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The impact of tonic immobility reaction on the prognosis of posttraumatic stress disorder

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ABSTRACT

Tonic immobility is the last defense reaction to entrapment by a predator. In humans, peritraumatic tonic immobility was correlated with PTSD severity and poor response to treatment. This study compared the role of peritraumatic dissociation, panic physical symptoms and tonic immobility as predictors of response to standard pharmacotherapy for PTSD. Thirty-six PTSD patients underwent a naturalistic pharmacological treatment. The Posttraumatic Stress Disorder Checklist – Civilian Version (PCL-C) and the Clinical Global Impressions Severity of Illness item scores (CGI-S) were employed at baseline and endpoint to examine treatment outcome. Peritraumatic reactions were assessed using the Physical Reactions Subscale, the Peritraumatic Dissociative Experiences Questionnaire and four motor questions of the Tonic Immobility Scale. After controlling for confounders, tonic immobility was the best predictor of a poor response to treatment, either considering the PCL-C or the CGI-S scores. Tonic immobility seems to have a greater negative impact on PTSD prognosis than peritraumatic panic or dissociation. Additional translational and clinical research may inform about particular mechanisms underlying tonic immobility and open new avenues for prevention and treatment of PTSD.

1. Introduction

Several pre-, peri- and posttraumatic variables have been implicated in the development of posttraumatic stress symptoms. Recently, there has been a surge in interest and literature devoted to understanding the role of peritraumatic responses in predicting the development of posttraumatic stress disorder (PTSD). The influent meta-analysis by Ozer and collaborators (2003) found peritraumatic dissociation to be the strongest predictor of PTSD or of its symptoms among several variables, such as trauma characteristics, prior exposure and adjustment, or concurrent psychopathology. Some studies have also emphasized the importance of peritraumatic panic attacks in explaining PTSD development (Nixon and Bryant, 2003; Bracha et al., 2004; Lawyer et al., 2006; Marmar et al., 2006). It has been suggested that peritraumatic physical symptoms of panic are likely to be valuable for both PTSD prognosis and diagnosis in a variety of trauma-exposed populations (Bracha et al., 2004).

Tonic immobility, a more recently investigated peritraumatic reaction in humans (Galliano et al., 1993; Heidt et al., 2005) has been studied in animals for over three centuries. It is characterized by involuntary immobility, analgesia and relative unresponsiveness to external stimulation (Gallup, 1974), and considered the last-ditch defense against entrapment by a predator within a sequence of defensive responses, namely freeze, flight, fight and tonic immobility (Marx et al., 2008). The more threatened the animal, the more likely tonic immobility is to occur (Gallup, 1974). In humans, this phenomenon was reported to be induced in the context of life threat and to be accompanied by intense fear and physical immobility (Heidt et al., 2005; Rocha-Rego et al., 2009). It has also been associated with greater posttraumatic symptomatology (Heidt et al., 2005; Bovin et al., 2008). Indeed, peritraumatic tonic immobility was shown to predict both the severity of posttraumatic stress symptoms (Rocha-Rego et al., 2009) and a poorer response to treatment (Fiszman et al., 2008; Lanius et al., 2003) in patients with posttraumatic stress disorder (PTSD).

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PTSD is a chronic and disruptive disorder; it is also difficult to treat, as many patients are unresponsive to the updated pharmacological treatment (Berger et al., 2009). The few studies on predictors of treatment response to pharmacologic agents in PTSD focused on baseline clinical factors, trauma intensity and type of trauma (Davidson et al., 1993, 1997; Katz et al., 1994; Connor et al., 2001; Martenyi et al., 2002; Fiszman et al., 2008).

The present investigation intends to compare the role of three peritraumatic reactions – dissociation, panic physical symptoms and tonic immobility – as predictors of response to standard pharmacological treatment for PTSD.

2. Methods

2.1. Participants

The sample comprised 36 (19 males) victims of armed robbery (n = 28, 77.8%), motor vehicle accident (n = 5, 13.9%), sexual assault (n = 2, 5.6%), and burn (n = 1, 2.8%) who were admitted to an outpatient university clinic specialized in posttraumatic stress assessment and pharmacological treatment. The mean age was 39.6 (SD = 5.1) for male and 41.5 (SD = 9.5) for female. Twenty-seven subjects were married (75%), five were high school dropouts (13.9%), nine were high school graduates (25%), 16 were college graduates (44.4%) and six had university degree (16.7%). At the first interview, those with symptoms suggestive of PTSD were invited to participate in a study of naturalistic follow-up in which standard pharmacological treatment is employed. After a description of the diagnostic and therapeutic procedures to the patients, a written informed consent was obtained. Patients were not informed about the aim of this study. Diagnosis of PTSD was confirmed using the Structured Clinical Interview for DSM-IV Axis I (SCID) (Del-Ben et al., 2001). Cases of psychotic disorders, severe personality disorders, or significant cognitive impairment were excluded.

Patients underwent a naturalistic treatment with antidepressant drugs administered in adequate doses and time according to the recommended guidelines for PTSD (American Psychiatric Association, 2004). They were initially treated with a selective serotonin reuptake inhibitor (SSRI) (fluoxetine, sertraline, paroxetine, or citalopram) or a selective serotonin and norepinephrine reuptake inhibitor (SNRI) (venlafaxine or milnacipram) in the maximum tolerated doses. The choice of a particular drug took into account its availability, patient's current clinical profile, and response to previous therapies. Patients who did not show significant clinical improvement or turned out to be drug intolerant were then shifted to another SSRI or SNRI, a tricyclic antidepressant (nortripline, amitriptiline, or imipramine) or a MAOI (tranilcipromine). The number of therapeutic trials ranged from 1 to 4. The investigation was carried out in accordance with the latest version of the Declaration of Helsinki, and the protocol has been approved by the Ethical Committee Review Board of the Federal University of Rio de Janeiro.

2.2. Measurements of response to treatment

This is a non-concurrent cohort study (Miller et al., 2005). Patients were asked to fill out the Posttraumatic Stress Disorder Checklist – Civilian Version (PCL-C) (Weathers et al., 1994) at baseline and every following visit in order to monitor the course of the posttraumatic stress symptoms. The Clinical Global Impressions Severity of Illness (CGI-S) item scores (Guy, 1976) were employed to assess the patients' overall psychiatric condition at baseline and every visit. The assistant physicians responsible for assessment and treatment were unaware of the objectives of the study. The last available PCL-C and CGI-S scores (endpoint scores) were used as measures of treatment outcome (dependent variables).

2.3. Measurements of peritraumatic reactions

Independent evaluators who were blind to treatment conditions probed peritraumatic panic physical symptoms, dissociation, and tonic immobility. The Physical Reactions Subscale (PRS) (Resnick, 1997) was used to measure peritraumatic panic attack symptoms. The severity ratings of the 10 items included in the PRS are made on a four-point Likert type scale: from 1 (not at all) to 4 (an extreme amount during the incident). The total score ranges from 11 to 44. Peritraumatic dissociation was assessed using the Peritraumatic Dissociative Experiences Questionnaire (PDEQ) (Marmar et al., 1998). Each of the 10 items consists of a statement indicating a dissociative experience and a 5-point Likert type response scale anchored by 1 (not at all true) and 5 (extremely true). The total score ranges from 10 to 50.

Our evaluation of peritraumatic tonic immobility was based on the questionnaire developed for investigating this phenomenon in humans, the Tonic Immobility Scale Child Abuse Form (TIS-C) (Fuse et al., 2007). To avoid item overlap with PDEQ and PRS measures, a four-item measure of motor aspects of tonic immobility were used, referred here as TI-4: rate the degree to which you (...) during or immediately after the event. (1) Froze or felt paralyzed (from 0 = not at all frozen or paralyzed to 6 = completely frozen or paralyzed). (2) Were unable to move even though not restrained (from 0 = could move freely to 6 = could not move at all). (3) Felt unable to call out or scream (from 0 = felt able to scream to 6 = wanted to scream but felt unable). (4) Felt unable to escape (from 0 = felt able to escape to 6 = wanted to escape but remained "fixed"). An unpublished exploratory factor analysis conducted among a subsample (506 victims of violence) of a cross-sectional epidemiological survey carried out in São Paulo, Brazil, (Andreoli et al., 2009) supported this procedure. A three factors solution was extracted, with the above mentioned four "motor" items of the TIS-C forming the first factor, which accounted for 48% of the variance. Internal consistency of the "motor" subscale of the TIS-C was deemed satisfactory (Cronbach's α = .83).

Further Information was also obtained for socio-demographic factors (age, gender, educational level, and marital status), length of treatment, and type of trauma. Baseline scores for depressive and anxiety symptoms were measured using the Beck Depression Inventory (BDI) (Beck et al., 1961) and the Beck Anxiety Inventory (BAI) (Beck et al., 1988).

2.4. Statistical analysis

Three simple linear regression models were fitted separately for peritraumatic tonic immobility (TI-4), panic symptoms (PRS) and dissociation (PDEQ) as predictors of treatment outcome (PCL-C or CGI-S endpoint scores). In order to adjust for confounding variables we used stepwise multiple linear regression models following the proposal by Kleinbaum et al. (1998), including PCL-C or CGI-S baseline scores, gender, age, treatment length, BDI baseline scores, and BAI baseline scores. Finally, the three peritraumatic variables were included in the same model to compare their contribution for predicting treatment outcome (PCL-C or CGI-S endpoint scores). p-Values equal or less than .05 were considered statistically significant while those between .06 and .10 were regarded as borderline. Statistical analysis was conducted using the Stata program, version 9.

3. Results

The prevalence of psychiatric comorbidities were 94.4% for major depression, 52.8% for obsessive compulsive disorder, and 33.3% for panic disorder with agoraphobia. The mean PCL-C (Posttraumatic Stress Disorder Checklist – Civilian Version) and CGI-S (Clin-