Sequelae of traumatic stress: psychopathology, cortisol, and attentional function in the aftermath of a disaster
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Summary
On May 13, 2000 a fireworks storage facility exploded in a residential district in Enschede. This unexpected and massive traumatic event affected and shocked many people. It caused the loss of lives and injuries in the community and the destruction of the residential area. The Dutch government declared it a national disaster.

Following a disaster, survivors may suffer from mental health disturbances. They may 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 may feel like disaster will again strike any minute. Usually these reactions disappear within a few weeks. 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. Symptoms may succumb into mental disorders, such as post-traumatic stress disorder (PTSD) and depressive disorder. After the fireworks disaster the Ministry of Health therefore launched a comprehensive aftercare program and a health monitoring study for a period of multiple years. The study resulted in many scientific publications. This thesis is part of this large health monitoring study.

The aims of the thesis were as follows. First, the purpose was to longitudinally describe the community prevalence of psychiatric disorders after the disaster and to identify predictors for the course of disorders in order to anticipate on consequences of future disasters and other traumatic events. Furthermore, the goal was 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, we aimed to identify the sequelae of symptom severity on attentional function, as difficulties in attentional function are frequently reported by people who have PTSD and depression.

Prevalence and course of psychiatric disorders post-disaster. In most disaster-studies only PTSD has been addressed, while it has widely been recognized that other mental disorders like depression and specific phobia show an increased risk of onset post-trauma also. Furthermore, comorbidity between disorders, particularly PTSD, is common. To get an insight into the prevalence and course of post-disaster psychopathology a
A community sample of survivors of the Enschede fireworks disaster was followed from 2-3 weeks to four years post-disaster. Diagnostic interviews to determine mental disorders in accordance with DSM-IV (Composite International Diagnostic Interview; CIDI) and childhood stressor interviews were administered at two years post-disaster (n=260). The CIDI was repeated at four years post-disaster (n=201, response 77.3%). At two years post-disaster approximately half of all survivors suffered from any mental disorder. The most common disorders were PTSD (21.8%), depression (16.1%) and/or specific phobia (21.5%). These disorders were highly comorbid. The majority of survivors recovered from their mental disorder over the course of time, although depression and specific phobia still exhibited a substantial risk at four years post-disaster. 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 like depression or specific phobia. On the other hand, it was unlikely to have a course starting off with depression followed by an anxiety disorder. Depression in the absence of a co-existing anxiety disorder showed to be a remitting disorder over the course of time.

The course of the three entangled disorders - PTSD, depression and specific phobia - was studied by constructing four groups of survivors based on the diagnostic status at two and four years post-disaster: healthy, recovered, chronic and delayed onset. Initial depressive symptoms, absence of maternal care during ones childhood, childhood physical abuse, and the magnitude of disaster exposure were found to discriminate between the four groups, predicting long-term mental health problems.

We conclude that clinicians should conduct thorough diagnostic assessments, including a history of trauma, as patients might present themselves with depressive symptoms while this is a change in symptom profile over time that hides an underlying PTSD. This is necessary since it has significant implications for the choice of treatment. Furthermore, clinicians should be alert to signal comorbidity in patients with trauma-related disorders. Findings showed that child abuse and neglect form extra risk factors for chronic psychopathology in adulthood. Since depressive symptom severity within a few weeks post-disaster showed to have a predictive value, this offers concrete suggestions for early screening of trauma survivors at risk for long-term mental health problems. Findings also emphasize that PTSD is not an exclusive outcome of trauma, as depressive disorder and specific phobia are highly prevalent disturbances post-disaster as well, specifically on the longer term (Chapter 2).
Associations between stress-hormone cortisol and PTSD. The sequelae of trauma also manifest itself in neurobiological phenomena. The hypothalamic-pituitary-adrenal (HPA) axis plays a major role in the adaptive response to stress. This system is responsible for the release of hormones (e.g. cortisol) in reaction to both psychological and physical stressors and is frequently studied for its role in the onset and persistence of psychopathology following traumatic stress. In scientific literature, PTSD has inconsistently been associated with lower levels of cortisol. To elucidate these inconsistencies, we performed a systematic review and meta-analysis to compare basal cortisol levels between adults with current PTSD and a control group of people without psychiatric disorders. Findings showed that across 37 studies, people with PTSD (N=828) and controls (N=800) did not differ in cortisol levels. Subgroup analyses revealed that studies assessing cortisol in plasma or serum showed significantly lower levels in people with PTSD than in controls who were not exposed to trauma. Lower levels were also found in people with PTSD when solely females were included, in studies on physical or sexual abuse, and in afternoon samples. Thus, low basal cortisol levels in PTSD were only found in sub-analyses under certain conditions. Future research should elucidate whether low cortisol is related to gender or abuse and depends on the measurement methods used (Chapter 3).

Cortisol, smoking and post-disaster psychopathology. Cortisol levels are influenced by smoking, while PTSD and major depressive disorder have been associated with increased rates of tobacco usage and dependence. At the same time tobacco also affects the HPA axis. We therefore examined the relationships between PTSD, post-traumatic depression, smoking and levels of circadian cortisol in the cohort of survivors from the fireworks disaster. The sample consisted of 38 healthy survivors, 40 subjects with PTSD, and 17 subjects with post-traumatic depression. Salivary cortisol samples were collected at home immediately upon awakening, 30 min after awakening, at noon, and at 10 p.m. Quantity of smoking was measured through self-report. The results of the study showed that salivary cortisol concentrations were higher in smoking subjects. In survivors with PTSD and healthy individuals the usual dynamic pattern of increase in cortisol past awakening was present, while we did not observe this in post-traumatic depression. Survivors with depression following the disaster had a flatter diurnal cortisol curve than subjects with PTSD or healthy survivors. These survivors with depression tended to use
more tobacco per day, and the cortisol group differences could only be revealed when we adjusted for quantity of smoking. We concluded that smoking mediates the relationship between traumatic stress symptoms and the HPA-axis. Smoking may be an important palliative coping style in dealing with posttraumatic arousal symptoms in the short-term, in the sense that it modulates tension and makes the situation more tolerable without directly taking care of the underlying problem (Chapter 4).

**Attentional function and PTSD symptom severity.** Subtle difficulties in memory and concentration in the aftermath of a disaster may play an important role in dysfunction in work, study and daily life and are frequent disturbances among people who have PTSD and depression. Unfortunately, research on neurocognitive functioning following trauma has exclusively focussed on PTSD. PTSD showed to be frequently associated to deficits in sustained attention which cause difficulties in executing long-lasting tasks. Since PTSD and depression are highly comorbid and have overlap in symptoms, it has however been suggested that the observed attentional deficits in PTSD can be attributed to co-existing depressive symptoms. We therefore investigated whether the ability to sustain attention is still related to PTSD symptom severity when we controlled for the influence of depressive symptoms and other potential factors of influence. We measured attentional function in a sample of survivors of the fireworks disaster by administering the Paced Auditory Serial Addition Task (PASAT). The objective of this test is to add 60 pairs of randomized digits in the range of 1 to 6, in each of 5 separate subtests that differ in the rate of speed between successive digits. Analyses revealed low but significant partial correlations between PTSD symptoms and the subtests with the lower speed rates, ruling out the effects of age, education, depressive symptomatology, and sleep disturbances. We concluded that PTSD symptoms are associated with attentional dysfunction in the aftermath of disaster (chapter 5).

**Long-term effects of PTSD and depressive symptoms on attentional functioning.** Over the course of time, PTSD and depressive symptoms may diminish naturally or by means of psychological/pharmacological interventions. It is assumed that improvements in health and functioning are mirrored in recovery of attentional functioning. However, this has barely been studied. We therefore examined the longitudinal effects of PTSD and
depressive symptoms on attentional function. PTSD and depressive symptom severity measures were repeatedly administered in a community-based sample of survivors between 2-3 weeks and 4 years post-disaster. Attentional function was measured with the PASAT in 135 survivors at 2 and 4 years post-disaster. Results showed that the initially high PTSD and depressive symptoms significantly diminished over the course of years and that attentional performance improved. PTSD symptoms as early as 3 weeks post-disaster were associated to attentional dysfunction 2 years post-disaster. No differences in predictive power of PTSD symptoms whether measured at 3 weeks or at 18 months post-disaster were revealed. Deterioration in attention at 4 years was predicted by depressive symptoms at two years post-disaster, but not by change in depressive or PTSD symptom severity. We conclude that PTSD symptoms are early signs and stable predictors for long-term attentional dysfunction. Findings elucidate the burden of comorbidity between PTSD and depressive symptoms for chronic difficulties with regard to attention, while targeting at improvement of PTSD or depressive symptoms appears to be insufficient for enhancing attentional dysfunction (chapter 6).

In the general conclusions and discussion (chapter 7) the main results of the previous chapters are summarized and discussed, along with the limitations of the studies, the clinical implications, and suggestions for further research. In sum, we came to the following conclusions and recommendations. First, since 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. We confirm earlier recommendations to re-evaluate the need to diagnose comorbid depression in PTSD. The DSM should be adapted by including a more prominent role for numbing and dysphoria symptoms in PTSD. We advise for future studies to focus on possible clusters of anxious-depressive symptoms for more comprehensive descriptions of the whole spectrum of trauma-induced psychopathology.

Second, disentangled the relationship between PTSD and cortisol is more complex than it first appears. Numerous factors - which are frequently overlooked - may have a confounding influence on cortisol levels. In order to increase validation of findings, large studies and consensus in data collection and sampling protocol of basal diurnal cortisol are needed.
Furthermore, the significance of early adverse life experiences, such as abuse and absence of maternal care in childhood, is pointed out both as risk factor for chronic mental disorders and for physiological changes in cortisol. It appears that maternal absence during developmentally critical periods is the link between childhood trauma and pathophysiological changes in the HPA axis and subsequent psychopathology in adulthood.

Fourth, since smoking appears to mediate the relationship between traumatic stress symptoms and the HPA-axis, supporting survivors to cease smoking may help to alleviate psychological problems. Intervention programs aiming at depressive symptoms and cessation of smoking simultaneously may need to be developed in the future.

Finally, occupational doctors should be informed about attention problems in survivors with PTSD and depression. Even when survivors have recovered from these illnesses, these problems may exist and influence job-performance negatively. Although time appears to improve attentional function, mild dysfunctions could persist for a long-period that may require adjustment of work-load and jobs that involve dangerous task. 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.