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Psychoneuroendocrinology

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



Decreased use of active coping styles contributes to elevated allostatic load index in first-episode psychosis



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ARTICLE INFO

Keywords: Schizophrenia Allostasis Stress Coping

ABSTRACT

Accumulating evidence indicates that stress plays an important role in the development of psychotic disorders. Recent studies have revealed that patients with first-episode psychosis (FEP) present systemic biological dysregulations related to stress-exposure in terms of elevated allostatic load (AL) index. However, the mechanisms underlying this observation remain unknown. Therefore, in this study we aimed to investigate the AL index with respect to stress coping strategies in 36 FEP patients and 31 matched controls. We found significantly higher AL index in FEP patients compared to controls after co-varying for potential confounding factors. Patients with FEP were less likely to use active and task-focused coping. Lower odds of using these coping styles, planning as well as positive reinterpretation and growth were related to higher AL index in FEP patients, but not in controls. Depressive symptoms were associated with lower likelihood of using task-focused coping as well as positive reinterpretation and growth. Additionally, depressive symptoms were related to higher AL index. Finally, depressive symptoms mediated the effects of task-focused coping as well as positive reinterpretation and growth on the AL index. Our results confirm systemic biological dysregulation indexed as AL in FEP patients. Lower odds of using active coping styles might contribute to higher AL index via the mediating effect of depressive symptoms in patients with FEP. Longitudinal studies are required to establish causal inferences between coping styles, depressive symptoms and the AL index in early psychosis.

1. Introduction

Stressful life events play an important role in the development, course and outcome of psychotic disorders. It has been shown that a history of childhood and adult life adversities accounts for about threefold increase of psychosis risk (Beards et al., 2013; Varese et al., 2012). A history of childhood trauma has been also related to early non-response to antipsychotic treatment, more severe psychotic symptoms and poor long-term outcomes in this group of patients (Misiak et al., 2017a,b, 2016; Misiak and Frydecka, 2016; Mondelli et al., 2015). Finally, exposure to stressful life events might predict the likelihood of psychotic relapse (Nuechterlein et al., 1994).

Psychosocial stress might play an important role in the pathophysiology of psychotic disorders. Indeed, there are studies showing blunted cortisol awakening response, increased dehydroepian-drosterone sulfate (DHEA-S) and decreased stress-induced release of cortisol (Berger et al., 2016; Ciufolini et al., 2014; Misiak et al., 2018). Dopamine release in response to stress has been found to be increased in distinct brain regions in drug-naïve schizophrenia patients and individuals at clinical high risk of psychosis (Mizrahi et al., 2012). There are also studies showing that childhood traumatic events might contribute to a number of biological dysregulations reported in patients with psychosis, including subclinical pro-inflammatory state, lipid profile alterations and decreased brain-derived neurotrophic factor (BDNF) (Di Nicola et al., 2013; Misiak et al., 2015; Theleritis et al., 2014). Our group has recently proposed that the allostatic load (AL) concept might be useful in describing biological alterations related to stress exposure in patients with schizophrenia (Misiak et al., 2014). The

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term "allostasis" captures a range of biological processes that are activated in response to stress to meet the demands of new situations (McEwen and Stellar, 1993). Mediators of allostasis include several hormones, neurotransmitters, neurotrophins, oxidative stress and immune-inflammatory response markers (Misiak et al., 2014). Although short-term activation of these mechanisms enables adaptation to new situations, their chronic activation might be deleterious. The latter scenario has been named as AL by McEwen (2006). In turn, disease outcomes attributable to AL have been defined as allostatic overload (McEwen and Wingfield, 2003). It is important to note that the AL concept is not only a theoretical framework providing a comprehensive conceptualization of stress response. Indeed, the AL index, capturing endocrine, immune-inflammatory, metabolic and cardiovascular markers is a useful measure predicting unfavourable stress-related outcomes (Juster et al., 2010). Emerging evidence indicates elevated AL index in patients with psychotic disorders at various stages of illness. In addition, it has been found that higher AL index might be related to more severe psychotic symptoms, lower functional capacity, reduced cortical thickness and abnormalities of the fornix structural connectivity (Berger et al., 2018; Chiappelli et al., 2017; Nugent et al., 2015; Savransky et al., 2017). Although increased AL index has been reported already in first-episode psychosis (FEP) (Berger et al., 2018), the exact mechanisms underlying this observation remain unknown.

Recent studies from non-clinical populations have suggested that positive coping strategies might buffer biological dysregulations associated with chronic stress exposure. It has been found that maladaptive coping strategies, including disengagement style or avoidance coping are associated with higher AL index (Fernandez et al., 2015; Juster et al., 2016). Patients with psychotic disorders tend to use maladaptive coping strategies that can be observed in the early course of illness. Recent studies of FEP patients revealed higher levels of emotion-focused as well as lower levels of task-focused or active coping (Allott et al., 2015; Pruessner et al., 2011). Therefore, the primary aim of this study was to investigate the AL index with respect to perceived stress, lifetime stressful events and stress coping strategies in patients with FEP. In addition, we aimed to determine the association between the AL index and clinical manifestation of FEP.

2. Material and methods

2.1. Participants

Participants were 36 patients with FEP (20 males and 16 females, aged 27.5 \pm 7.4 years) and 31 healthy controls (12 males and 19 females, aged 25.2 \pm 6.6 years). The study protocol was approved by the Ethics Committee at Wroclaw Medical University (Wroclaw, Poland) and all participants gave written informed consent. Patients were diagnosed according to the DSM-IV criteria and represented the following diagnostic categories: schizophrenia (n = 15), schizophreniform disorder (n = 12), brief psychotic disorder (n = 4), schizoaffective disorder (n = 4) and delusional disorder (n = 1). A diagnosis of FEP was validated using the Operational Criteria for Psychotic Illness (OPCRIT) checklist (McGuffin, 1991). They were recruited from consecutive admissions at two clinical sites: Lower Silesian Centre of Mental Health (Wroclaw, Poland) and Department and Clinic of Psychiatry (Pomeranian Medical University, Szczecin, Poland) in the years 2016 - 2018. There were following exclusion criteria in the group of FEP patients and healthy controls: 1) comorbid neurological disorders; 2) intellectual disability; 3) physical health impairment that might affect biochemical markers measured in the study (diabetes, hypertension, coronary artery disease, autoimmune disorders, inflammatory diseases, endocrine disorders) and 4) drug and/or alcohol dependence (except for nicotine). Cigarette smoking was assessed using the Fagerström Test for Nicotine Dependence (FTND) (Pomerleau et al., 1989). Patients with FEP were eligible for participation in the study if their antipsychotic treatment duration did not exceed 30 days. This treatment duration criterion was established due to a number of questionnaires that might be difficult to administer in acute phase of psychosis.

Community controls were recruited at Wroclaw Medical University (Wroclaw, Poland) through advertisements. They had negative present, past and family history of psychotic and affective disorders. Healthy controls did not receive any incentives for participation in the study. In addition, they had never been treated because of any psychiatric disorders. Patients with FEP and healthy controls were matched for age, sex and parental education as a proxy measure of socioeconomic status.

2.2. Measures

2.2.1. Psychopathology and general functioning

Psychopathological manifestation was assessed using the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987), Scale for Assessment of Positive Symptoms (SAPS) and Scale for Assessment of Negative Symptoms (SANS) (Andreasen, 1990). Additionally, affective symptomatology was evaluated using the Hamilton Depression Rating Scale (HDRS) (Hammilton, 1960) and the Young Mania Rating Scale (YMRS) (Young et al., 1978). The Global Assessment of Functioning (GAF) (Hall, 1995) as well as the Social and Occupational Functioning Assessment Scale (SOFAS) were used to record functional capacity (Goldman et al., 1992).

2.2.2. Stress

The Perceived Stress Scale (PSS) was used to measure self-perception of stress over the past month (Cohen et al., 1983). It is a widely used instrument that consists of 10 questions which are rated on a 5-point Likert scale, ranging from 0 (never) to 4 (very often). Total scores range from 0 to 40.

The List of Threatening Experiences (LTE) was administered to record lifetime stressful events (Brugha and Cragg, 1990). It consists of 12 dichotomously scored questions (positive or negative history of a particular event) regarding the following experiences: 1) serious illness, injury or assault to self; 2) serious illness, injury or assault to close relative; 3) death of parent, child or spouse; 4) death of close friend or other relatives; 5) separation due marital problems; 6) broke of a steady relationship; 7) serious problems of close friend, neighbour or relative; 8) becoming unemployed or seeking work > 1 month; 9) sacked from job; 10) major financial crisis; 11) problems with police and court appearance and 12) something valuable lost or stolen.

2.2.3. Coping styles

Coping strategies were evaluated using the Coping Inventory for Stressful Situations (CISS) (Endler and Parker, 1990) and the COPE Inventory (Carver et al., 1989). The CISS is a 48-tem self-rating scale that assesses the ways people react to stressful situations. Scores from distinct items are summarized in distinct subscales for 5 specific coping styles: 1) task-focused (a problem-oriented strategy that involves taking direct action to reduce the level of stress evoked by distinct situations); 2) emotion-focused (focusing on the emotional arousal evoked by stress but not on the situation); 3) avoidance-focused coping (efforts to avoid dealing with the stressor); 4) distraction (engaging in other activities to avoid dealing with the stressor) and 5) social diversion (seeking social interactions in case of stressful events). The COPE is a 60-item selfreport that evaluates a broader range of stress coping styles: 1) active coping (taking action and exerting efforts to remove or circumvent stressors); 2) planning (thinking about how to confront stressors); 3) instrumental social support (ability to ask for advice or help); 4) emotional social support (ability to ask for emotional support and understanding); 5) suppression of competing interests (limiting the activities not connected to the problem); 6) religious coping (engagement in religious activities); 7) positive reinterpretation and growth (to growing in light of a stressful situation that is perceived in a positive light); 8) restraint (passive waiting for the right time to resolve the problem); 9) acceptance (accepting the situation as something irreversible, trying to

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