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Biological and psychological predictors of posttraumatic stress disorder onset and chronicity. A one-year prospective study

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ABSTRACT

Background: Few studies have prospectively examined risk factors for posttraumatic stress disorder (PTSD) in the aftermath of a traumatic exposure. The aim of this study is to identify the concurrent influence of psychological and biological diatheses on PTSD onset and maintenance, taking into account socio-demographic factors and psychiatric antecedents.

Methods: A total of 123 civilians (61.8% of women) recruited in emergency units, were assessed using validated instruments during the first week and then at 1, 4, and 12 months post-trauma. Baseline assessment included evaluation of the psychological diathesis (i.e. psychiatric history and peritraumatic distress and dissociation), and the biological diathesis [i.e. cortisol, norepinephrine, epinephrine, c-reactive protein, total cholesterol, HDL cholesterol, glycosylated haemoglobin, waist-to-hip ratio (WHR), body mass index, diastolic and systolic blood pressure (SBP), and heart rate].

Results: Multivariate logistic regression analyses demonstrated both psychological and biological diatheses to be independent risk factors for PTSD. Peritraumatic distress and dissociation predicted onset (1-month) and mid-term PTSD (4-months), respectively. PTSD risk was associated positively with SBP and negatively with WHR, throughout the follow-up. In addition, a higher level of 12 h-overnight urinary norepinephrine independently predicted mid-term PTSD (4-months).

Conclusions: This prospective study shows that peritraumatic psychological and biological markers are independent predictors of PTSD onset with specificities according to the stage of PTSD development; the psychological diathesis, i.e. peritraumatic distress and dissociation, being a better predictor of short-term dysfunction whereas biological diathesis was also predictive of development and maintenance of PTSD.

1. Introduction

Posttraumatic stress disorder (PTSD) occurs in people who have experienced, witnessed, or been confronted with an event involving actual or threatened danger. This event is followed by specific symptoms which have been recently reclassified in four diagnostic clusters in the DSM-5: re-experiencing, avoidance, negative cognitions and mood, and arousal symptoms (American Psychiatric Association, 2013). The majority of people exposed to trauma however do not develop PTSD, most victims maintaining, or rapidly returning to a normal functioning. The stressor initiates traumatic memories, and the onset of PTSD symptoms actually

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depends on the ability of the individual to modify the associated hyperarousal and neurobiological cascade (McFarlane, 2000). This transition phase is likely to be the period when risk and protective factors are of greatest significance (McFarlane, 2000) and consequently an important window for intervention strategies, thus stressing the importance of developing risk models at this stage.

PTSD is a heterogeneous disorder with variable expressions of clinical distress immediately after exposure to a traumatic event and thus variable clinical presentations. Two principal clinical subtypes of PTSD have been described, primarily characterized either by the expression of hyperarousal symptoms or by symptoms of dissociation, numbness and physiological unresponsiveness (Lanius et al., 2010a; Weston, 2014). These two sets of symptoms are associated with different aspects of emotion dysregulation and distinct patterns of physiological and brain activation upon exposure to reminders of traumatic events (Lanius et al., 2010b). The etiological factors of PTSD thus encompass both psychological and biological aspects of the individual.

Of the theoretical diathesis-stress models proposed to identify vulnerability factors or predictors of PTSD development, the most recent models proposes that pre-trauma individual risk factors (diatheses) contribute to a constitutional vulnerability to a situational stressor (trauma) (Bomyea et al., 2012; Elwood et al., 2009; McKeever and Hiff, 2003). This stressor must be sufficiently severe to activate the diathesis and promote the development of PTSD. It is hypothesized that the less favorable the individual's diathesis, the less severe will be the trauma susceptible to initiate PTSD. According to Elwood et al. (2009) a comprehensive diathesis-stress model of PTSD should take into account not only pre-, but also peri- and post-trauma factors, as well as different types of vulnerability (e.g. biological, psychological and cognitive) (Elwood et al., 2009).

Predictors of psychological vulnerability were classified based on the weighted effect sizes and temporal proximity with the traumatic event. Peritraumatic distress (high level of emotion) and peritraumatic dissociation (dissociative experiences) during or in the immediate aftermath of the traumatic event are the most proximal to the traumatic event. They were recognized as the most robust predictors of PTSD symptoms (see for meta-analyses (Brewin et al., 2000; Ozer et al., 2003)), more than other pre-trauma factors (e.g. prior history of trauma, education, sex and age) and a lynchpin in the development of PTSD symptoms (Bremner et al., 1992; Marmar et al., 2006).

Regarding biological vulnerability, increased sympathetic nervous system (SNS) and decreased hypothalamic-pituitary-adrenal (HPA) functioning, within one month after trauma, have been reported to contribute to PTSD onset and maintenance through the formation of over-consolidated memories (Pitman, 1989). However none of these factors has individually demonstrated the ability to be a marker of PTSD development (Morris and Rao, 2013; Ostrowski and Delahanty, 2014; Pitman et al., 2012). Another approach considered the cost to the individual of adapting to cumulative stress across a range of physiological systems (McEwen and Stellar, 1993). This cost or allostatic load (AL) refers to the cumulative physiological wear and tear that results from repeated efforts of the organism to adapt to stressors over time (McEwen and Stellar, 1993). AL is evaluated by assessing biomarkers of multiple systems including primary mediators of stress systems (e.g. cortisol, epinephrine and norepinephrine) as well as biomarkers known to exhibit change in response to interaction with a primary mediator of stress (e.g. C-reactive protein (CRP)) or to represent secondary outcomes of these mediating processes, namely systolic and diastolic blood pressure (SBP and DBP, respectively), glycosylated haemoglobin (HbA1c) and visceral fat depositing. Although high AL was hypothesized to be a major contributor to the development of PTSD (Charney, 2004; McEwen, 2002), this has not been demonstrated. The validity of this concept is also questioned notably in the field of stress related disorders in which insufficient glucocorticoid signaling may play a significant role in the etiology (Fries et al., 2005; Heim et al., 2000; Raison and Miller, 2003).

Actually, it is becoming evident that simple biological models could not account for the complex etiology of PTSD which should consider together psychological and biological aspects and their relative weight in the onset and maintenance of PTSD overtime. However, to our knowledge, no study on PTSD etiology has studied both aspects concurrently. Our prospective study aimed to examine the effect of both psychological (psychiatric history and peritraumatic reaction) and a large range of potential markers of biological diatheses on PTSD onset (after 1-month) and maintenance (4- and 12-months), in people who have recently experienced a traumatic event of the civilian life, while taking into account sociodemographic pre-trauma factors.

2. Methods

2.1. Study population

People having experienced an event satisfying criterion A1 and A2 for trauma exposure (DSM-IV) (American Psychiatric Association, 1994) within the previous 7 days, were consecutively recruited in the emergency and forensic medicine departments of the Montpellier University Hospital (France) between 2006 and 2011 (the Phoenix study). The exclusion criteria were: 1) having experienced significant head injury defined as an external injury to the brain leading to a loss of consciousness for 10 min or more, 2) previously suffering from a psychotic illness or mental retardation, 3) being homeless, 4) use of corticosteroid medications which could interfere with cortisol measurement. A fifth exclusion criterion concerned domestic violence which is mostly woman specific, frequently chronic and associated with high prevalence of current PTSD which may introduce a methodological bias regarding causality. The study protocol was approved by the South-Mediterranean Ethics Committee and written informed consent was obtained from each participant.

Participants were administered standardized questionnaires by a single Master level research nurse at baseline and after 1, 4 and 12 month of follow-up. The first interview was within 2–7 days after trauma exposure [median (IQR) = 5 (4–6) days]. Venous blood samples were collected during the interview and 12 h-overnight urine during the subsequent night. Of the 123 individuals recruited, 89 completed the 1-month follow-up [median (IQR) = 39 (30–49) days], 85 the 4-month follow-up [median (IQR) = 136 (123–152) days], and 57 the 12-month follow-up [median (IQR) = 387 (361–413) days]. The subjects lost to follow-up more frequently reported lifetime psychiatric disorder ($p < 0.05$). Those lost specifically to the last follow-up after 12 months were also younger ($p = 0.04$) and with a higher peri-traumatic distress score ($p = 0.01$). No other significant differences were found between the participants included in analyses and those lost to follow-up.

2.2. Interview

2.2.1. Inclusion examination

The standardized interview included questionnaires on sociodemographic characteristics as well as clinical and biological evaluation and information relating to prescription drug and psychotherapy use over the last two years. Peritraumatic reaction and psychiatric history were also investigated as part of this baseline psychiatric evaluation. Peritraumatic distress was assessed using the validated French version of the Peritraumatic Distress Inventory