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# Startle reactivity in the long-term after severe accidental injury: Preliminary data

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ABSTRACT

An exaggerated startle response is one of the core hyperarousal symptoms of posttraumatic stress disorder (PTSD). Heightened startle eye-blink magnitude and reduced habituation of this response in PTSD patients have been reported in several studies. However, it is unclear whether this is an enduring characteristic of individuals vulnerable for PTSD or to which degree trauma-exposed individuals who do not develop PTSD also show exaggerated startle. Thirteen accident survivors with remitted PTSD, 12 trauma controls, and 16 non-trauma controls were examined. Four measures of startle reactivity were analyzed in response to 15 bursts of white noise (95 dB, 50 ms): eye-blink magnitude, eye-blink onset latency, skin conductance response, and heart rate response. The eye-blink reflex was measured over the left musculus orbicularis oculi. Reactivity and habituation were analyzed using linear mixed models. Remitted PTSD subjects did not differ from non-trauma controls regarding any of the startle reactivity or habituation measures. Unexpectedly, trauma controls showed larger eye-blink magnitude than non-trauma controls. These results suggest that the exaggerated startle response disappears after remission from PTSD. Further, they suggest that psychologically resilient trauma survivors might show a PTSD-like pattern of exaggerated physiological startle even many years after a traumatic event.


## 1. Introduction

Post-traumatic stress disorder (PTSD) is an anxiety disorder that can develop after exposure to terrifying events in which grave physical harm occurred or was threatened (American Psychiatric Association, 1994). Resilience on the other hand is a personality characteristic that moderates the negative effects of stress and promotes adaptation. The rates of PTSD among accident survivors vary considerably between studies, some showing high rates of up to 46% (Blanchard et al., 1994, 1995; Ehlers et al., 1998; Koren et al., 1999; Ursano et al., 1999). In contrast, in two studies in Switzerland less than 5% of severely injured accident survivors were found to suffer from PTSD (Schnyder et al., 2001, 2008), indicating high psychological resilience in this population.

According to the DSM-IV (American Psychiatric Association, 1994), the diagnosis of PTSD includes persistent symptoms of increased arousal like exaggerated startle responses, difficulty falling or staying asleep, anger, or hypervigilance. The startle reaction is a physiologic response to a sudden unexpected stimulus that contracts several muscles in order to protect the body from harm (Landis and Hunt, 1939). Startle reactivity can be measured using the eye-blink reflex, which is part of the startle reaction and can easily be elicited by loud acoustic stimuli (Lang et al., 1990). High startle reactivity is characterized by high eye-blink amplitudes and short eye-blink onset latencies. The startle reaction can also be accompanied by a rise of the skin conductance level (Shalev et al., 1992) and an increased heart rate (Shalev et al., 1992; Orr et al., 1995, 1997a, 1997b).

Studies exploring the association between startle reactions and PTSD have found inconsistent results. In victims of single potentially traumatic events such as combat, rape, or accidents evidence for heightened startle reactions in PTSD has been found compared to traumatized subjects without PTSD (Butler et al., 1990; Shalev et al.,

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1992, 1997; Orr et al., 1995; Morgan et al., 1996; Grillon et al., 1998) as well as compared to subjects without trauma history (Shalev et al., 1992; Morgan et al., 1996, 1997; Grillon et al., 1998). Victims of prolonged or repeated traumatic exposure such as childhood sexual abuse, on the other hand, might reveal a reversed pattern of lower startle reactivity. For example Medina et al. (2001) found that higher PTSD scores were associated with lower startle reactivity in women who had experienced childhood corporal punishment or intimate partner aggression. In a meta-analysis by Pole (2007) PTSD was reliably associated with larger responses to startling sounds. It is unclear, however, whether the exaggerated startle response is a stable trait characteristic of subjects vulnerable for PTSD (risk factor), or an acquired PTSD symptom that disappears after remission. In accordance with the former hypothesis, in a prospective investigation Guthrie and Bryant (2005) found a heightened startle reaction in firefighters prior to trauma to be a predictor for PTSD severity after traumatic events. On the other hand, Shalev et al. (2000) found that subjects who later developed PTSD showed elevated startle responses 1 month after trauma, while 1 week after trauma they did not differ from subjects who did not go on to develop PTSD. In a rat model of PTSD Nalloor et al. (2011) showed that higher acoustic startle reactions elicited by mild stress prior to a traumatic event were able to predict PTSD-like behavior after trauma. These results suggest a hidden risk factor for PTSD that can be seen under mildly stressing conditions. Additionally, studies investigating reactions to startle sounds in PTSD reported deficits in habituation, i.e. deficits in the decrease of physiological reaction after repeated exposure (Shalev et al., 1992, 1997; Orr et al., 1995). These findings point to a possible learning deficit in PTSD patients that could partly explain the hyperarousal symptoms and might have implications for treatment. Also studies investigating fear-potentiated startle reactions point into this direction by showing that the ability to inhibit fear reactions under safe conditions is impaired in PTSD patients (Jovanovic et al., 2009, 2013).

Taken together, these findings show that the relation between startle and PTSD is rather complex. The few studies that have compared startle reactions in remitted and current PTSD patients (Metzger et al., 1999; Carson et al., 2007) also found inconsistent results. While Carson et al. (2007) found that current PTSD patients showed higher heart rate responses than remitted PTSD patients and subjects who never had PTSD, Metzger et al. (1999) found higher heart rate responses and slower skin conductance habituation in current and remitted PTSD patients as compared to individuals who never had PTSD.

Further, it is unclear how subjects who are resilient against the development of PTSD after a traumatic event react physiologically compared to individuals who have never experienced any serious traumatic event. More specifically, it is not clear whether psychologically resilient subjects show a PTSD-like pattern at the physiological level or whether physiological changes only take place in association with psychological PTSD symptoms.

The aim of this study was to investigate whether remitted PTSD subjects still show heightened startle reactions. We examined the physiological startle reactivity of accident survivors, comparing remitted PTSD subjects with a group of accident survivors who did not develop PTSD (trauma controls) and a group of control subjects who had not experienced any trauma (non-trauma controls). On the assumption that heightened startle might be a pre-existing trait characteristic of subjects vulnerable for the development of PTSD, we expected the remitted PTSD subjects to have the largest startle response and slowest habituation. On the other hand, we expected the trauma control group to show the weakest startle response and fastest habituation as they seem to be resilient to stress. The non-trauma control subjects were expected to lie between the other two groups, because this group should comprise both resilient and susceptible individuals.

## 2. Methods

### 2.1. Participants

Twenty-two PTSD-remitted accident survivors and 16 resilient accident survivors who had not developed PTSD were recruited from two samples of physically injured subjects who had been hospitalized at the Department of Traumatology at the University Hospital Zurich 10 years ago and had taken part in earlier studies looking into the psychosocial consequences of accidental injuries (Schnyder et al., 2001, 2008). These patients had originally received a thorough psychiatric diagnostic assessment shortly after the accident and 6 and 12 months later. To recruit the subjects we called all the participants of the previous studies fulfilling our inclusion criteria, and informed them about our study. Additionally, 16 healthy controls were recruited from the general population through advertisements (non-trauma group). All subjects were over 18 years of age. To be included in the PTSD-remitted group subjects had to have been diagnosed with full or subsyndromal PTSD according to DSM-IV (American Psychiatric Association, 1994), as assessed by the German version (Schnyder and Moergeli, 2002) of the Clinician-Administered PTSD Scale (CAPS) (Blake et al., 1995) at least at one of the measurement points in the previous studies (full PTSD: fulfilling symptom clusters B, C and D; subsyndromal PTSD: fulfilling symptom clusters B plus either C or D but not both) but not in the present study. For participants to be included in the trauma-control group, it was required that they never had a diagnosis of full or subsyndromal PTSD during the previous studies. Inclusion criteria for the non-trauma group were that the participants had never experienced a trauma according to DSM-IV criteria. Exclusion criteria for all three groups were current mental disorders, chronic somatic and neurological diseases and insufficient command of German. All subjects were tested for normal hearing function. Groups were matched for age and gender (see Table 1). Participants were thoroughly informed about the procedures and gave written informed consent according to the Declaration of Helsinki before participating. This study was approved by the local ethics committee.

Six participants were excluded from the study due to current major depression or anxiety disorders. Two participants were excluded because of non-normal hearing, and three because of technical problems. One subject canceled the assessment, and one did not tolerate the face electrodes for the startle measurement. From the remaining 13 subjects in the PTSD-remitted group, one subject was excluded from skin conductance analysis and two from heart rate analysis because of poor data quality. Also, one of the remaining 12 subjects in the trauma-control group and two of the 16 subjects in the non-trauma group were excluded from skin conductance analysis for the same reason. The sample description is given in Table 1. Two subjects in the remitted PTSD group were taking psychotropic medication, one was taking antidepressants and one anticonvulsants. Analyses were performed both including and excluding these subjects (results without these two subjects are provided in the supplemental material). Two subjects of the remitted PTSD group had received psychotherapy.

### 2.2. Psychometrics

Current PTSD symptoms were assessed using the German version (Schnyder and Moergeli, 2002) of the Clinician-Administered PTSD Scale (CAPS; Blake et al., 1995). Axis I comorbidity was established by the Mini International Neuropsychiatric Interview (M.I.N.I.; Sheehan et al., 1998). Symptoms of depression were measured by the German version (Hautzinger et al., 1995) of the Beck Depression Inventory (BDI; Beck et al., 1961) and trait anxiety by the German version of the State Trait Anxiety Inventory (STAI, Laux et al., 1981). The absence of traumatic events in the non-trauma group was checked by the German version of the first part of the Posttraumatic Stress Diagnostic Scale (PDS; Foa, 1995).

### 2.3. Physiological measures

Recording of the physiological data was performed using a BIOPAC MP150 System (Biopac Systems, Inc., Goleta, CA). The eye-blink reflex was measured by electromyographic (EMG) recordings of activity in the left musculus orbicularis oculi (Fridlund and Cacioppo, 1986) using Ag/AgCl disposable snap connector electrodes filled with hydrogel jelly. Skin conductance electrodes were placed on the thenar and hypothenar eminence of the left palmar surface using Ag/AgCl electrodes filled with isotonic electrolyte gel. Electrocardiograms (ECG) were recorded from three Ag/AgCl disposable snap connector electrodes filled with hydrogel jelly located below the left and right collarbone and on the left rib cage. EMG and ECG were sampled at a 1000 Hz rate, skin conductance level at a 62.5 Hz rate.

### 2.4. Procedure

The study took place at the psychophysiological laboratory of the Department of Psychiatry and Psychotherapy, University Hospital Zurich, Switzerland. Sensors were attached while the subjects reclined in a comfortable chair. Subjects were