Psychoneuroendocrinology 74 (2016) 342–349

Contents lists available at ScienceDirect

Psychoneuroendocrinology

journal homepage: www.elsevier.com/locate/psyneuen

Associations among integrated psychoneuroimmunological factors and metabolic syndrome

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ARTICLE INFO

Article history:
Received 10 May 2016
Received in revised form
29 September 2016
Accepted 30 September 2016

Keywords:
Metabolic syndrome
Psychological distress
Perceived stress
Depression
Autonomic nervous function
Psychoneuroimmunology

ABSTRACT

Background: Metabolic syndrome (MetS) has been reported to cause considerable psychoneuroimmunology (PNI) disturbances such as, psychological distress, autonomic nervous imbalance, and impaired immune function. Associations among these psychoneuroimmunology (PNI) factors and their integrated effects with MetS and risk components of MetS necessitate further exploration.
Objective: This study investigated associations among psychoneuroimmunological factors, their integrated effects with MetS and risk components of MetS.
Methods: This was a cross-sectional study. Participants were recruited from two health management centers at a medical center in Northern Taiwan. Demographics and data on psychological distress (e.g., perceived stress and depression) were collected using self-reported questionnaires. Heart rate variability (HRV) and C-reactive protein values (CRP) were measured to evaluate participants' autonomic nervous function and immune reaction. The risk components of MetS (e.g., elevated blood pressure, impaired fasting glucose, dyslipidemia, and abdominal obesity) were identified according to the Taiwan-specific definition of MetS and were determined based on participants' health examination profiles.
Results: A total of 345 participants with complete data were included for data analysis. Compared with healthy controls, participants with MetS exhibited higher depression scores (11.2 ± 8.5 vs. 8.7 ± 7.0), higher CRP values (2.1 ± 2.5 vs. 0.7 ± 1.0), and lower HRV (total power: 758.7 ± 774.9 vs. 1064.4 ± 1075.0). However, perceived stress in participants with MetS did not significantly differ from that of their healthy counterparts ($p > 0.05$). Univariate analyses indicated that associations among psychoneuroimmunological factors and MetS risk components were statistically heterogeneous: a) perceived stress and depression were significantly associated only with high blood glucose ($p < 0.05$); b) CRP was significantly associated with all MetS risk components ($p < 0.05$); and c) HRV was significantly associated with high triglycerides and high fasting blood glucose ($p < 0.05$). Multivariate analysis indicated that the integrated effects of depression, CRP, and HRV were significantly associated with MetS ($p < 0.01$) after controlling for age and education level.
Conclusions: Higher depression scores, higher CRP values, and lower HRV are independently and additively associated with MetS and risk components of MetS. Accordingly, a multidisciplinary approach to alleviating psychological distress, immune dysfunction, and autonomic nervous imbalance is recommended for promoting well-being in people with subclinical metabolic abnormalities or MetS to minimize downstream health consequences.

1. Introduction

Metabolic syndrome (MetS) is regarded as a pre-disease related to an unhealthy lifestyle. MetS contains a cluster of risk components

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http://dx.doi.org/10.1016/j.psyneuen.2016.09.027
0306-4530/

(e.g., abdominal obesity, dyslipidemia, elevated blood pressure, impaired fasting glucose, and insulin resistance) that are linked to diabetes and cardiovascular diseases (CVDs) (Alberti et al., 2006; Wilson et al., 2005). Due to an increase in sedentary lifestyles and unhealthy dietary habits, the global prevalence of MetS has also been increasing in recent years (Beltran-Sanchez et al., 2013; Hwang et al., 2012). Prior research has indicated that people possessing four to five of the MetS risk components exhibited a 24.5-fold higher risk of developing chronic CVDs and a 2.5-fold higher risk of dying compared with those without MetS risk components (McNeill et al., 2005). According to a 2014 analysis of multiple cause-of-death data reported by the Taiwanese government, chronic diseases related to MetS (hypertension, diabetes, cerebrovascular disease, and heart disease) were among the top ten leading causes of death, and had mortality rates near to that of malignant cancer (Ministry of Health and Welfare, Taiwan., 2014).

Early identification and intervention are regarded as crucial prevention methods against the development of MetS and its progression to chronic diseases. Therefore, many studies have focused on the investigation of predictive risk factors, prevalence of MetS, and adverse prognostic effects in MetS including relationships between MetS and psychological factors, neuroendocrine functioning, and immunological responses. To date, research findings strongly suggest that the development of CVD through MetS is correlated with psychological distress (Roohafza et al., 2014), autonomic dysfunction (Licht et al., 2013), and immunologically mediated inflammation (Esser et al., 2014). Psychological distress is considered to be a critical risk factor for MetS, and a proposed bidirectional relationship exists between them (Roohafza et al., 2014). Stressful events and psychological distress appear to be correlated with visceral fat levels that may lead to metabolic abnormalities (Magnavita, 2015). In addition, self-perceived depression has been associated with MetS and its risk components irrespective of gender differences (Miettola et al., 2008; Raikkonen et al., 2007; Viinamaki et al., 2009). Furthermore, psychological distress is thought to be associated with several biological alternations in MetS, possibly causing autonomic nervous dysfunction, dysregulation of the hypothalamic–pituitary–adrenal axis (HPA axis) in the endocrine system, altered inflammatory reflex, and blunted serotonin function (Raikkonen et al., 2007).

Autonomic nervous dysfunction is regarded as a lack of dynamic flexibility innate to health and has been used to predict morbidity and mortality caused by CVDs and diabetes in people with MetS (Jarczok et al., 2013). Heart rate variability (HRV) is commonly used to assess autonomic nervous imbalance because indices from time and frequency domain analyses of HRV reflect modulation of sympathetic and parasympathetic activities of the nervous system (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996). A prospective study investigating autonomic nervous dysfunction to predict the 2-year development of MetS revealed that overexcitation of sympathetic nervous function and suppression of parasympathetic nervous function can reduce HRV, increase insulin resistance and hypertension, and induce abnormal lipid metabolism (Licht et al., 2013). Autonomic nervous dysfunction has been identified as a crucial factor in health monitoring for patients with MetS (Soares-Miranda et al., 2012; Stuckey et al., 2014). Furthermore, regular monitoring of HRV has been suggested as a means for early prediction of diabetes, thereby providing an opportunity for prompt intervention to modify risk factors and prevent diabetes-related complications (Meyer et al., 2016). Nevertheless, HRV has not been commonly used for managing MetS and its clinical utility is worth further exploration.

Research has found that people with MetS commonly exhibit chronic, low-grade inflammation (Yang et al., 2013). C-reactive protein (CRP) plays a crucial role in the inflammatory reaction in MetS. CRP levels are correlated with dyslipidemia, obesity, hypertension, insulin resistance, fasting hyperglycemia, endothelial dysfunction, and an increase in the number of risk components in MetS (Firdous, 2014; Yang et al., 2013). Moreover, an 8-year follow-up study indicated that CRP levels were an accurate independent predictor of the occurrence of future CVD events related to MetS (Ridker et al., 2003).

Psychoneuroimmunology (PNI) is a field of study related to associations among psychological factors and the neuroendocrine and immune systems. Cumulative findings regarding psychological distress, autonomic nervous dysfunction, and inflammation in MetS lend support to the idea that PNI can serve as a framework for preventing and treating MetS—confirming a link between the mind and the body (Ziemssen and Kern, 2007). Acute psychosocial stress may affect the body's highly-integrated allostatic systems, compromising the neurobiological network of the nervous, endocrine, and immune systems. The neurobiological network detects stress and initiates a cascade of reactions that activate the sympathetic nervous system, triggering inflammation, stimulating the HPA axis, and finally equilibrating with the parasympathetic nervous system to terminate the physiological arousal, thereby promoting short-term adaptation (Danese and McEwen, 2012). This adaptive response to stress or danger emerges from the psychological factors that modulate the reciprocal connection between the neuroendocrine and immune systems (Ziemssen and Kern, 2007). However, persistent activation of the allostatic systems that occurs with chronic stress can result in detrimental consequences (Danese and McEwen, 2012). Specifically, chronic stress may cause allostatic overload resulting in: (a) increasing dendritic growth in the amygdala, which enhances responses to unlearned and conditioned fear (McEwen and Gianaros, 2011), (b) remodeling of the hippocampus with plastic volumetric reduction, which leads to deficits in declarative, contextual, and spatial memory (McEwen and Gianaros, 2011); (c) enhancing the ability of the corticotropin-releasing hormone to withstand HPA axis activation and elevated inflammation levels (McEwen, 2007; Miller et al., 2007), and (d) ongoing elevation of inflammation levels resulting from repeated stimulation of the sympathetic nervous system, progressive downregulation of the anti-inflammatory pathways, the HPA axis (Tracey, 2002), and the parasympathetic nervous system (Thayer et al., 2010). Additionally, anatomical and physiological links indicate that the autonomic nervous system (ANS) consists of sympathetic and parasympathetic nerves that directly (through neural influences) and indirectly (through neuroendocrine humoral outflow) modulate lymphoid organs and regulate the immune system (Steinman, 2004). In other words, acute emotional or psychological distress may stimulate the immune response temporarily, but repeated or chronic distress may invert or imbalance the immune response, resulting in a slower recovery and an increased susceptibility to a variety of immune-related disorders (Dhabhar, 2013).

Despite numerous studies that have examined MetS, investigations focusing on the PNI framework for preventing and managing MetS are lacking. Thus, the goal of this study was to use subjective self-reports and objective physiological measures to examine relationships and interactions among psychological distress, autonomic nervous dysfunction, and inflammation in MetS.

2. Material and methods

2.1. Study population and data collection

This is a cross-sectional study using a convenience sample. With the approval of the Institutional Review Board of the Tri-Service General Hospital in Northern Taiwan, participants were recruited from the hospital's two affiliated health management centers.