



## LETTERS TO THE EDITOR

### Serum brain-derived neurotrophic factor levels in depression with and without melancholy and in healthy participants



Dear,

Brain-derived neurotrophic factor (BDNF) contributes to the pathophysiology of major depressive disorder (MDD). BDNF plays a major role in neuronal growth and survival, serves as a neurotransmitter modulator, and contributes to neuronal plasticity, all of which are associated with MDD. BDNF stimulates and controls the growth of new neurons from neural stem cells (i.e., neurogenesis), and BDNF protein and mRNA have been detected in various regions of the brain, including the olfactory bulb, cortex, hippocampus, basal forebrain, mesencephalon, hypothalamus, brainstem, and spinal cord.<sup>1,2</sup> We compared serum BDNF levels in three groups: individuals with major depression (MD) and melancholy, those with major depression without melancholy, and healthy participants. This study was approved by the Ethics Committee of the University of Occupational and Environmental Health, Japan. All participants provided informed consent. Seventy-eight in-/out-patients with MD (35 males and 43 females; average  $46.2 \pm 12.5$  years old) were recruited. Patients met the diagnostic criteria for MD according to the Diagnostic and Statistical Manual of Mental Disorders-5 criteria. Serum BDNF concentrations were measured by sandwich ELISA.<sup>3</sup> Depression severity was assessed using the 17-item Hamilton Rating Scale for Depression (HAM-D).<sup>4</sup> Antidepressants included escitalopram 24 ( $16.3 \pm 2.4$ ) mg/day, paroxetine 17 ( $27.3 \pm 9.6$ ) mg/day, duloxetine 16 ( $38.4 \pm 14.8$ ) mg/day, sertraline 12 ( $63.6 \pm 18.1$ ) mg/day, and milnacipran 9 ( $88.1 \pm 24.5$ ) mg/day. There were no differences in age or sex between the melancholy and non-melancholy groups. There was no difference in the HAM-D scores at week 0 between the melancholy ( $23.8 \pm 2.0$ ) and non-melancholy ( $22.8 \pm 1.9$ ) groups; however, following antidepressant treatment, there was a significant increase in the HAM-D scores (week 0–4) of the melancholy group compared with those of the non-melancholy group (Table 1). The present result was following with a previous study reporting a more evident global response to pharmacotherapy in melancholia compared to that in other depressive syndromes, particularly when selective serotonin uptake inhibitors are used.<sup>5</sup>

Serum BDNF concentrations at week 0 did not differ among the melancholy, non-melancholy, and healthy control groups (Table 2); there were also no significant changes in serum BDNF levels (week 0–4) following antidepressant administration between the melancholy and non-melancholy groups. We previously reported that serum BDNF levels are significantly reduced in drug-naïve first-episode patients with MD.<sup>3</sup> The results of the present study, in which pre-treatment serum BDNF concentrations did not differ among the three groups, were not consistent with our previous results.<sup>3</sup> It is plausible that the inclusion of patients with recurrent episodes and refractory patients ( $n = 38$ ) in the present study might have contributed to the discrepancy. There are no differences in plasma levels of 3-methoxy-4-hydroxyphenylglycol (MHPG) and homovanillic acid (HVA) between the melancholic and non-melancholic groups.<sup>6</sup> We also reported that BDNF does not interact with catecholamine metabolites, including MHPG and HVA.<sup>2</sup> These findings suggest that serum BDNF and plasma catecholamine metabolites are not differential indicators of melancholy or non-melancholy MD. In conclusion, it is difficult to categorize MD based on peripheral BDNF and catecholamine metabolites.

### Data sharing statement

All data are available from the corresponding author.

### Ethics approval

Was in accordance with ethical guidelines. The study was approved by the institutional review board (approved code UOHECRB21-57). Written informed consent was obtained from all participants. Study was conducted in accordance with the Declaration of Helsinki.

### Consent to participate

Was obtained from the patient.

### Consent for publication

Was obtained from the patient.

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**Table 1** Changes in the Hamilton Rating Scale for Depression (HAMD) scores; *p*-value tested using the Mann–Whitney U test.

	melancholy	non-melancholy	<i>p</i> -value
HAMD scores (week 0–4)	11.1 (4.20)	9.18 (4.15)	0.040

**Table 2** Serum brain-derived neurotrophic factor (BDNF) levels in the melancholy, non-melancholy, and healthy control groups; *p*-value tested using the Kruskal–Wallis test.

	Healthy controls	Melancholy	Non-melancholy
BDNF (week 0)	8.97 (1.13)	8.14 (2.18)	8.62 (1.83)

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## Disclosure

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Reiji Yoshimura\*, Naomichi Okamoto, Atsuko Ikenouchi

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

\* Corresponding author at: Department of Psychiatry, University of Occupational and Environmental Health, 1-1 Iseigaoka, Yahatanishi-ku, Kitakyushu, Japan.

*E-mail address:* yoshi621@med.uoeh-u.ac.jp (R. Yoshimura).

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