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Medically unexplained symptoms and between-group differences in 24-h ambulatory recording of stress physiology

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Abstract

People with medically unexplained symptoms (MUS) often have a comorbid history of stress and negative affect. Although the verbal-cognitive and (peripheral) physiological stress systems have shown a great degree of independence, at the same time it is claimed that chronic stress and negative affect can result in a disregulated physiological stress system, which may lead to MUS. Previous studies could not demonstrate a straightforward between subject relationship between MUS and stress physiology, supporting the view of independence. The aim of the current study was to further explore this relationship using an improved methodology based on ecologically valid 24-h real-life ambulatory recordings. Seventy-four participants (19 male; 55 female) with heterogeneous MUS were compared with 71 healthy controls (26 male; 45 females). Momentary experienced somatic complaints and mood, heart rate, cardiac autonomic activity, respiration and saliva cortisol were monitored using electronic diary and ambulatory registration devices. Participants with MUS reported much more momentary complaints and negative affect as compared to controls. Although MUS seemed to be associated with elevated heart rate and reduced low and very-low frequency heart period variability, these effects disappeared after controlling for differences in sports behaviour. No group differences were found for cardiac autonomic activity, respiration, end-tidal CO_2 and saliva cortisol. Our 24-h real-life ambulatory study did not support the existence of a connection between MUS and disregulated peripheral stress physiology. Future studies may instead focus on central measures to reveal potential abnormalities such as deviant central processing of visceral signals in MUS patients.

Keywords: Medically unexplained symptoms; Cortisol; Heart rate; PEP; Respiration; RSA

1. Introduction

When somatic symptoms cannot (or not conclusively) be explained by an organic disease, they are considered to be epiphenomena of underlying psychological problems (like anxiety, chronic stress or depression) and are labelled as 'psychosomatic', 'functional somatic' or 'medically unexplained' symptoms (Barsky and Borus, 1999; Costa and McCrae, 1985; Da Costa, 1871; Watson and Pennebaker, 1989; Wessely et al., 1999). Medically unexplained symptoms have a high prevalence and are a burdening problem in primary and secondary health care. These symptoms are more common among women, younger age groups and people from lower social economic background (Nimnuan et al., 2001a). Several distinct syndromes have been identified such as fibromyalgia, chronic fatigue syndrome, irritable bowel syndrome, multiple chemical sensitivity, noncardiac chest pain and hyperventilation syndrome. However, these syndromes show a considerable overlap and their specificity has been questioned (Barsky and Borus, 1999; Nimnuan et al., 2001b; Wessely et al., 1999).

Medically unexplained symptoms have been associated with stress and negative affect within subjects (changes over time) and between subjects (group differences). Experimental manipulations aimed at inducing somatic complaints (e.g., by inhalation of CO_2-enriched air) in participants high on medically unexplained symptoms showed increased self-reports of distress, state anxiety and negative mood, and experimental manipulations aimed at inducing mental distress showed increased self-reports of somatic complaints (Houtveen et al., 2003; Wientjes and Grossman, 1994). Group differences in medically unexplained symptoms are also closely tied to group differences in current and past reports of anxiety, trauma, neuroticism, negative affect and

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depression (Barsky and Borus, 1999; Houtveen et al., 2003; Pennebaker, 2000; Van Diest et al., 2005; Watson and Pennebaker, 1989; Wessely et al., 1999; Wientjes and Grossman, 1994). The within and between subject relationship between unexplained bodily symptoms and (stress-related) negative affect has been taken as a starting point for the current psychophysiological study.

A negative emotional state may become manifest in the verbal-cognitive system (self-reported measures), the behaviour-motor system (behavioural measures) and in the (peripheral) physiological stress system (stress-physiological measures). The within subject relationship between negative affective states and peripheral stress physiology has been studied extensively. Within-subject changes in self-reported negative emotional state as a result of mental stress clearly coincide with changes in activation of the cardiac sympathetic and parasympathetic divisions of the autonomic nervous system. Mental stress generally leads to increased heart rate, reduced pre-ejection period (PEP) and reduced heart rate variability in the respiratory frequency range (i.e., respiratory sinus arrhythmia; RSA), reflecting increased sympathetic (beta-adrenergic) and decreased parasympathetic (vagal) influences on the heart respectively (Allen and Crowell, 1989; Berntson et al., 1993,1994; Kamphuis and Frowein, 1985; Langewitz and Ruddel, 1989; Sherwood et al., 1986). For most individuals, mental stress also leads to respiratory changes (Boiten et al., 1994; Grossman, 1983) which could result in reduced partial pressure of CO_2 (Han et al., 2000; Ley and Yelich, 1998; Suess et al., 1980). Finally, short-term stress, specifically the stress associated with social evaluation and uncontrollability, gives rise to cortisol elevation (Dickerson et al., 2004).

The between subject association between individual differences in self-reported negative affect (i.e., negative affective traits) and peripheral stress physiology is less clear. A related issue, and of importance for the current study, is whether subjects suffering from medically unexplained symptoms have a disregulated peripheral stress physiology. Frequent and/or intense stressors have been claimed to result in a disregulation of one or more of the physiological stress systems (De Kloet et al., 2005; McEwen, 1998,2003). This is in line with some traditional psychophysiological models of medically unexplained symptoms in which unexplained complaints are suggested to be *reactions* to disregulated (i.e., exaggerated) peripheral manifestations of stress and anxiety (Sharpe and Bass, 1992). This concerns, for example, the role of muscle tension in low back pain, respiration and CO_2 in the hyperventilation syndrome, and disruptions of the autonomic balance or the stress hormone cortisol in chronic fatigue syndrome. It has, however, frequently been observed that the verbal-cognitive and the physiological stress systems show a great degree of independence (Lang, 1994; Wilhelm and Roth, 2001). The discordance between self-reported and stress-physiological measures may be especially true when comparing subjects. Previous between subject (group-comparing) studies on the relationship between medically unexplained symptoms and stress-physiological measures have shown mixed results. Although in some of these studies autonomic, respiratory or HPA-axes irregularities have been reported in relation to medically unexplained syndromes and anxiety disorders (Bystritsky et al., 2000; Coryell et al., 2001; Heim et al., 2000; Hoehn-Saric et al., 1991; Thayer and Brosschot, 2005; Wilhelm et al., 2001), many null-findings have also been reported (Hornsveld et al., 1996; Houtveen et al., 2003; Kirschbaum et al., 1992; Mommersteeg et al., 2006a,b; Troosters et al., 1999; Wientjes and Grossman, 1994). Thus, although efforts to demonstrate a between subject correspondence between self-reported medically unexplained symptoms, stress, anxiety on the one hand and peripheral stress physiology on the other have not yet been very successful in the past, this issue remains of importance for validation or falsification of the traditional psychophysiological models that claim a role for disregulated stress physiology to explain medically unexplained symptoms.

The aim of the current study was to further explore the between subject relationship between medically unexplained symptoms and peripheral stress physiology using an improved methodology. Physiological measures are traditionally taken in a laboratory situation under artificial baseline conditions or in response to artificial stressors. However, this way of testing has a low ecological validity. For example, generalisation of individual differences in cardiovascular stress reactivity from laboratory situations to real-life situations has been shown to be moderate at best (Gerin et al., 1994; Kamarck et al., 2003; van Doornen et al., 1994). Moreover, circadian variation has been demonstrated in baseline and reactivity values of cardiac autonomic levels (van Eekelen et al., 2004a,b), respiration (Mortola, 2004) and HPA axis activity (Buijs, 1999; Van Eekelen et al., 2003), and physiological group differences may be specifically manifest in specific windows of the diurnal cycle. For these reasons (ecological validity of the test situation and the possibility of circadian variation of group differences), between subject differences in physiological stress profiles preferably should be assessed in a real-life situation by using ambulatory measurement devices and last a full circadian timeframe. As an example of the utility of this approach, Vrijkotte et al. (2000) found that men reporting high work stress (classified with Siegrist's model as an imbalance between high effort and low reward at the workplace) had increased heart rates, lower heart period variability and increased sleep-leisure-work differences as compared to men low in stress (Vrijkotte et al., 2004). These results show how ambulatory recordings can reveal stress-physiological differences related to between subject differences in self-reported mental stress.

In the current 24-h ambulatory study, self-reported measures and stress-physiological measures were assessed simultaneously. The aim of the current study was to relate group differences in medically unexplained symptoms to group differences in (the set-points of) stress physiology. Momentary experienced somatic complaints and mood were assessed with electronic diaries to demonstrate the presence of symptoms and negative emotional states during the measurement day. The use of a more reliable assessment of complaints by way of a diary excludes the possibility that an absence of the expected relationship is due to the role of retrospective bias when using