Sequelae of traumatic stress: psychopathology, cortisol, and attentional function in the aftermath of a disaster
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Chapter 1

General introduction
1.1 News flash of the Enschede fireworks disaster

Saturday May 13, 2000 it was briefly after 2 p.m. in the residential area Roombeek in Enschede when the sight of a small fire next to a fireworks-storage facility attracted many people in the neighbourhood (RTV Oost, 2000). Firemen tried to keep spectators at a distance. For unknown reasons the fire reached the storage bunkers. Without any understanding of the seriousness of the situation people were watching the firemen. Slowly the crowd became aware of the increasing danger of the flames and fireworks. All of a sudden their curiosity turned into panic. The fire led the fireworks to detonate.

The blast was felt up to 30 kilometers away. The explosions had an unbelievable destroying effect. Quickly the residential area turned into a black-burned ruin with hundreds of people wounded and 23 killed. Rescue workers reacted fast. Fire-trucks from all over Twente and even from Germany were being employed. Over 100 ambulances and several trauma-helicopters were actively engaged in the transportation of the deceased and critically injured victims. Hospitals in the wide vicinity were full to the bursting point with victims. More than 10,000 people had to be evacuated for one or more days, and 1,200 people lost their homes completely.

1.2 Disasters in the Netherlands

Disasters are collectively experienced traumatic events. Whether natural (e.g. flood, earthquake), industrial (e.g. mining accident, factory explosion), or man-made (e.g. terrorist attack), disasters are relatively uncommon in the Netherlands. Table 1 shows an overview of disasters in the Netherlands after World War II (Yzermans, 2011).

Despite the fact that the Netherlands borders the sea and that parts of the country are under sea level, only a few large floods occurred in recent Dutch history. The most disastrous one was in 1953 when a great deal of the provinces of Zeeland and Zuid-Holland were flooded. Psychological after-effects and disturbances of this disaster have hardly been described (Ellemers, 1956). Due to this flood a tremendous masterplan was initiated – the Delta works – to defend the country in the near future against the sea.

It was in 1992 that the country was shaken by the air crash of a cargo plane on a residential area, the Bijlmermeer in Amsterdam (Carlier & Gersons, 1997; Gersons & Carlier, 1993). Apart from the loss of lives, injured people and the destruction of the
residential area, this disaster is notorious of the many eyewitnesses and rescue workers who complained over many years about psychological problems and unexplained physical symptoms. This culminated in uncertainty and distrust in authorities and finally ended up in a parliamentary inquiry (Yzermans & Gersons, 2002). In the aftermath of the fireworks disaster in the city of Enschede the Dutch government implemented the lessons learned from the Bijlmermeer disaster. The authorities were keen to address the needs of the survivors and the community as best as possible. Additionally they intended to restore trust in the government. The Ministry of Health launched an effective and efficient aftercare program and a masterplan for a health monitoring study for a period of three to five years. The ongoing gathering of data aimed to specify the needs of the population and to monitor their wellbeing. Services could be up- or downscaled accordingly. This Health Monitoring Victims Enschede Firework Disaster (Gezondheidsmonitoring Getroffenen Vuurwerkramp Enschede; GGVE) has resulted in

<table>
<thead>
<tr>
<th>Year</th>
<th>Place</th>
<th>No of Dutch victims deceased</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1946</td>
<td>Apeldoorn</td>
<td>24</td>
<td>Airplane crash on secondary school</td>
</tr>
<tr>
<td>1953</td>
<td>Zeeland</td>
<td>1835</td>
<td>Dike collapse and subsequent flood</td>
</tr>
<tr>
<td>1962</td>
<td>Harmelen</td>
<td>93</td>
<td>Train accident</td>
</tr>
<tr>
<td>1976</td>
<td>Schiedam</td>
<td>24</td>
<td>Train accident</td>
</tr>
<tr>
<td>1977</td>
<td>Amsterdam</td>
<td>33</td>
<td>Hotel fire (Hotel Polen)</td>
</tr>
<tr>
<td>1977</td>
<td>Tenerife, Spain</td>
<td>583</td>
<td>Airplane crash</td>
</tr>
<tr>
<td>1989</td>
<td>Zanderije, Suriname</td>
<td>175</td>
<td>Airplane crash</td>
</tr>
<tr>
<td>1992</td>
<td>Bijlmermeer</td>
<td>43</td>
<td>Airplane crash on residency</td>
</tr>
<tr>
<td>1992</td>
<td>Faro, Portugal</td>
<td>56</td>
<td>Airplane crash</td>
</tr>
<tr>
<td>1996</td>
<td>Eindhoven</td>
<td>34</td>
<td>Airplane crash (Herculus disaster)</td>
</tr>
<tr>
<td>1996</td>
<td>Texel</td>
<td>32</td>
<td>Airplane crash (Dakota disaster)</td>
</tr>
<tr>
<td>1999</td>
<td>Bovenkarspel</td>
<td>28</td>
<td>Legionella epidemic after Flower Festival</td>
</tr>
<tr>
<td>2000</td>
<td>Enschede</td>
<td>23</td>
<td>Explosion of fireworks-depot in residential area</td>
</tr>
<tr>
<td>2001</td>
<td>Volendam</td>
<td>14</td>
<td>Fire in pub on New Year’s eve</td>
</tr>
<tr>
<td>2004</td>
<td>Asia</td>
<td>3</td>
<td>Tsunami Indian Ocean</td>
</tr>
<tr>
<td>2010</td>
<td>Tripoli, Libya</td>
<td>70</td>
<td>Airplane crash</td>
</tr>
</tbody>
</table>
a wealth of scientific articles (see appendix) and several PhD studies. This thesis is one of them. While most others studies in general have an epidemiological character this thesis is an in-depth study on a subgroup of subjects to address some specific (neuro) psychological and biological issues.

1.3 Trauma and psychological problems

The current knowledge on the sequelae of traumatic stress has come from studies investigating survivors who experienced a diversity of traumatic events. Traumatic events may consist of one or multiple events which are extremely frightening or shocking. Other examples of traumatic events than disasters are war, rape, traffic accidents, violent crimes and other situations in which one felt severely repulsed or felt like one’s life was in danger. In the Netherlands the lifetime prevalence of any potential trauma is about 80 percent (de Vries & Olff, 2009) which resembles rates found in the United States (Breslau et al., 1998).

After a traumatic event survivors often feel tense, frightened, irritable and sad. Additionally, the memory of the traumatic event may be unwillingly and frequently recalled and survivors may suffer from disturbed sleep. People typically may have difficulties in concentrating at work or study and they feel like disaster will again strike any minute. Usually these reactions disappear within a few weeks (Bonanno, 2004).

However, in some survivors of traumatic events these disturbances persist for a longer duration. They cause clinically significant distress or impairment in social, occupational, or other important areas of functioning and daily life. In an attempt to regain control over life all kinds of situations and activities that remind them of the trauma are avoided. Survivors lose trust in themselves and others and can get a sense of powerlessness and hopelessness. Alcohol or sedative substances may be used to suppress negative feelings and hyperarousal. These survivors suffer from severe and disabling psychological problems and it has widely been recognized that trauma and environmental adversities have a role in the genesis of mental disorders like post-traumatic stress disorder (PTSD) (Brom, Kleber, & Witztum, 1992), major depression (Kendler, Karkowski, & Prescott, 1999), specific phobia (Onder, Tural, Aker, Kilic, & Erdogan, 2006), social phobia (Marteinsdottir, Svensson, Svedberg, Anderberg, & von
Knorring, 2007), panic disorder (Scocco, Barbieri, & Frank, 2007), and alcoholism (Zucker & Gomberg, 1986).

PTSD and major depression occur frequently following traumatic exposure, both as separate disorders and concurrently. In adults with chronic PTSD, comorbid depression occurs in nearly 50 percent of all individuals (Kessler, Sonnega, Bromet, Hughes, & Nelson, 1995; Orsillo et al., 1996). In favour of the correct choice of treatment for patients it seems important to disentangle the overlap between PTSD and depression.

1.4 Physiological response to stress: cortisol

The sequelae of trauma also manifest itself in neurobiological phenomena. The hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic nervous system play a major role in the adaptive response to stress. Both systems are responsible for the release of hormones in reaction to both psychological and physical stressors and are frequently studied for their role in the onset and persistence of psychopathology following traumatic stress. Lately, the secretion of cortisol as a measure of HPA axis activity has received increasing attention.

During acute stress, such as exposure to a disaster, there is a dose-dependent increase in both catecholamines and cortisol: the levels of both hormones increase relatively to the severity of the stressor. The catecholamines from the sympathetic nervous system, adrenaline (or epinephrine) and noradrenaline (or norepinephrine), facilitate the availability of energy to vital organs. They initiate certain physiological changes to prepare the body for action (fight or flight reaction). Typically these changes involve an increase in heart-rate, blood-pressure and perspiration, dilation of the pupils and heavy breathing. It also influences our awareness of time. Time seems to pass very slowly, which helps us to respond faster. Cortisol, on the contrary, functions as an “antistress” hormone. It helps to contain or shut down the neural defensive reactions that have been initiated by stress (Munck, Guyre, & Holbrook, 1984; Yehuda, 2001). Cortisol also has a function in preserving information acquired during stressful events, so that it can be stored for future use (Joëls, 2008). Numerous studies suggest that basal cortisol levels may be higher in individuals with a depressive disorder, whereas these levels are presumed to be lower in those with PTSD.
1.5 **Neurocognitive difficulties: attention**

Intrusions, avoidance and hyperarousal symptoms of PTSD are all well described in the aftermath of a disaster (Kleber, 2008). However, more subtle symptoms of difficulties in memory and concentration have been studied much less even though they play an important role in dysfunction in work and daily life. Neurocognitive difficulties are frequent complaints among people who have PTSD and depression. People with depression, for instance, have difficulties concentrating and making decisions. Typical cognitive-processing distortions in PTSD are on the one hand that people suffer from involuntary intrusions of the traumatic event (flashbacks) and are preoccupied with threatening stimuli, while on the other hand they may have difficulty remembering important aspects of the trauma (psychogenic amnesia). The most common findings in studies on neurocognitive functioning in PTSD are impairments in attention and immediate memory. It is emphasized that immediate memory deficits in itself could be attributable to attentional dysfunction (for review see (Horner & Hamner, 2002)) since attention lies at the basis of all adequate information processing (Ashcraft, 1994). Similarly to PTSD, impairment in attention is frequently reported in the acute phase of depression (for review see (Hammar & Ardal, 2009)). Furthermore, it has been found that attentional dysfunctions persist during remission of the disorder (Paelecke-Habermann, Pohl, & Leplow, 2005).

1.6 **Health Monitoring Victims Enschede Firework Disaster**

In this paragraph we will describe the design and main results of the health monitoring studies that documented short- and long-term effects of the Enschede fireworks disaster, see appendix for all published studies on the fireworks disaster.

Between two to three weeks the first post-disaster health survey started. Blood and urine samples were analysed for trace elements indicative of exposure to fireworks-related substances. Results of the analyses showed no systematic increase of heavy metal levels in the residential group and in relief workers (Projectteam Gezondheidsonderzoek Vuurwerkkramp Enschede, 2001). At the same time, the immediate health effects and personal experiences during the disaster were assessed by a comprehensive questionnaire. From a scientific point of view an additional advantage of this speed of assessment was that it prevented a possible bias in the recollection of
disaster experiences and emotions during and immediately after the disaster (van Kamp et al., 2006; Roorda, van Stiphout, & Huijsman-Rubingh, 2004). These questionnaires were repeatedly administered at approximately 18 months and 4 years post-disaster. A different track was to use the records of the GP’s before and after the disaster. By use of electronic medical records extracted from GP’s it appeared feasible to measure the health of survivors before and after the disaster. This cohort study took place from 16 months pre-disaster to 5 years post-disaster. In the Dutch health system every citizen is enrolled in the practice of just one GP who acts as a gatekeeper to secondary care, therefore these GP’s medical records encompass a good overview of all health care problems.

The main results of the studies revealed that mental health problems declined over the course of time. However, severe anxiety and sleeping problems were still elevated at 4 years post-disaster in survivors (n=662) in comparison to an unaffected control group (n=526). Severe intrusions and avoidance of reminders of the disaster (total score >25) at 2-3 weeks, 18 months, and 4 years post-disaster were 70.6%, 36.8% and 23.7%, respectively. Self-rated post-traumatic stress disorder (SRS-PTSD) at 18 months was 13.4% and 9.7% at 4 years post-disaster (van der Velden et al., 2006b).

During the first 2 post-disaster years, survivors had more contact with their GP than pre-disaster. This was especially the case for bereaved survivors and those with mental health problems (den Ouden et al., 2007; Dorn et al., 2006). In the fifth year post-disaster, differences in the amount of contact with the GP between affected and matched non-affected residents were still significant. Pre-disaster no differences were apparent between survivors and matched controls in the prevalence of psychological problems. However, in the six months after the disaster a six-fold increase of psychological problems occurred followed by a fast decrease and a plateau which lasted for almost three years. At 5 years post-disaster survivors still presented more psychological problems than pre-disaster.

Sick leave among rescue workers (n=1403) increased during the 18 months after the explosions: the prevalence of absences attributed to psychological problems increased from 2.5 percent of workers during the 6 months before the disaster to 4.6 percent during the first 6-month period after the explosions and 5.1 percent during the following year (Morren, Dirkzwager, Kessels, & Yzermans, 2007).
1.7 Aims of this thesis

Several limitations have been observed in the above described health monitoring studies. Classifying mental health problems into possible mental disorders is necessary to be able to identify the underlying psychological dysfunction. This enables clinicians to intervene with the appropriate treatment. The validity of self-rated questionnaires is limited when it comes to classifying psychological problems into mental disorders. Sleeping problems and exhaustion, for instance, may be associated to several mental disorders like depression, PTSD, substance abuse, but also to cheerful experiences like having a new born baby.

Secondly, people might not understand the questions or interpret them wrongly. In the study that used electronic medical records of residents, classification of problems was the result of patient–doctor interaction. No systematic examination of post-traumatic psychological distress was performed by GP’s. It appeared that the identification of problems by GP’s depended on several factors like the GP’s own level of self-reported post-trauma mental health, the number of contacts survivors had with their GP and the level of survivors’ disaster-related experiences. This might have led to an under-estimation of psychological problems (Drogendijk et al., 2007; Kessler, Lloyd, Lewis, & Gray, 1999).

Currently, much of the psychological knowledge on how adults cope with trauma comes from survivors who sought treatment or exhibited great distress (Bonanno & Mancini, 2008). Yet, many people are exposed to traumatic events at some point in their lives and continue to have positive emotional experiences and show only minor and transient disruptions in their ability to function. Therefore, the aim of this thesis is to longitudinally describe the community prevalence of psychiatric disorders after mass-trauma and identify predictors for its course in order to be able to anticipate on consequences of future disasters and other traumatic events. We endeavoured to cover the limitations of the health studies by administering structured clinical interviews in a random sample of traumatised inhabitants of the affected area (the “in-depth cohort”).

Furthermore, the goal is to evaluate associations in the existing literature between PTSD and the stress-hormone cortisol, and examine the associations between cortisol and trauma-related psychopathology in the cohort of survivors of the fireworks-disaster.
Finally, as difficulties in attentional function are frequent symptoms among people who have PTSD and depression, we aimed to identify the sequelae of symptom severity on attentional function. We investigated short- and long-term effects on attentional function since deficits in this matter may disrupt normal functioning in social interactions, work and study, even in the remitted state of mental disorders.

In sum, this thesis focused on the following questions:

- 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?

1.8 Brief overview of the study design

With the exception of a systematic review, studies in this thesis are based on the Enschede in-depth cohort. It is a unique and relatively large sample of trauma survivors, as they all experienced the same disaster and were followed from two weeks till four years post-disaster. The participants of the in-depth cohort study were recruited as part of the large prospective study monitoring health after the disaster (van Kamp & van der Velden, 2001). In the in-depth cohort study survivors were assessed with a structured clinical interview at 2 and 4 years post-disaster. A subsample of the interviewed survivors was asked to participate twice in the biological study for neuroendocrine assessments and neuropsychological testing. Figure 1 shows the flow chart of the cohort of participants in the large health survey and the cohort in the in-depth study (overall and biology).
1.9 Outline of this thesis

Although nearly everyone is exposed to a traumatic incident at some point in their lives, only a minority of people have succumbed to PTSD, depression, or other serious mental health problems. Survivors of traumatic events may follow various courses with regard to the development of psychopathology. Luckily, most survivors remain psychologically healthy. Some survivors, however, will have chronic courses of mental disorders, while others will recover, or develop a delayed onset of disorders. In chapter 2 we aimed to get insight into these courses. We studied survivors of the Enschede fireworks disaster from 2-3 weeks up to 4 years post-disaster aiming to assess how many survivors suffer from mental disorders, which specific mental disorders are prominent, and how long survivors suffer from—or are at risk of development of—these potential mental disorders. This longitudinal study also aimed to investigate predictors for the course of the most prevalent disorders in disaster survivors.

Despite a general consensus that basal levels of the stress-hormone cortisol are low in individuals with PTSD compared to controls (i.e. research papers and even reviews on this topic cite in favour of this view), many studies could not confirm these findings. Some studies even found higher basal levels of cortisol in PTSD. Chapter 3 aimed to disentangle these inconsistencies. It describes a systematic review and meta-analysis on studies examining basal cortisol levels in adults with current PTSD in comparison to mentally healthy individuals.
Cortisol levels are influenced by tobacco, and PTSD and major depressive disorder have been associated with increased rates of tobacco usage and dependence. Chapter 4 describes the relationships between PTSD, post-traumatic depression, smoking and levels of circadian cortisol in the cohort of survivors from the fireworks disaster.

Most studies on attentional function in PTSD included patients with significant psychiatric comorbidity. The extent to which the observed attentional deficits were specifically attributable to PTSD remained unclear. Comorbid depression has been put forward as a factor to explain attentional dysfunction in PTSD. In chapter 5 we therefore investigated whether attentional dysfunction in survivors of the Enschede fireworks disaster is related to PTSD symptom severity independently from depressive symptoms. Furthermore, to assure that attentional performance is not the consequence of sleep disturbances, we also examined the effect of sleep disturbances in the relationship between PTSD symptoms and attention.

While symptoms of PTSD and depression after trauma may improve over time, it is unclear whether this improvement is mirrored in recovery of attentional functioning. Chapter 6 describes the longitudinal study on the natural course of attentional functioning in the above mentioned population-based disaster sample. The main research question was whether improvement in attentional functioning can be predicted by PTSD or depressive symptoms, and whether improvement in attention is related to change in symptom severity.

In chapter 7, the general conclusions and discussion are presented, along with the limitations of the studies, the clinical implications, and suggestions for further research.
Reference List


