-disaster.
7.2 Main findings

How many survivors suffer from mental disorders, and which specific mental disorders are prominent?

Nearly half of the survivors (48.3%) suffered from one or more mental disorders 2 years after the fireworks disaster. The most prevalent disorders were PTSD (21.9%), specific phobia (21.5%), and depression (16.2%). Social phobia and somatoform disorder followed with 4.6% and 6.1%, respectively. Comorbidity between disorders was considerable. Two-thirds of the survivors with PTSD had one or more co-existing disorders, and around three quarters of survivors with depression and specific phobia had at least one other mental disorder.

How long do survivors suffer from –or are at risk of development of- these potential mental disorders?

The course of mental disorders post-disaster appears to takes four forms. Survivors may sustain mentally healthy, recover from mental disorders, have chronic disorders, or a late-onset of disorders post-disaster. Findings showed that the percentage of survivors with any mental disorder in the past 12 months decreased from 48.3% at 2 years to 29.5% at 4 years post-disaster. When survivors were healthy at 2 years post-disaster, they most likely sustained healthy at 4 years. The majority (58.2%) of survivors with PTSD, specific phobia, and depression at 2 years post-disaster no longer met diagnostic criteria of any mental disorder at 4 years. Nonetheless, although many survivors recovered from depression and specific phobia, approximately half as many developed a new onset of these disorders. Hence, rates of survivors with depression (9.5%) and specific phobia (12.4%) were still elevated in comparison to the Dutch population. (Bijl, de Graaf, Ravelli, Smit, & Vollebergh, 2002) (depression 5.65% (CI:4.7%-6.5%); specific phobia 6.88% (CI:6.0-7.8%)). Late onset of one disorder was in two out of three times preceded by another disorder. This regularly showed to be a shift in diagnostic classification from PTSD to depression.
Are there particular risk factors for chronic mental disorders among survivors?

We identified pre-, peri- and post-disaster risk factors for development and persistence of mental disorders. Pre-disaster risk factors entailed the unavailability of a maternal caregiver and abuse during childhood. The severity of traumatic exposure experienced peri-disaster contributed to a higher risk of development of mental disorders and a chronic course. Shortly after the disaster (2-3 weeks), high depressive symptom severity appeared to predict chronic anxious-depressive mental disorders at 4 years post-disaster.

Looking at predictors at a later stage (2 years post-disaster), survivors with PTSD or specific phobia at this time point showed an increased risk of depression at 4 years post-disaster.

Do survivors with post-trauma mental disorders differ from survivors without mental disorders in their level of the stress-hormone cortisol?

Our systematic review and meta-analysis on the existing literature on basal cortisol levels and PTSD showed that subjects with PTSD and non-psychiatric controls did not differ in cortisol levels in general. Nevertheless, support was found for low cortisol levels in PTSD depending on the type of control groups and specific subpopulations. Significantly lower cortisol levels were found in subjects with PTSD when compared with non-exposed controls, while no differences were found between trauma exposed subjects with and without PTSD. Subgroup analyses further revealed lower cortisol in those subjects who seem to be at the greatest risk for developing PTSD, i.e. women and physically or sexually abused people.

In our cohort study survivors with a depressive disorder following the Enschede fireworks disaster had a flatter diurnal cortisol curve than subjects with PTSD or mentally healthy survivors. No differences were found between survivors with PTSD and healthy individuals. In both these groups the usual dynamic pattern of increase in cortisol past awakening was present, while we did not observe this in the group of survivors with post-traumatic depressive disorder. These survivors with depression tended to use more tobacco per day, and the group differences in cortisol could only be revealed when we adjusted for quantity of smoking.
What is the burden of symptoms of PTSD and depression on attentional function in the short- and long-term?

Our cross-sectional study showed that PTSD and depressive symptoms, and sleep disturbances independently contributed to attentional dysfunction in disaster survivors. Our longitudinal study revealed that PTSD symptoms within 3 weeks post-disaster were predictive of poorer sustained attention in the following years. Attentional function was predicted equally well by PTSD symptom severity whether measured as early as 3 weeks or at 18 months post-disaster. This finding showed that PTSD symptoms are early signs and stable longitudinal predictors for attentional dysfunction up to at least 4 years after trauma. Although PTSD symptoms diminished and attentional functioning considerably improved over time, no association between changes in symptoms and changes in attention was found. Severity of depressive symptoms at 2 years was associated with a lack of progression in attentional function in the following years.

7.3 Methodological considerations: strengths and limitations

Design and sample of the cohort

An obvious strength of the studies in survivors of the Enschede fireworks disaster is the longitudinal design that rapidly started after the disaster and followed survivors and rescue workers for several years (van der Velden et al., 2006a; van der Velden et al., 2006b). In that matter we were able to collect information about disaster exposure and possible health consequences nearly on the spot, discarding a possible recollection bias of survivors.

The cohort study of residents is the first epidemiologic disaster study in which affected subjects were interviewed face-to-face at 2 different points in time. Our sample is also unique as the majority of trauma studies have used samples of patients undergoing treatment for PTSD. Such individuals might be expected to have more severe PTSD symptomatology, or possibly more comorbid psychopathology, than individuals who meet diagnostic criteria for PTSD but who are not specifically seeking treatment.

The cohort in this thesis is drawn from a Western European country, and as far as we know, all survivors had access to money, food and accommodation in the aftermath.
of the disaster. The migrants in this disaster-struck community were not included in our study when they mastered the Dutch language insufficiently. They were studied in a separate study (see (Drogendijk et al., 2011)). We are aware that survivors who have lost everything, as is frequently the case in developing countries, generally have a worse health outcome due to the so-called secondary disaster. Therefore, findings in our cohort of survivors of the fireworks disaster may not simply be generalizable to other disaster-exposed populations.

**Studies on cortisol**

In our systematic review (chapter 3) we were able to include the large number of 1628 people in total across 37 published and unpublished studies, with 828 individuals with PTSD and 800 controls. This large sample size emphasizes the robustness of findings of no differences in basal cortisol between people with PTSD and healthy controls. Results in specific subgroups have been found in post-hoc analysis with much smaller numbers of survivors. Therefore, these findings can only be considered as a hypothesis that needs further testing and not as a solid conclusion. Furthermore, in the systematic review substantial differences in the methodology of studies hampered comparison. For instance, time of cortisol measurements, restrictions regarding smoking, alcohol, coffee, and food-intake varied widely across studies. Although we attempted to pool data of studies on important characteristics, these restrictions and comorbid conditions known to confound cortisol levels remained unattended. In our cohort study (chapter 4) we addressed these issues regarding restrictions, and disentangled the role of smoking as a mediator between levels of basal cortisol and post-disaster psychopathology. We used saliva sampling in order to be able to plot the diurnal cycle of cortisol related to time of awakening. Saliva sampling has the advantage of measuring cortisol under relatively stress-free (i.e. basal) conditions. Many people fear blood-tests. We even had several survivors with a blood-injection phobia in our cohort. Therefore, saliva sampling is preferred as blood sampling would definitely have activated the stress-system to a higher account.
Factors of influence on attentional function

Studies that investigated associations between attention and PTSD have almost exclusively focused on treatment-seeking patients with combat-related PTSD in Vietnam. Vietnam veterans may have been exposed to toxic agents like pesticides during missions which are associated with increased risks of mild cognitive dysfunction (Bosma, van Boxtel, Ponds, Houx, & Jolles, 2000). The community sample of survivors of the Enschede fireworks disaster had the advantage that blood and urine samples of survivors, collected within the first weeks post-disaster, were negatively screened for toxic exposure to substances during the disaster (van der Velden, Yzermans, & Grievink, 2009). Additionally, attentional problems due to heavy drinking and substance abuse may have surpassed attentional problems related to PTSD of veterans in some studies, while in our sample a history of alcohol or substance abuse/dependence was rare. The studies on attentional function (chapters 5 and 6) were the first studies that controlled subjects in their food, beverages, and smoking before testing to rule out possible cognitive enhancing effects of these factors. However, in some subjects it might have been the case that the restrictions themselves (e.g. skipping a meal due to the prescribed one hour restrictions before testing) may have led to a subsequent unwanted loss of concentration.

7.4 Relevance of findings

Findings of this thesis have several parallels with those of other studies on post-trauma psychopathology in survivors. This thesis also offers several unique and distinctive findings that add important information to the trauma and disaster literature.

Anxiety and depression after trauma

Nowadays PTSD is well documented as a possible outcome in the aftermath of trauma. However, this thesis emphasizes that it is not an exclusive outcome of trauma (chapter 2). Findings show that depressive disorder and specific phobia are highly prevalent disturbances post-disaster as well.

The majority of survivors recovered from their mental disorder over the course of time, although depression and specific phobia still exhibited a substantial risk in the
long-term. PTSD, on the other hand, showed to be a transient disorder. However, a common feature in our cohort was a shift from PTSD into another diagnostic status over time. These findings are in line with a longitudinal study of briefer duration (O’Donnell, Creamer, & Pattison, 2004). Nearly half of all survivors with a diagnosis (PTSD/depression) at 3 months no longer met criteria at 12 months and none of the survivors with a single diagnosis of depression developed PTSD later on. We similarly found no increased risk for anxiety disorders to follow up on a depressive disorder.

Interestingly, depression in the absence of a co-existing anxiety disorder showed to be a remitting disorder over the course of time, while findings showed an increased risk for a superimposed depression on PTSD or specific phobia. Breslau and colleagues also showed that that there was an increased risk for depression in respondents who had also developed PTSD, but no increased risk in respondents who were exposed to trauma without developing PTSD (Breslau, Davis, Peterson, & Schultz, 2000). Thus, anxiety disorders may lead to later depression, while a course starting off with depression followed by an anxiety disorder is not very likely.

Severity of depression showed to have a link with severity of intrusive trauma memories in both inpatients and outpatients with depression (Carlier, Voerman, & Gersons, 2000; Kuyken & Brewin, 1994). It has been suggested that numbing or dysphoria, i.e. a lack of emotional responsiveness and social withdrawal, is a consequence of uncontrollable anxious arousal (Foa & Riggs, 1993). It appears as if depression follows when active avoidance is not effective enough. As PTSD and depression after trauma have been found to be very closely related, there is a need to reconsider the current diagnostic classification of PTSD for the upcoming DSM-5. Suggestions will be discussed in a later paragraph.

**Cause and function of cortisol alterations**

Based on our findings, the general consensus in the field of psychotraumatology that PTSD is related to low basal cortisol oversimplifies facts. First, an important finding of this thesis is that hypocortisolism is not per definition related to PTSD. Chapter 3 stressed that there is no systematic difference in basal cortisol levels between people with PTSD and controls, as this is only found in specific subgroups and when PTSD subjects were compared to non-trauma exposed individuals. Second, low cortisol is not
unique for PTSD, as it has been associated with several other conditions and coping styles. In chapter 4, low cortisol in people with a depressive disorder following the disaster was associated with a palliative coping style of smoking. Additionally, in a review of the literature on depression by Heim and colleagues (Heim, Ehlert, & Hellhammer, 2000a) was shown that in clinical samples, passive coping, repression, and denial of a stressful event were related to low cortisol. Furthermore, considerable evidence for HPA axis dysregulation was found in patients suffering from bodily disorders. These include chronic fatigue syndrome, fibromyalgia, other somatoform disorders, rheumatoid arthritis, and asthma. Many of these disorders have been related to stress (Heim et al., 2000a). Finally, low cortisol, does not seem to be an exclusive correlate of stress-related pathology, but has also been reported for healthy subjects exposed to trauma as well as for healthy subjects living under ongoing stress (Klaassens, Giltay, van Veen, Veen, & Zitman, 2009).

The manifestation of low basal levels of cortisol can be attributed to several factors, as these low cortisol levels may reflect alterations on different levels of the HPA axis (CRF in the hypothalamus, ACTH in the pituitary, and cortisol in the adrenals). Cortisol inhibits the HPA axis through a negative feedback loop by binding with receptors in the pituitary and the hypothalamus. It inhibits the release of CRF and ACTH, which in turn results in less secretion of cortisol (Jacobson & Sapolsky, 1991). Several findings indicate that lower basal cortisol, as found in PTSD, might be due to a higher number—and sensitivity—of glucocorticoid receptors in the pituitary (Stein, Yehuda, Koverola, & Hanna, 1997; Yehuda, Boisoneau, Lowy, & Giller, Jr., 1995) that would result in a greater sensitivity of negative feedback of cortisol. In this enhanced negative feedback model, the inhibiting function of cortisol on the hypothalamus is dampened, which explains why studies find hypersecretion of CRF in PTSD (Baker et al., 1999; Bremner et al., 1997) and that low cortisol in afferent pathways could lead to increased sympathetic activity.

Although low cortisol is assumed to be an etiological factor in onset of disease, it is also suggested that low cortisol has protective effects for the individual. One of the arguments was that a down-regulation of the HPA axis in chronically stressed subjects protects those subjects against the harmful effects for the body and brain resulting from chronic overactivity or inactivity of physiological systems that are normally involved in adaptation to environmental challenge (for review see (Fries, Hesse, Hellhammer, & Hellhammer, 2005). Thus, low cortisol might be a functional adaptation or correlate of
living under extreme stress instead of an etiological factor in the onset and persistence of stress-related psychopathology.

Future studies are needed to get more insight into the function of cortisol in relation to traumatic stress. Since cortisol is under the influence of many factors, large samples and consensus in data collection (e.g. time of awakening, quantity of smoking) and sampling protocols (e.g. assessment times, dietary restrictions) are needed to rule out concomitant conditions of psychopathology such as sleeping problems and heavy smoking.

**Childhood stressors**

Abuse and absence of maternal care in childhood were found to be predictive for chronic mental disorders in adulthood after the fireworks disaster (chapter 2). Furthermore, post-hoc analysis in the systematic review on cortisol and PTSD (chapter 3) showed low cortisol in people with PTSD due to physical or sexual abuse in comparison to healthy controls. Findings in both these chapters point out a significant influence of early adverse life experiences.

It appears that maternal absence during developmentally critical periods interacts between childhood trauma and subsequent changes in the HPA axis. First childhood trauma has been associated with pathophysiological changes of the HPA axis and subsequent adult psychopathology (Heim, Newport, Mletzko, Miller, & Nemeroff, 2008). In particular exposure to stress during developmentally critical periods might result in persisting hyper-reactivity of the HPA axis and the autonomic nervous system (Heim et al., 2000b). Second the effect of exposure to stress on the HPA axis and amygdala showed to be modulated by absence of caregivers during critical periods of development as was shown in rodent pups (Moriceau & Sullivan, 2006). Maternal absence during acute stress resulted behaviorally in avoidance of associated stimuli of the stressor, which is a major symptom in anxiety disorders, and physiologically in amygdala activation and corticosterone secretion (rat equivalent to human cortisol). It appears that during a sufficiently supported development, an amygdala-dependent emotional circuit develops that is able to appropriately differentiate threatening from non-threatening environmental stimuli (Gillespie, Phifer, Bradley, & Ressler, 2009).
In humans some evidence has shown that early life stress and neglect may also affect the HPA axis due to a compromised oxytocin system (see for review (Olff, Langeland, Witteveen, & Denys, 2010)). Furthermore, we know that sexual and physical abuse both promote overwhelming emotional arousal and often take place in a family context in which caregivers offer little soothing or guidance in effective coping. Abuse is generally chronic and often starts in early development. It is suggested that adults who repeatedly experienced abuse as a child often lack a sense of emotional awareness, have poor emotion regulation skills, and have diminished expectations of social support (Cloitre, Stovall-McClough, Zorbas, & Charuvastra, 2008; Gladstone et al., 2004; Rademaker, Vermetten, Geuze, Muijlwijk, & Kleber, 2008). As a child, they may not have learned to identify and cope with emotions, as parents might have reacted negatively in general to emotions of the child. Notwithstanding, child-abuse in itself is an experience in which the emotions of a child have been seen as unimportant, have been ignored or mislabelled by the offender. Furthermore, parents might have given an inadequate example of their own regulation of emotions by having anger outbursts, smoking and drinking alcohol. As a consequence abused children did not have a proper example from their parents on how to cope with stressors. Inadequate coping may cause stressors to continue for a longer duration or even lead to chronic stress.

**Association between smoking, cortisol and depression**

A model of traumatic stress has to deal with several factors (see (Kleber & Brom, 1992; Olff, Langeland, & Gersons, 2005)). Coping style and dispositions might be crucial mediating factors in the development of psychopathology following childhood adverse experiences. Palliative coping is a way of modulating tension and making the situation more tolerable or keeping it under control without directly taking care of the problem (Lazarus & Folkman, 1984; Olff, Langeland, & Gersons, 2005). In this thesis, support has been found for a mediating role of palliative coping (i.e. smoking) between low cortisol and psychopathology (chapter 4).

Salivary cortisol concentrations were higher in survivors who smoked tobacco, and survivors with depression tended to smoke more per day. When the amount of tobacco was accounted for, depressive survivors showed low cortisol. Thus, in survivors with depression smoking seemed to have a role in elevating cortisol to a normal level.
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(i.e. comparable to healthy survivors). Nicotine withdrawal symptoms and craving, on the other hand, resemble a stress response reflected by elevation of baseline cortisol levels (Cohen, al’Absi, & Collins, Jr., 2004), which likely leads to more smoking. This suggests a biological explanation for smoking as a way of palliative coping with stress on the short-term.

Findings in rescue workers involved in the Enschede fireworks disaster, showed that smoking at 2-3 weeks post-disaster predicted PTSD at 18 months post-disaster (van der Velden, Kleber, & Koenen, 2008). Another large prospective study among nearly 1200 adults in Norway (Klungsoyr, Nygard, Sorensen, & Sandanger, 2006) found a dose-response relation between quantity of smoking and increased risk for depression. Smoking and depression appear to be a self-perpetuating circle, as depression early in adolescence in turn resulted in more tobacco use 3.5 years later (Sihvola et al., 2008). Thus smoking may help to cope with stress in the short term, but appears to have unfavourable effects in the long-term.

Thus far, findings in the literature were inconclusive on what comes first, maladaptive (palliative) coping by smoking or depression. However, they may also have a mutual underlying cause, as is suggested in a study among 6050 twins in which findings showed that a history of childhood sexual abuse was associated with both a significant risk for subsequently occurring regular smoking and a significantly earlier onset of regular smoking (Nelson et al., 2006).

In sum, findings suggest a pathway of adverse life events, like childhood trauma, leading to a self-perpetuating circle of smoking, depression, and cortisol dysregulations.

**Attentional function and symptoms of PTSD and depression**

In studying the burden of symptoms of PTSD and depression on attentional function, chapter 5 showed that although depressive symptoms and sleep disturbances contributed to attentional dysfunction in disaster survivors, these concomitant symptoms of PTSD explained only part of the difficulties. Attentional dysfunction showed to be still directly related to PTSD symptoms also. Most previous studies have compared PTSD subjects to normal controls, thereby confounding the effects of PTSD and trauma exposure. Our correlational study showed that there is at least an additional effect of PTSD symptoms over trauma on attentional dysfunction. Chapter 6 described the
longitudinal study that aimed to elucidate whether improvement in PTSD and depressive symptoms over time, is mirrored in recovery of attentional functioning. Although findings showed that while PTSD symptoms diminished and attentional functioning considerably improved over time, it failed to show an association between changes in symptoms and changes in attention. Restoring pre-trauma levels of attention and concentration perhaps needs more time. However, since our study covered four years this explanation seems unlikely. Although these findings appear to show an irreversible loss of attention after remission of PTSD and depressive disorder, a longitudinal study in young adults who experienced a widespread fire collected data before and after the disaster showed that poorer neurocognitive function was not only an outcome of PTSD symptoms, but may also be a vulnerability factor for developing symptoms of PTSD (Parslow & Jorm, 2007). In light of these findings, we might need to temper our conclusions that PTSD symptoms are stable and early predictors of attentional function, since this might as well indicate an inverse causal relationship. In clinical practice, however, patients with PTSD clearly indicate that their ability to sustain attention has decreased post-trauma, and that they have experienced difficulties to concentrate on their study and jobs ever since. Thus, it seems most likely that PTSD and attention will mutually influence one another.

7.5 Clinical implications and suggestions for further research

Adaptation of current PTSD classification in DSM-5

Findings on exchange between - and comorbidity of - mental disorders question whether the DSM-IV adequately classifies PTSD, depression and perhaps even specific phobia as separate disorders. Lately, several suggestions to adapt PTSD for the upcoming DSM-5 have been recommended by researchers in the field of trauma (Kleber, 2008; McNally, 2009). We pinpoint the discussion below to PTSD and depression.

First, some researchers proposed to narrow the criteria for PTSD specifically for the cluster of reexperiencing (Brewin, Lanius, Novac, Schnyder, & Galea, 2009). They comment that daytime images accompanied by horror or fear and nightmares are the only reexperiencing symptoms that differentiate PTSD from other disorders, for involuntary intrusive recollections are often seen in depressed patients as well. Depressed patients, with or without trauma in their history, often experience unwanted memories
of one or more significant events in their lives that intrude frequently into their minds (e.g., Birrer, Michael, & Munsch, 2007; Brewin, Hunter, Carroll, & Tata, 1996; Kuyken et al., 1994; Patel et al., 2007). In studies to date the proportion of depressed unipolar patients reporting intrusive visual memories has varied from 44% (Patel et al., 2007) to 87% (Brewin et al., 1996). Like in PTSD, in depression these memories are vivid, full of sensory details, distressing, absorbing, and associated with intense negative emotions, although they lack the “here and now” character of intrusions in PTSD (Michael, Ehlers, Halligan, & Clark, 2005). An accordingly narrow description of intrusive memories in PTSD would help to differentiate it from depression.

Second, in contrast to narrow the classification of PTSD, several researchers proposed to broaden it. Empirical data in clinical and epidemiological samples suggest to split the avoidance cluster of PTSD in the current DSM-IV into two different factors: active avoidance and emotional numbing/dysphoria (Carragher, Mills, Slade, Teesson, & Silove, 2010; Olff, Sijbrandij, Opmeer, Carlier, & Gersons, 2009). The first factor consists of actively avoiding thoughts or feelings about the event or doing things that remind the person of the event. The second factor describes emotional numbing or dysphoria as in having difficulty enjoying things or having sad feelings, feeling distant from other people or finding it hard to imagine fulfilling future goals. Question remains whether it is necessary to have both numbing and avoidance symptoms to fulfil the criteria of PTSD or that these factors may exclude one another. Foa et al implied that avoidance and numbing may be functionally similar (i.e. both provide escape from emotional pain) but represent two separate phenomena reflecting different mechanisms (Foa, Riggs, & Gershuny, 1995). Avoidance would be an effortful and strategic psychological process, whereas emotional numbing, i.e., a lack of emotional responsiveness and social withdrawal, may be mediated by a more automatic mechanism resembling those underlying freezing behaviour. Numbing would occur when effortful avoidance is ineffective in reducing arousal (Schnurr et al. (Schnurr, Friedman, & Bernardy, 2002) took it a step further and inferred that comorbid PTSD/depression could be seen as a depressive subtype of PTSD instead of two different disorders, and that it is distinctly different from major depression alone.

Several findings in this thesis support the second point of view to broaden the classification of symptoms of PTSD. PTSD and post-trauma depression appear closely
related, both in their overlapping symptom profiles, in their biological profile and in the course of symptoms.

Our data showed that comorbidity between PTSD and depression, and a shift in diagnostic status over time from PTSD to depression in our cohort was common (chapter 2). Neurobiological findings in the meta-analysis on PTSD and basal cortisol (chapter 3) showed that basal cortisol levels in comorbid PTSD/depression did not differ from levels in PTSD alone. Furthermore, (chapter 4) subgroups of survivors with PTSD and PTSD/depression were similar in presentation (demographics, PTSD symptom severity, and smoking habit) and showed to be different from survivors with major depression. Accordingly, cortisol levels adjusted for smoking differed in survivors with depression alone from the group with PTSD with or without comorbid depression. Thus, this thesis underlines previous comments that suggest to re-evaluate the need to diagnose comorbid depression in PTSD. We should rather adapt the DSM by including a more prominent role for numbing/dysphoria symptoms in PTSD.

Treatment of intrusive visual memories regardless of diagnostic status

Regardless of issues in how to classify overlap in symptoms of depression and PTSD, all psychiatric patients should receive a thorough diagnostic assessment, including a history of trauma, as patients might present themselves with depressive symptoms while there is an underlying PTSD. This has significant implications for choice of treatment since depression, in contrast to PTSD, is treated with more generic treatments as activation, cognitive therapy, and interpersonal therapy. Noteworthy is that evidence has emerged recently that the first choice therapy of PTSD (i.e. imaginal exposure), is beneficial for some depressive patients as well. Brewin et al. (Brewin et al., 2009) found that imagery rehearsal and rescripting therapy has potential as a brief stand-alone treatment for a subgroup of chronically depressed individuals with intrusive visual memories. These new treatment findings once again point to a similar function of avoidance in PTSD and numbing in depression and PTSD. As Foa et al mentioned (Foa et al., 1995), these mechanisms both provide escape from emotional pain. Future studies may give more insight whether post-trauma intrusive visual memories -regardless of diagnostic status- should guide the choice of treatment.
Instructing health practitioners on the sequelae of trauma

Early depressive symptom severity was found to be a significant predictor for an unfavourable course of psychopathology, which in the long-term more often entailed depression and specific phobia than PTSD (chapter 2). It is advisable to create awareness in general practitioners (GP’s), victim support services, and other health professionals to focus on sequelae of trauma. Health practitioners should be informed about a more comprehensive psychological response of patients to trauma than just PTSD with specific attention for early depressive symptoms as risk factor for later disorders and also about the comorbidity between anxiety disorders and depression in survivors post-trauma. Findings in this thesis point out that just checking whether the first onset psychological disorder is in remission is not sufficient, as it may have shifted into another disorder. Since most survivors stay healthy, implementing surveys in the affected populations with large screening questionnaires to identify people at risk of mental health problems would unnecessarily strain survivors who need their time and energy to deal with many issues in the aftermath of trauma.

Furthermore, the association between smoking and psychopathology is worthwhile to point out to health practitioners. Supporting survivors to cessate smoking may help to alleviate psychological problems. However, since depressive symptom severity prospectively predicted a lower likelihood of smoking cessation (Kenney et al., 2009), intervention programs aiming at both smoking addiction and depression might need to be developed in the future.

Occupational doctors should be informed about attention problems in survivors with PTSD or depression. Even when survivors have recovered from these illnesses, these problems may exist and influence job-performance negatively (Kleber & van der Velden, 2009). Time appears to improve attentional function. However, mild dysfunction may persist for a long-period. Adjustment of work-load and jobs that involve dangerous task may be necessary.

Cortisol sampling

Cortisol sampling has previously been thought to show opportunities for an objective determination of the PTSD diagnosis in patients. It has even been mentioned that measuring the level of this hormone would detect if someone is malingering PTSD
(Mason, Giller, Kosten, Ostroff, & Podd, 1986). This thesis unambiguously showed that basal cortisol levels have no value for diagnosing PTSD since cortisol did not distinguish healthy traumatized individuals from those with PTSD.

However, cortisol appears to have a role in PTSD. Several studies have shown that subjects with PTSD who responded to psychological treatment had lower cortisol levels before than after treatment (Gerardi, Rothbaum, Astin, & Kelley, 2010; Olff, de Vries, Guzelcan, Assies, & Gersons, 2007). Furthermore, infusion of an intravenous hydrocortisone (cortisol) enhanced elements of working memory performance in a group of survivors with PTSD (Yehuda, Harvey, Buchsbaum, Tischler, & Schmeidler, 2007). Since cortisol helps to preserve information acquired during stressful events to store it for future use (Joëls, 2008), using cortisol as a pharmacological agent as a surplus in the exposure treatment of patients with trauma-related mental health problems may have some benefits as is shown in the first case described by Yehuda et al. (Yehuda, Bierer, Pratchett, & Malowney, 2010), although care should be taken not to imprint fearful memories. Notwithstanding, low cortisol in trauma survivors might be an adaptive response or just a correlate, instead of the cause of psychopathology.

### 7.6 Conclusions

This thesis described studies in a cohort of survivors of the fireworks disaster in Enschede in May 2000. It showed that nearly half of all survivors had a mental disorder in the past 12 months at 2 years post-disaster, and that the rate dropped to 30 percent at 4 years. The most prevalent disorders were PTSD, specific phobia, and depression. Comorbidity between disorders and a shift from one mental disorder into the other occurred regularly. Findings showed that when survivors were healthy at 2 years post-disaster, they most likely remained healthy at 4 years. For the purpose of DSM-5 it would be interesting to conduct factor analysis of a comprehensive picture of psychological symptoms post-disaster instead of factor analysis within a current diagnostic classification, as this reckons with the overlap in constructs of mental disorders in the current diagnostic classes of the DSM-IV.

Pre-disaster risk factors for development and persistence of mental disorders entailed absence of a maternal caregiver and abuse in childhood. High depressive
symptom severity within weeks post-disaster showed to precede chronic mental disorders at 4 years post-disaster.

In a systematic review of the scientific literature no alterations in the basal levels of the stress-hormone cortisol were found in subjects with PTSD compared to mentally healthy individuals. Though, low cortisol levels in PTSD were shown depending on the type of control groups and specific subpopulations. In our cohort of survivors of the fireworks disaster, evidence was found for low cortisol in post-disaster depression. However, low cortisol in relation to depression was only found when we took into account that smoking has an enhancing effect on cortisol. Since numerous factors may have a confounding influence on cortisol levels, disentangling the relationship between PTSD and cortisol is more complex than it first appears. Large samples and consensus in data collection and sampling protocol of basal diurnal cortisol is needed as this would improve validation of future findings.

Furthermore, this thesis described that PTSD and depressive symptoms are independently associated with poor attentional function. PTSD symptoms appeared to be early and stable longitudinal predictors for attentional dysfunction, whereas mid-term depressive symptoms predicted a lack of improvement in the long-term. Improvement of PTSD or depressive symptoms appeared insufficient for enhancing attentional dysfunction.

Future research should focus on interventions to improve attentional function of survivors with mental health problems post-trauma, as better neurocognitive function may lead to improved (emotional) information processing and day-to-day function.
Reference List


