

## THERMAL SIGNATURE OF FEAR CONDITIONING IN MILD POST TRAUMATIC STRESS DISORDER

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**Abstract**—Fear conditioning has been proposed as an important factor involved in the etiology of posttraumatic stress disorder (PTSD). We examined fear processing in PTSD patients with mild symptoms and in individuals who did not develop symptoms (both groups consisting of victims of a bank robbery), through the study of fear-conditioned response. Conditioned responses were quantified by the skin conductance response (SCR) and the facial thermal response, the latter being measured by high-resolution functional thermal infrared (fIR) imaging. We found: (a) a change of the physiological parameters with respect to the baseline condition in both control subjects and PTSD patients during the conditioning phase; (b) the permanence of the conditioning effect in the maintenance phase in both control and PTSD patients; (c) patients and controls did differ for the variation across the phases of the physiological parameters rather than for their absolute values, showing that PTSD patients had a prolonged excitation and higher tonic component of autonomic activity. These results, although preliminary, indicate that the analysis of SCR and facial thermal response during the conditioning paradigm is a promising psychometric method of investigation, even in the case of low level of PTSD symptom severity. To the best of our knowledge, this study is the first attempt to discriminate between control subjects and PTSD patients with mild symptoms through infrared thermal imaging. It may suggest feasible approaches for diagnostic screening in the early phases of the disorder and in the assessment of preventive measures and therapies.  
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**Key words:** conditioning, emotion, thermal imaging, post traumatic stress disorder (PTSD).

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**Abbreviations:** ANOVA, analysis of variance; ANS, autonomic nervous system; ASR, Acoustic Startle Response; CAPS, Clinician-Administered PTSD Scale; CS, conditioned stimulus; fIR, functional infrared imaging; GSR, Galvanic Skin Response; PTSD, post-traumatic stress disorder; SCR, skin conductance response; US, unconditioned stimulus.

### FEAR IS AN EVOLUTIONARY RESPONSE

Transient fear state is an advantage mechanism, which could turn into a pathological condition if occurring for long-term. Pathological fear is a distinctive feature of patients suffering from post-traumatic stress disorder (PTSD), a clinical condition characterized by both psychological and physiological components. Indeed, PTSD patients present symptoms involving intrusive re-experiencing of traumatic events, avoidance of reminders, emotional numbing and hyper-arousal (American Psychiatric Association, 2000, Diagnostic and Statistical Manual of Mental Disorders, 4th ed. DSM-IV-TR).

According to the DSM IV, PTSD patients may present high physiological arousal (Criterion B5) to situations that have low similarity with the experienced trauma, but that could overlap or share with them particular sensory impressions (e.g., similar color, smell or sound; Ehlers and Clark, 2000). Furthermore, exaggerated startle response (Criterion D5) expressed by significant increases in the autonomic nervous system (ANS) response is usually observed.

Fear conditioning is a basic form of associative learning, well studied at both the behavioral and neural levels (Maren and Quirk, 2004; Quirk et al., 2006; Burgos-Robles et al., 2007), to investigate the augmented physiological and emotional reactivity in PTSD patients (Foa et al., 1992; Rasmussen and Charney, 1997; Quirk and Mueller, 2008).

From a fear conditioning point of view, a traumatic event serves as an unconditioned stimulus (US) that elicits an unconditioned response like fear and high arousal. The US is associated with any stimuli (sights or smells) present in the traumatic environment. As a consequence, such stimuli could become conditioned stimuli (CS). Thereafter, despite the absence of the US, CS–US association produces conditioned responses, e.g. intense fear, at those stimuli similar to those presented in the traumatic context. Therefore the conditioned response persists even after the termination of the conditioning (Fendt and Fanselow, 1999; LeDoux, 2000), becoming a persistent conditioned response in PTSD (Friedman, 2006; Amstadter et al., 2009). Conversely, repeated presentations of the CS without the US extinguishes the fear responses elicited by the CS (Brooks and Bouton, 1993) and it may represent a model for the emotional regulation in healthy individuals, as the fear response is attenuated or extinguished by the absence of the fear-related stimuli. Habituation

allows individuals to ignore innocuous events by producing a progressive decline in response to repeated presentations of a neutral stimulus via non-associative learning (Hettema et al., 2003). Therefore, deficits in the extinction of the fear responses may reflect an abnormal emotional regulation similar to what observed in the PTSD patients (Sherin and Nemeroff, 2011).

Functional imaging studies have shown a correlation between blood-oxygen-level-dependent (BOLD) signal in the amygdala and the skin conductance response (SCR) amplitude and occurrence in response to the presentation of emotional stimulus (Liberzon et al., 2000; Williams et al., 2001; Hoffman et al., 2007). These responses include increases in ANS arousal (such as sweating, heart rate, blood pressure) and the release of stress hormones (LeDoux, 1998). The enhanced amygdala activity together with arousal systems excitation are thought to allow the cortex to distinguish fear signals from other arousal responses to novel stimuli (Damasio, 1995; LeDoux, 1996).

Previous studies about idiographic trauma imagery have shown that PTSD patients report more pronounced heart rate acceleration than control subjects and stronger facial expressions of displeasure concordant with more extreme aversive ratings (Pitman et al., 1987; Cuthbert et al., 2003; Pole, 2007). Patients also exhibit a stronger startle reflex response than controls during idiographic threat-related imagery, consistent with enhanced limbic (in particular, amygdalar) and paralimbic activation. Indeed, PTSD patients interpret innocuous stimuli as a potential threat (Lanius et al., 2006; Brunetti et al., 2010). An example of this is the Acoustic Startle Response (ASR), which consists of a sequence of reactions caused by muscular and neural responses to sudden and intense acoustic stimuli. Conversely to healthy controls, a lack of habituation to the ASR has been reported in PTSD patients, thus indicating a difficult evaluation of the sensory stimuli and of the appropriate mobilizing levels of neural and physiological reactivity (Van der Kolk, 2003; Glover et al., 2011). SCRs to subliminal salient emotional stimuli were also delayed in PTSD patients with damage in the left or right amygdala (Gläscher and Adolphs, 2003).

Furthermore, PTSD patients show higher levels of arousal in response to both conditioned (CS+) and unconditioned (US) stimuli (Peri et al., 2000; Orr et al., 2000; Norrholm et al., 2011) in paradigms based on fear-potentiated startle response, that is characterized by the increase in the magnitude of the acoustic startle reflex elicited from a CS previously paired with an US.

In this pilot study, we wanted to assess whether the psychophysiological responses of PTSD patients with mild symptoms during a new variant of conditioning paradigm differ from those observed in the subjects who did not develop symptoms. To this end we measured both the SCR and the facial thermal response, the latter being measured by high-resolution functional thermal infrared (fIR) imaging (Merla and Romani, 2007).

In fact, fIR imaging has proven to be a robust and ecologically valid method to monitor an individual's arousal through the effects that the autonomic activity

exerts on the facial cutaneous temperature (Shastri et al., 2009; Ebisch et al., 2012; Manini et al., 2013). In particular, we focused on the tonic component of the SCR, which is the slowly changing component of the signal and it is related to the arousal level of the subject (Lim et al., 1997), and on the nose tip temperature, which is closely related to the tonic component of the SCR (Shastri et al., 2009).

We expected that mild PTSD patients would have higher tonic average values in the conditioning and maintenance phases than controls. Moreover, we did expect to find reduced differences between conditioning and maintenance phases in patients with respect to controls. The same hypotheses hold for the nose tip temperature.

## EXPERIMENTAL PROCEDURES

### Subjects

Ten PTSD patients and 10 healthy controls (Table 1) were recruited for this study. All the participants were bank clerks, victims of one or more armed bank assaults in the last 10 months before the experiments (range of 2–18 months). All participants underwent to an extensive clinical examination carried out by an expert psychiatrist (GS) and a clinical psychologist (MB).

A broader range of traumatic event types, including car accidents and criminal attacks, was assessed using the event checklist of the Clinician Administered PTSD Scale (CAPS) (Blake et al., 1998). Standardized clinical instruments were used for the assessment of DSM-IV diagnoses by trained researchers: CAPS (Blake et al., 1990; Pieraccini et al., 1999) for the diagnosis and quantification of PTSD and related dissociative features (MB) and Mini International Neuropsychiatric Interviews (MINI) (Sheehan et al., 1994; Conti et al., 1999) for diagnoses of DSM-IV Axis I disorders (GS). At the time of the present study, participants met DSM IV diagnostic criteria for the following current co-morbid diagnoses: dysthymia ( $n = 1$  PTSD subject), agoraphobia without history of panic attack disorder ( $n = 1$  PTSD subject), and social phobia ( $n = 1$  control subject). None of the

**Table 1.** Demographic and clinical characteristics of the two subject groups

Variable	PTSD group ( $n = 10$ )	Control group ( $n = 10$ )
Mean age in years (SD)	39.7 (6.34)	36.8 (12.1)
Mean school educ. in years (SD)	16 (2.5)	14 (2.1)
Females N (%)	6 (60)	6 (60)
Nicotine dependence N (%)	4 (40)	4 (40)
Trauma load [mean number (range)]	5 (1–8)	4 (1–5)
CAPS PTSD symptom score, mean (SD)	30.8 <sup>*</sup> (11.2)	6.2 <sup>*</sup> (6.9)

CAPS = Clinician Administered PTSD Scale.

<sup>\*</sup> Indices represent the results of ANOVA: ( $F(1,18) = 34.9, p \leq 0.01$ ).

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