Original Article

Absence of an association between serum interleukin-6 and brain-derived neurotrophic factor in drug-naïve first-episode major depression

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ABSTRACT

Peripheral and central cytokine interleukin-6 (IL-6) levels play an important role in the pathophysiology of major depression (MD). We investigated the association between serum levels of IL-6 and brain-derived neurotrophic factor (BDNF) in drug-naïve, first-episode patients with MD. This study included 28 patients (male/female: 11/17; mean [standard deviation] age, 46.7 [11.9] years) who met the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition criteria for MD without any physical diseases. We evaluated the severity of depression using the Hamilton Rating Scale for Depression. No associations were found between serum levels of IL-6 and BDNF (r=-0.102, *P*=0.605). These results suggest that IL-6 does not influence BDNF and vice versa, but both act in a peripheral manner.

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Keywords: interleukin-6; major depression; neuroinflammation; brain-derived neurotrophic factors

Introduction

Major depression (MD) is an important cause of reduced quality of life worldwide [1]. MD is associated with increased levels of circulating cytokines and soluble receptors [2]. We recently reported that higher plasma interleukin 6 (IL-6) activity is associated with refractory depression, and plasma IL-6 levels might be a predictor of the response to selective serotonin reuptake inhibitors or serotonin and norepinephrine reuptake inhibitors [3]; thus, IL-6 levels play an important role in the pathophysiology of MD [4]. Brain-derived neurotrophic factor (BDNF) is also involved in the pathophysiology of MD [5]. Peripheral levels of BDNF in patients with MD are reduced, and use of antidepressants recovers them [6]. Evidence suggests that the interaction between IL-6 and BDNF is scarce; only one previous report demonstrated that BDNF levels were positively associated with IL-6 levels in patients with melancholic depression [7]. However, the association between peripheral IL-6 and BDNF in patients with MD remains to be elucidated.

The aim of the present study was to investigate the association between serum levels of IL-6 and BDNF in drug-naïve, first-episode patients with MD. To the best of our knowledge, this is the first report examining the association of these factors in patients with first episode of MD who are drug-naïve.

Materials and methods

This study included 28 patients (male/female, 11/17; mean [standard deviation] age, 46.7 [11.9] years) who met the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition [8] criteria for MD and were without any physical diseases.

We evaluated the severity of depression using the Hamilton Rating Scale for Depression (HAMD) [9]. Blood samples were taken at 7:00 am before breakfast (at least 12 h after the last medication, because two patients took a laxative agent) before starting the medication. After overnight rest, 15 mL of venous blood was drawn from the patients in the supine position. The serum samples were immediately separated using a centrifuge (2000 *g*, 10 min, 4°C) and stored at −80°C until they were used for the assays. Serum levels of IL-6 and BDNF were measured using enzyme-linked immunosorbent assays. Pearson's coefficient correlation was used as the statistical method, and statistical significance was defined as $P<0.05$. All participants enrolled in the study signed an informed consent document that explained the study protocol and the potential risks involved. The study was approved by the ethics committee of the University of Occupational and Environmental Health, Kitakyushu, Japan (approval number: H25-13; May 8, 2013) and was conducted while upholding the stipulated ethical standards.

Results

The demographics of the patients were shown in Table 1. No associations were found between serum levels of IL-6 and BDNF (r=-0.102, *P*=0.605) (Figure 1).

Discussion and conclusion

A meta-analysis reported increased blood IL-6 levels [10], and another study reported reduced blood BDNF levels in MD patients [11]. Our study found no correlation between serum levels of IL-6 levels and BDNF in patients with MD. In short, the results of the present study suggest that IL-6 does not influence BDNF and vice versa, but both act in a peripheral manner. Our results,

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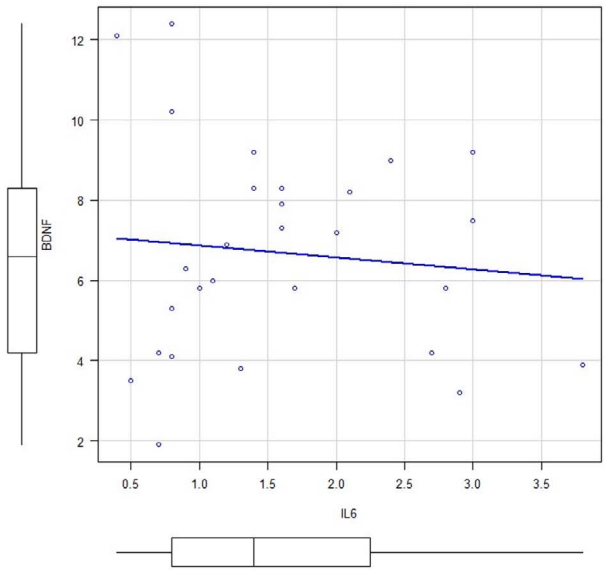

Figure 1. Serum BDNF and serum IL-6. r=-0.102, P=0.605. BDNF, brain-derived neurotrophic factor; IL, interleukin.

Table 1. Demographics of the patients

male (%)	11 (40.7)
age (mean±s.d.)yr	46.9±11.9
married (%)	20 (71.4%)
years of education (mean±s.d.)yr	13.5±1.7
HAMD (mean±s.d.)	22.4±3.7
IL-6 (pg/mL) (mean±s.d.)	1.6±0.8
BDNF (ng/mL) (mean±s.d.)	6.6±2.5

however, are not in accordance with the results of a study that reported a positive association between serum BDNF levels and IL-6 levels in patients with MD [7]. The reason for this discrepancy remains unknown. The inclusion of drug-naïve patients with first-episode MD in our study might be related to this discrepancy. In conclusion, the dynamics of IL-6 and BDNF in the periphery may be complicated in patients with MD. We cannot speculate on the association between IL-6 and BDNF in the brain based on this preliminary peripheral result. The study had several limitations including a small sample size, cross-sectional, discrepancy between peripheral and brain. Further studies considering above points must be performed.

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