Psychiatry Research 186 (2011) 326–332

Contents lists available at ScienceDirect

Psychiatry Research

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

Relationships between stress, social adaptation, personality traits, brain-derived neurotrophic factor and 3-methoxy-4-hydroxyphenylglycol plasma concentrations in employees at a publishing company in Japan

Kanae Okuno, Reiji Yoshimura *, Nobuhisa Ueda, Atsuko Ikenouchi-Sugita, Wakako Umene-Nakano, Hikaru Hori, Kenji Hayashi, Asuka Katsuki, Hsin-I Chen, Jun Nakamura

Department of Psychiatry, University of Occupational and Environmental Health, 1-1 Iseigaoka, Yahatanishi-ku, Kitakyushu, Fukuoka 8078555, Japan

ARTICLE INFO

Article history:
Received 2 April 2009
Received in revised form 21 July 2010
Accepted 23 July 2010

Keywords:
BDNF
MHPG
Psychological job stress
Personality trait
Biological markers

ABSTRACT

There is growing evidence that blood levels of brain-derived neurotrophic factor (BDNF) and 3-methoxy-4-hydroxyphenylglycol (MHPG), a major metabolite of noradrenaline, are related to depression-associated personality traits as well as to depressive, suicidal and anxious states. Psychological job stress is well known to lead to symptoms of depression, anxiety and suicide. We have recently reported that psychological job stress among hospital employees altered blood levels of BDNF and MHPG (Mitoma et al., 2008). In the present study, we re-examined the effects of social adaptation and personality traits, as well as those of psychological job stress, on plasma levels of BDNF and MHPG in healthy employees ($n = 269$, male/female = 210/59, age = 49 ± 10 years) working in a publishing company in Japan. The values (mean ± SD) of scores on the Stress and Arousal Check Lists (s-SACL and a-SACL), Social Adaptation Self-evaluation Scale (SASS), plasma MHPG levels and plasma BDNF levels were 6.0 ± 3.4, 5.7 ± 2.3, 33.7 ± 6.8, 5.8 ± 4.3 and 4.6 ± 3.1 ng ml^{-1}, respectively. A positive correlation was found between plasma MHPG levels and scores on the s-SACL, but not the a-SACL. A positive correlation was also found between SASS scores and plasma MHPG levels and between SASS scores and plasma BDNF levels. A negative correlation was found between plasma BDNF levels and s-SACL scores. Furthermore, a positive correlation between NEO-Five factor Inventory (Openness) scores and plasma MHPG levels was observed, as well as between NEO-Five factor Inventory (Extroversion) scores and plasma BDNF levels. These results suggest that levels of plasma BDNF and plasma MHPG might be associated with psychological job stress and certain personality traits among employees in the publishing industry in Japan.

1. Introduction

Brain-derived neurotrophic factor (BDNF) is a major neurotrophic factor that has been found to play a critical role in long-term potentiation, a cellular mechanism of learning and memory, which suggests that this neurotrophic factor exerts an influence on neuroplasticity (Korte et al., 1995; Figurov et al., 1996). In addition, BDNF is required for the survival and guidance of neurons during development and for the survival and function of neurons during adulthood (Thoenen, 1995; McAllister et al., 1999; Duman et al., 2000). Atrophy and loss of hippocampal or cerebral cortical neurons and/or glia can result from various factors (e.g., stress-induced loss of neurotrophic factors, certain processes that compromise neuronal function and activity and insults associated with an individual's genetic background) (Sapolsky, 2000; Shelton, 2000). In a number of studies, decreased BDNF expression, measured under stressful conditions, has suggested that this neurotrophic factor plays a crucial role in inducing depression and anxiety in animal models (Duman et al., 1997; Duman and Monteggia, 2006). In other words, many different types of acute and chronic stress paradigms decrease the expression of BDNF in the hippocampus. Initial studies examined the influence of acute immobilisation stress and reported significant reductions of BDNF messenger RNA expression in the major subfields of the hippocampus. Subsequent studies found that other types of stress, including unpredictable, footshock, social isolation, social defeat, swim stress and maternal deprivation, also decreased the expression of BDNF in the hippocampus. Several human studies have demonstrated decreased blood levels of BDNF in patients with depression (Karege et al., 2002; Shimizu et al., 2003; Gonul et al., 2005; Yukimasa et al., 2006; Yoshimura et al., 2007a,b), suicidal

Abbreviations: BDNF, brain-derived neurotrophic factor; MHPG, 3-methoxy-4-hydroxyphenylglycol; SACLI, stress and arousal check list (SACLI accepted this revised manuscript as it is); SASS, social adaptation self-evaluation scale.

* Corresponding author. Department of Psychiatry, University of Occupational and Environmental Health, 1-2 Iseigaoka, Yahatanishi-ku, Kitakyushu, Fukuoka 8078555, Japan. Tel.: +81 936917253; fax: +81 936924894.
E-mail address: yoshi621@med.uoeh-u.ac.jp (R. Yoshimura).

0165-1781/$ – see front matter © 2010 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.psychres.2010.07.023

behaviour (Kim et al., 2007) and anxiety disorders (Kobayashi et al., 2005). A meta-analysis conducted by Sen et al. (2008) revealed that serum BDNF levels are lower in depressed subjects than in healthy control subjects, and that levels rise after antidepressant treatment. Thus, while serum BDNF levels may be abnormally low in depressed patients, they can be elevated following a course of antidepressant therapy. Brunoni et al. (2008) also performed a systematic review and meta-analysis of clinical studies of major depression and BDNF levels, and found that blood BDNF levels are associated with clinical changes in depressive patients. Taking these findings into account, the blood BDNF level is a good candidate biological-state marker of depression. Serum BDNF levels are approximately 100–250 times greater that those in platelet-poor plasma. Platelets are the major source of serum BDNF, as they sequester large quantities of it for release during clotting. Sources of circulating plasma BDNF include vascular endothelial cells as well as brain cells (Lommatzsch et al., 2005). Platelets have a life span of approximately 10 days (Harker et al., 2000), whereas plasma BDNF is minimally affected by the amount stored in platelets, and, therefore, is likely to be a more suitable index of brain BDNF levels (Marano et al., 2007). Nonetheless, the extent to which peripheral levels reflect brain levels of BDNF remains unknown (Podusto and Curran, 1996).

In a previous study, Lang et al. (2004) observed decreased serum BDNF levels in healthy volunteers with neuroticism, a depression-related personality trait. The authors also reported association between BDNF gene Val66Met polymorphism and anxiety-related personality traits (Lang et al., 2005).

Plasma levels of 3-methoxy-4-hydroxyphenylglycol (MHPG), a major metabolite of noradrenaline, are reported to reflect noradrenergic neuronal tone in humans (Kopin, 1985). However, when the central and peripheral activities of norepinephrine are associated, plasma MHPG levels can be difficult to interpret. Although Maas et al. (1979) reported that approximately 60% of plasma MHPG originates in the brain, it is currently believed that only 20–30% of total MHPG is of brain origin (Nagaoka et al., 1997; Yoshimura et al., 2000; Umene-Nakano et al., 2010). Mitchel et al. (2009) recently reported that the sympathetic innervations of the cerebral vessels can be delineated into an extrinsic and an intrinsic system. Extracerebral blood vessels receive postganglionic fibres arising from the superior cervical ganglion. Within the brain parenchyma, the cerebral arteries lose their extrinsic innervation and are supplied by noradrenergic neurons within the brain. The author's assumption is that brain noradrenaline spillover derives from the extrinsic cerebrovascular sympathetic nerves. Thus, it is reasonable to consider that both cerebral and sympathetic nerves contribute to plasma MHPG levels. Previously, we reported that plasma MHPG levels correlated with the severity of anxiety in depressed patients (Ueda et al., 2002; Shinkai et al., 2004; Yukimasa et al., 2006). Taken together, the findings reported to date suggest that blood levels of MHPG may serve as biomarkers of stress-related symptoms such as depression and anxiety. In addition, Fukuda et al. (1996) observed a significant positive correlation between plasma MHPG and psychological stress in healthy volunteers. Mizuki et al. (1992) reported an increase in dopamine turnover (homovanillic acid/dopamine) during the performance of a mental task in a normal control group. These results suggest that catecholaminergic activity might be associated with psychological stress in normal subjects. We recently reported that serum BDNF levels and plasma MHPG levels (but neither plasma levels of interleukin-6 nor tumour necrosis factor) are candidate biological markers reflective of psychological job stress in hospital employees.

Social behaviours have been shown to exert a strong influence on determining acceptance and rejection between strangers and friends (Paddock and Nowicki, 1986). Deficits in social skills (e.g., lack of smiling, sad facial expression, avoidance of eye contact, monotonic speech and lack of verbal responses) have been shown to be common among those with low levels of social contact (Cohen et al., 1986) and depressed patients (Segrin and Abramson, 1994). These sorts of behaviour were found to result in social rejection by strangers (Tse and Bond, 2003) and friends. Moreover, such behavioural traits have been suggested to play an important role in the aetiology and maintenance of depressive symptoms. In other words, social adaptation skills are considered important for adjustment to the workplace and in the aetiology of depressive disorders. Bosc et al. (1997) demonstrated that social motivation could be measured by the Social Adaptation Self-evaluation Scale (SASS), a 20-item self-report questionnaire. The SASS has been shown to possess adequate psychometric properties and good internal consistency. Dubini et al. (1997) found that depressed patients reported lower SASS scores than did healthy volunteers. Furthermore, depressed patients have been found to have less social support in general. The Japanese version of the SASS was produced by Goto et al. (2005), who confirmed that the translated instrument was suitable for evaluating social adaptation in the Japanese population. Interestingly, Dubini et al. (1997) demonstrated that depressed patients treated with reboxetine, a noradrenaline reuptake inhibitor, were found to improve significantly more in terms of social motivation, as measured by the SASS, than those treated with fluoxetine, a selective serotonin reuptake inhibitor (SSRI). Taking these findings into account, the SASS can be considered to possess adequate psychometric properties, and is considered a valid tool for assessing the motivational aspect of social adjustment, which is associated with noradrenergic activity.

The Stress and Arousal Check Lists (SACL) is a self-rating scale for assessing psychological stress and arousal that consists of 30 adjectives expressing stress and arousal (Mackay et al., 1978). The category of stress includes 17 items regarding psychological stress and 13 items regarding mental arousal. A higher score is indicative of a relatively greater degree of psychological stress and mental arousal. The Japanese version of the SACL was produced by Kumashiro (2002), who also demonstrated that it was suitable for evaluating stress in occupational health workers in Japan. We have recently reported finding significant correlations between SACL scores and serum BDNF levels or plasma MHPG levels in Japanese hospital employees (Mitoma et al., 2008), which suggests both of these biological markers as reflective of psychological job stress.

In the present study, we investigated the relationships among plasma levels of BDNF and MHPG in terms of psychological job stress, and we used a large sample for SASS measurement and assessment of personality traits using the NEO-Five-factor Inventory (NEO-FFI) (Costa and McCrae, 1992) and the SACL in healthy volunteers working in a publishing company in Japan. The aims of the present study were to compare the results of these two studies, and if possible, to reconfirm the results of our last study. In addition, we also examined the roles of social adaptation and various personality traits on psychological stress.

2. Methods

2.1. Subjects

Included in this study were 269 Japanese employees working in a publishing company. We chose this particular sample because, during the course of the study, one of the present authors was engaged as a mental health consultant for employees at this company. However, no conflict of interest exists with regard to this relation. The Mini International Neuropsychiatric Interview (M.I.N.I.) (Sheehan et al., 1998) was used to rule out psychiatric disorders among candidate subjects, and none of the subjects selected for the final analysis had received any drugs for at least 2 weeks prior to the study. All participants were physically healthy. Of the subjects, 210 were male and 59 were female, and their age ranged from 22 to 68 (mean ± S.D.: 49 ± 10) years. The levels of perceived psychological stress and social adjustment of the participants were evaluated by SACL and SASS, respectively. The personality traits of the subjects were assessed using the NEO-FFI. The protocol of this study was approved by the Ethics Committee of the University of Occupational and Environmental Health. Written informed consent was obtained from all subjects.

2.2. Procedures

Blood was drawn from the participants at 8:00 a.m. before breakfast. We used ethylenediaminetetraacetic acid disodium salt as an anticoagulant for collected plasma