



## PTSD, but not childhood maltreatment, modifies responses to unpleasant odors

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### ABSTRACT

Childhood maltreatment (CM) as well as posttraumatic stress disorder (PTSD) is said to result in functional changes to amygdalae and orbitofrontal cortex. Thus, it might be expected to change olfactory function in adults with a CM-history and current PTSD symptomatology as amygdalae and orbitofrontal cortex are of major importance for olfactory information processing. To explore this we investigated olfactory function in 31 women with current psychopathology and a history of CM, 28 without CM, and 27 healthy women. We used the “Sniffin’ Sticks” threshold and identification test and analyzed chemosensory event-related potentials. Participants were also asked to complete a questionnaire to assess current symptoms of posttraumatic stress disorder (PTSD). We found no significant difference between the CM-Group and the two control groups, but PTSD severity correlated significantly with odor identification scores and with parameters of event-related potentials in response to unpleasant stimuli. The results indicate preferential processing of unpleasant stimuli in PTSD patients irrespective of the childhood history.

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### 1. Introduction

The aim of this study was to investigate relations between emotional information processing and the sense of smell by exploring olfactory function in groups of individuals that are characterized by psychopathology involving emotion regulation deficits. This was based on the idea that some studies indicate functional and structural changes in amygdalae and orbitofrontal cortex following psychosomatic and psychiatric disorders involving emotion regulation deficits. Both regions are highly important for olfactory information processing. For this exploratory study, we focused on patients with psychosomatic disorders and with a history of childhood maltreatment (CM), as well as on adults suffering from posttraumatic stress disorder (PTSD) symptomatology.

In contrast to other patients with psychopathology, *patients with CM* are often seen as a special group, requiring special treatment. This is due to a conspicuous emotion regulation deficit in these patients, involving hyperarousal and depression (Herman, 1992; Sack, 2004). CM constitutes a major social issue. For example, approximately 10% of German students report severe physical abuse by their parents (Pfeiffer et al., 1999). Similar estimates exist for the USA. In a retrospective study with over 17,000 participants, 12% of USAmerican adults report severe maltreatment in their childhood (Anda et al.,

2006). Maltreated children not only perform worse in tests of language and cognitive function (Hoffman-Plotkin and Twentyman, 1984; Beers and Bellis, 2002; Prasad et al., 2005), they also suffer to adulthood from their childhood experiences. Adults with a history of CM are more likely to develop psychiatric diseases, like depression, anxiety or substance abuse (Anda et al., 2006).

In contrast to the biographical experience of CM, PTSD is a psychosomatic disorder. It is described by the criteria of hyperarousal, intrusion and avoidance following an extreme traumatic experience (American-Psychiatric-Association, 2000). Lifetime prevalence of PTSD is estimated at about 8% (Kessler et al., 1995). The prevalence of trauma survivors developing PTSD is estimated at about 25% (Yehuda, 2002). It is important to note, that although adults with a history of CM have an enhanced risk to develop psychiatric diseases (Anda et al., 2006), not all of them get PTSD. On the other side, not all PTSD patients have traumatic childhood experiences, but might develop PTSD after traumatic adulthood experiences.

Neurostructural changes have been described in the context of CM and PTSD. Some authors suggest a reduced brain volume in CM patients (DeBellis et al., 1999; DeBellis and Keshavan, 2003). More specifically, volume reduction is reported in parts of the limbic system, including amygdalae (Driessen et al., 2000; Teicher et al., 2003; Vermetten et al., 2006), hippocampus (Bremner et al., 1997) and anterior cingulate cortex (Kitayama et al., 2006). In all of these studies, the participants also suffered from psychopathology, mostly PTSD. Thus, one could argue that the smaller volumes of these structures are not the result of traumatic experiences, but that smaller volumes in these brain regions enhance the risk to develop psychopathology, especially PTSD in participants with CM.

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Based upon these previous studies the present investigation intended to analyze the influence of CM and PTSD on olfactory perception. There is overlap between structures proposed to be affected in patients with CM and PTSD and the structures involved in olfactory information processing. In contrast to any of the other sensory modalities, most of the olfactory fibers bypass the thalamus and project very rapidly and directly into the piriform cortex, amygdalae and entorhinal cortex; regions implicated in emotional and memory processing (Landis et al., 2005). Furthermore, orbito-frontal and hippocampal areas are very important in olfactory processing (Zatorre et al., 1992; Lesa Betha, 1999; Sobel et al., 2003).

Accordingly, we wanted to explore whether participants with a history of CM exhibit altered olfactory perception in comparison to controls. Furthermore, it was planned to investigate whether possible changes in olfactory function relate to PTSD. To explore these questions, we used a comprehensive battery of psychophysical tests of olfactory function including tests for odor identification and odor thresholds (Hummel et al., 2007). On an electrophysiological level, event-related potentials generated in response to olfactory and trigeminal stimuli were recorded (Hummel and Kobal, 2001). We compared three groups of participants: inpatients of a psychosomatic clinic with CM, inpatients of the same clinic without CM, and a healthy control group. To measure PTSD, participants answered a questionnaire exploring the presence and severity of PTSD-symptoms (Impact of Event Scale-Revised; IES-R, (Horowitz et al., 1979; Maercker, 2003)). To control depressive symptoms, which are reported to be related to olfactory function (Pause et al., 2003), participants answered a depression questionnaire (Beck Depression Inventory; BDI (Beck and Steer, 1987; Hautzinger et al., 1995)). Thus correlation of olfactory function and PTSD in healthy and in depressive women with and without CM was possible.

## 2. Methods and materials

### 2.1. Participants

To analyze the influence of CM on odor perception, three groups of participants were recruited. The *CM-Group* included 31 women with CM, especially with a history of sexual and physical abuse. Participants were recruited from inpatients at our clinic for psychosomatic disorders. Due to the fact, that a reduced olfactory sensitivity is often described in depressed people (Pause et al., 2003), we tried to control for the possible influence of depressive symptoms. Thus 28 women without CM but with depressive symptomatology were also invited to participate. They were inpatients at the same clinic (*Patient-Control-Group*). In addition, 27 women without CM and without mental disorders were tested (*Healthy-Control-Group*). Participants were aged between 19 and 60 years (mean  $\pm$  standard deviation =  $39.9 \pm 10.2$  years).

The investigations were performed according to the Declaration of Helsinki on Biomedical Research Involving Human Subjects. The protocol was approved by the University of Dresden Medical Faculty Ethics Review Board. After complete description of the study to the participants, written informed consent was obtained.

#### 2.1.1. Whole sample of participants

There were no significant differences between the groups in relation to age, smoking behavior, or alcohol consumption. There were also no significant differences in the depressive symptoms (BDI) or pharmaceutical therapies, the *CM-Group* and the *Patient-Control-Group*. CM was quantified using a childhood-trauma-questionnaire (CTQ (Bernstein and Fink, 1998; Gast et al., 2001)) and validated by therapists' ratings. In contrast to both control groups, participants in the *CM-Group* exhibited significantly higher scores in this questionnaire (CTQ:  $F=39.3$ ,  $df=2$ ,  $p<0.001$ ) and in the subscales of a questionnaire exploring symptoms of PTSD (IES-R;  $F=13.8$ ,  $df=2$ ,

$p<0.001$ ). Combining the three IES-R subscales with a regression formula (Maercker, 2003) allows an appraisal of the presence or absence of PTSD. Doing so, 22/31 participants of the *CM-Group*, 5/28 of the *Patients-Group* and none of the *Healthy-Control-Group* is classified as suffering from PTSD. Descriptive statistics from the three research groups are shown in Table 1. Clinical diagnoses of the participants of the *Patients-Group* with and without CM are presented in Table 2. All participants received tests for odor thresholds and odor identification.

#### 2.1.2. Samples of chemosensory event-related potentials

Chemosensory event-related potentials were collected from 18 women in the *Trauma-Group*, from 11 of the *Patient-Control-Group* and from 20 of the *Healthy-Control-Group*. In this partial sample, there were no group differences in age, smoking behavior or alcohol. There was no significant difference between depressive symptoms (BDI) in *CM-Group* and the *Patient-Control-Group*. In contrast to both control groups, participants in the *CM-Group* scored significantly higher in the CTQ and the subscales of the IES-R-questionnaire evaluations (CTQ:  $F=35.5$ ,  $df=2$ ,  $p<0.000$ ; IES-R:  $F=17.7$ ,  $df=2$ ,  $p<0.000$ ). Both control groups did not differ significantly according to the CTQ and IES-R questionnaires.

#### 2.2. Testing of odor thresholds and odor identification

Odorants were presented using the validated and reliable "Sniffin' Sticks" tests resembling pen-like odor dispensers (Burghart GmbH, Wedel, Germany; compare (Hummel et al., 2007)). Instead of liquid dye the tampon of the pen is filled with a liquid odorant. To present the odor the pen's cap was removed by the experimenter for approximately 3 s and the tip of the pen was placed 1–2 cm in front of the nostrils. The interval between presentations of individual pens from a triplet was approximately 3 s.

Odor thresholds were obtained for phenyl ethyl alcohol (PEA, a rose-like odor) diluted in propylene glycol. Employing a 3-alternative, forced-choice (3-AFC) paradigm, the participants had to identify the pen that contained the odorant presented at various concentrations. Two successive correct identifications of the pen containing the odor, or one incorrect identification, triggered a reversal of the staircase to the next higher or the next lower dilution step, respectively. Odor thresholds were determined as the average of the final 4 of 7 staircase reversals.

Odor identification was assessed by means of 32 common odors, each presented in one pen. Using a 4-alternative forced-choice paradigm, identification of each individual odors was performed from a written list of four descriptors. The test result was the sum of correctly identified odors (Haehner et al., 2009).

#### 2.3. Chemosensory event-related potentials (CSERP)

CSERP were recorded in participants naive to these recordings. They were instructed to keep their eyes open. During CSERP recordings, participants were asked to perform a simple tracking task on a computer screen directly in front of them. Monomodal chemosensory nasal stimulation was performed using a stimulator (Olfactometer OM2S, Burghart Instruments, Wedel, Germany) which allows administration of chemical stimuli without causing concomitant mechanical or thermal sensations.

This was achieved by embedding chemical stimuli of 200 ms duration in a constantly flowing air stream (8 l/min) applied to the nasal cavity through a canula with an inner diameter of 2 mm inserted approximately 1 cm into the nostril beyond the nasal valve area. Temperature and humidity of the air stream was kept constant (36.5 °C, 80% relative humidity). Rise time of the stimulus concentration was less than 20 ms (measured as described by Kobal, 1981), specifically, the switching of the olfactometer's vacuum was

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