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Temporal analysis of heart rate variability as a predictor of post traumatic stress disorder in road traffic accidents survivors

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ABSTRACT

Background: Road Traffic Accidents (RTA) are most probably the leading cause of post traumatic stress disorder (PTSD) in developed countries. The autonomic nervous system (ANS) disturbances, due to psychological trauma, are part of the pathophysiology of PTSD. The aim of the present study was to determine whether early heart rate variability (HRV) measurement, a biomarker of the ANS function, could act as a predictor of PTSD development after a RTA.

Methods: We prospectively investigated 35 survivors of RTA with both physical injury and psychological trauma. HRV data were obtained from 24-h Holter ECG monitoring, which was performed on the second day after the accident. Time domain analysis was applied to the inter-beat (RR) interval time series to calculate the various parameters of HRV. PTSD status was assessed 2 and 6 months after RTA.

Results: There was a global diminution of HRV measurements in the PTSD group at both 2 and 6 months. The variability index was the best predictor of PTSD with the area under the receiveroperating curve for discriminating PTSD at 6 months at 0.92 (95% CI: 0.785; 1.046). A cut-off at 2.19% yielded a sensitivity of 85.7% and a specificity of 81.8% for PTSD. Positive and negative predictive values were respectively 75% and 90%. However, initial heart rate (HR) data were relevant at 2 months but not at 6 months.

Conclusion: RTA survivors exhibiting lower parasympathetic modulation of HR, indexed by temporal analysis of HRV, are more susceptible to developing PTSD as a short and long-term outcome.

1. Introduction

The psychological trauma related to Road Traffic Accidents (RTA) is the cause of many acute and chronic psychopathological disorders, some of which can generate a serious disability. Post traumatic stress disorder (PTSD) is one of the most common sequelae of RTA in developed countries. Its prevalence in these countries in the months following RTA is estimated between 20% and 45% among drivers and passengers (Blanchard and Hickling, 2004). PTSD could have serious, far-reaching consequences for victims as well as for society as a whole, resulting in suicidal attempts in 27% of the cases (Blanchard and Hickling, 2004; Vaiva G et al., 2011). Accordingly, identifying victims who are at risk of developing PTSD in the aftermath of trauma would appear to be mandatory for early prevention and management, in order to reduce the frequency and intensity of PTSD. Among the multiple studies that targeted the fate of psycho-traumatised subjects, only a few clinical and biological factors of vulnerability such as psychiatric scales, cortisol and GABA blood level have been proposed, which have also limited predictive ability and require time-consuming measures (Bryant, 2003; Delahanty et al., 2003; Vaiva et al., 2004).

The association between elevated basal heart rate (HR), the most prominent autonomic feature, and PTSD, has been well

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documented (Buckley and Kaloupek, 2001). However, studies investigating initial HR (measured within one week of traumatic injury) as a predictor of subsequent PTSD raise a controversy (Bryant, 2006). While many current studies reported that initially elevated HR following trauma was associated with later PTSD (Bryant et al., 2008; Zatzick et al., 2005; Kassam et al., 2005), other studies did not find such a link (Buckley et al., 2004; Kuhn et al., 2006). Furthermore, a negative correlation between initial HR and chronic PTSD was reported (Blanchard et al., 2002), but this study had some methodological limitations (retrospective, unrepresentative sample). It is worth noting that whereas many large studies tended to confirm the association between elevated HR and later PTSD, there was much variability in the HR levels and subsequent PTSD. In addition, a current study with a large sample size concluded that the initial HR was a weak and non independent predictor of PTSD. However, the prevalence of PTSD was low (Kraemer et al., 2008). Recently, a study with a large sample reported that only HR measured at the scene of RTA and not HR measured at hospital admission predicted later PTSD (Coronas et al., 2011).

Further studies have examined the relationship between PTSD and HR using indices of heart rate variability (HRV), a biomarker of the autonomic nervous system (ANS) function. The fluctuations between consecutive normal inter-beat (RR) intervals provide a "dynamic map" of the interaction between both branches of ANS (parasympathetic and sympathetic). HRV measurement may be a more revealing physiological assessment of PTSD than HR activation. While measures of elevated HR habitually assess sympathetic arousal, HRV measures the relative influence and interaction of both branches of ANS on HR responsiveness. Furthermore, standardized investigations of HRV represent an economical, non-invasive procedure allowing not only a qualitative, but also a good semi-quantitative estimation of the ANS function (Task Force, 1996). Besides, it is probable that decreased HRV indicating autonomic dysfunction explains the negative cardiovascular outcome in PTSD (Kubzansky et al., 2007).

It was previously reported that autonomic dysfunction due to increased sympathetic and/or reduced vagal activity demonstrated by low HRV, was involved in a variety of psychiatric and physiological disorders, including depression (Kemp et al., 2010), anxiety (Miu et al., 2009), and insomnia (Bonnet and Arand, 1998), all of which are known to be highly comorbid with PTSD. As regards PTSD, many studies reported its association with low HRV by using symptom provocation cue protocols. These studies indicated that lower basal and elicited respiratory sinus arrhythmia (RSA), a measure of parasympathetic cardiac modulation, were frequently associated with PTSD diagnosis and severity. Certain studies found that participants with PTSD had lower baseline RSA amplitude compared to normal control subjects (Cohen et al., 1997; Blechert et al., 2007). However, other studies showed that RSA amplitude was only lower in the PTSD group during the trauma cue and not at baseline (Sahar et al., 2001; Keary et al., 2009). These disparate findings concerning RSA at baseline might be explained by two studies that examined HRV and PTSD severity. When HRV assessment studies ranked participants with PTSD according to their HRV amplitude, they found that only those with the lowest indices had an elevated HR (Hopper et al., 2006) and a more pronounced HR arousal (Sack et al., 2004). These results suggested that more severe autonomic dysregulation might influence elevated HR as well as later PTSD.

Moreover, an increase in HRV has been associated with a decrease in PTSD symptoms in a few pilot intervention studies. Recent studies provided preliminary support for the efficacy of RSA biofeedback (pacing breath rhythms at approximately six breaths-per-minute) in facilitating the increase in HRV amplitude and improving the physiological and psychological health of individuals with PTSD (Zucker et al., 2009).

The present study hypothesized that: 1) RTA survivors with lower parasympathetic mediated HRV parameters would have a higher risk of PTSD compared to those with higher HRV; 2) PTSD severity would be related to the magnitude of a decrease in parasympathetic mediated HRV indices. To test these hypotheses, we measured temporal parameters of HRV soon after trauma exposure in a subset of RTA survivors of a prospective pilot study, whose aim was to assess low post-trauma GABA plasma levels as a predictive factor in the development of acute PTSD (Vaiva et al., 2004). We followed up the patients to define the short and long-term (2, 6 months) psychopathological outcome.

2. Materials and methods

2.1. Participants

Men and women aged 18 years and over who had life-threatening traffic accidents with physical injuries and who required hospitalization up to 72 h, were recruited from the Traumatology Department of Lille University Hospital and Douai Hospital. We excluded patients with head trauma with initial loss of consciousness for more than 15 min (based on reports of paramedics and witnesses), patients with organic brain disease or dementia, patients receiving long-term treatment with benzodiazepines or anticonvulsants, patients with a history of alcohol abuse or addiction and victims who were drunk at the time of the accident. Specific exclusion criteria for the validity of HRV measurements included the following: treatment with medication affecting the central or peripheral ANS (i.e., psychiatric medication [hypnotics and anxiolytics], antihypertensive drugs [including β-blockers and calcium channel blockers]) which was a restrictive criterion, illnesses known to be associated with a reduction in HRV (e.g., cardiac diseases, apoplexy, diabetic or alcoholic autonomic neuropathy) and difficulty with installation of a Holter device on the anterior chest wall. The study received the approval of the regional ethics committee (CPP 02/30). Written informed consent was obtained from all participants in the study.

2.2. Instruments

General characteristics of the subjects, the whole circumstances of the accident and the Injury Severity Score calculation (ISS) were assessed (Smith, 1990). The Peritraumatic Distress Inventory (PDI) was evaluated to determine whether the subject fulfilled the inclusion criteria of A1 and A2 of the DSM-IV for PTSD (Brunet et al., 2001). The Mini International Neuropsychiatric Interview items (M.I.N.I) for Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) were used to assess the current and past psychopathological state of each patient (Lecrubier et al., 1997). A validated modified version of the Clinician-Administered PTSD Scale (CAPS) completed by telephone was used (Blake et al., 1995; Aziz and Kenford, 2004). The CAPS is widely considered to be the "gold standard" in PTSD assessment. It is a 30-item scale that examines the frequency and severity of PTSD symptoms as defined by DSM-IV. In addition to these items, there were other tests to assess social and occupational functioning, global PTSD symptom severity, and response validity. This evaluation was performed at 2 and 6 months following the accident.

2.3. Analysis of heart rate variability

Twenty-four hour Holter ECG monitoring using a two channels ELA Medical record was undertaken at the patient's bedside on day