Letter to the Editor

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Plasma levels of paroxetine are not associated with the increase of serum levels of brain-derived neurotrophic factor in major depression

Reiji Yoshimura, Naomichi Okamoto, Yuki Konishi, Atsuko Ikenouchi

Department of Psychiatry, University of Occupational and Environmental Health, Japan

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To the Editor: Brain-derived neurotrophic factor (BDNF) is associated with synaptic neuroplasticity and memory [1] and has been implicated in the pathophysiology of major depressive disorder (MDD) [2]. According to our meta-analysis, blood levels (serum and plasma levels) of BDNF are lower in MDD patients than in healthy subjects [3] Conversely, treatment with antidepressants increased peripheral BDNF levels [4]. We previously reported that serum BDNF levels in individuals who responded to paroxetine, significantly increased (2.6-fold) 8-weeks after treatment. This would suggest that paroxetine improved the depressive symptoms by increasing serum BDNF levels [5].

Herein, we investigated the association between plasma concentrations of paroxetine and serum levels of BDNF in other samples of our previous study [5]. The participants met the following criteria: 1) diagnosed with MDD according to the DSM-5, 2) received paroxetine monotherapy for 8 -weeks, 3) were considered to be in remission for at least 8 weeks (7 point or less in the Hamilton Rating Scale for Depression-17; HAMD17) until 8 weeks starting paroxetine (mean ± sd=27.1 ± 9.7 mg/day). Eighteen individuals who had been diagnosed with MDD but were in remission (M/F:7/11, age: 46.4 ± 9.3 yrs) were enrolled in the present study. The HAMD17 score was taken at baseline and at 8 weeks (23.3 ± 3.3 and 5.6 ± 1.2, respectively). Blood sampling was performed twice, ie before paroxetine treatment and then 8-weeks after treatment. Plasma levels of paroxetine and serum levels of BDNF were measured as previously described [5,6]. The protocol and procedures of this study were approved by the Ethics Committee of the University of Occupational and Environmental Health, Kitakyushu, Japan. Written informed consent was obtained from all subjects.

Serum BDNF levels were significantly increased 8-weeks after treatment with paroxetine (from 8.0 ± 2.0 ng/ml to 8.9 ± 1.6 ng/ml, respectively; paired t-test: p=0.007). A significant association was not found between the change of the HAMD17 score and the change of serum BDNF level before and 8-weeks after treatment with paroxetine (Pearson's correlation coefficient: r=0.0654, p=0.796, Figure 1). Moreover, no correlation was also observed between the change in serum levels of BDNF and plasma concentrations of paroxetine (Pearson's correlation coefficient: r=-0.150, p=0.560, Figure 2).

We have previously reported that no association was found between plasma levels of fluvoxamine and the changes of serum levels of BDNF in MDD patients [7]. The results of the present study using paroxetine were in accordance with our previously published report using fluvoxamine. In short, plasma concentration of antidepressant drugs might be independent of the changes of BDNF level. [7]. We had previously reported the association was found between the change of BDNF and the change of HAMD17 score MDD patients treated with paroxetine [5], which is in disagreement with the pre-

Corresponding author: Reiji Yoshimura, Department of Psychiatry, University of Occupational and Environmental Health 1-1 iseigaoka, Yahatanishi-ku, Kitakyushu, Fukuoka8078555, Japan. Tel: +81936917253, Fax: +81936924894, E-mail: yoshi621@med.uoeh-u.ac.jp

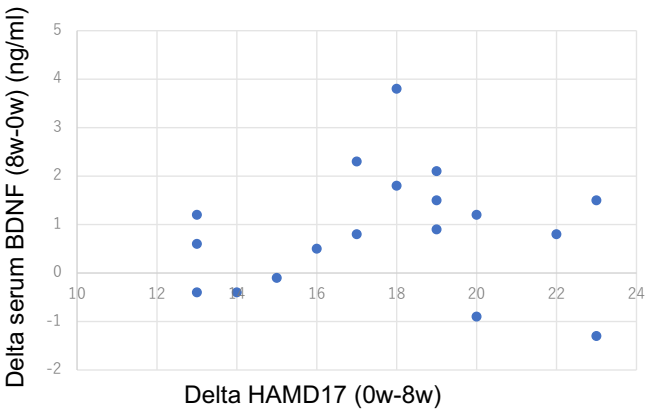

Figure 1. The change of the HAMD17 score and the change of serum BDNF level at week 0 and week 8.

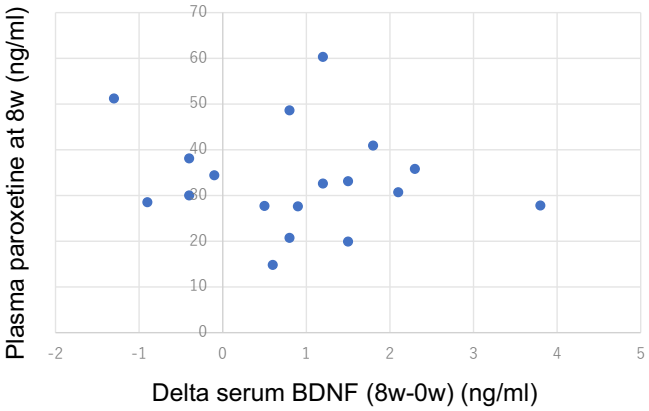

Figure 2. Plasma levels of paroxetine at week 8 and the change of serum of BDNF at week 0 and week 8.

sent findings. We considered one of the reasons for the discrepancy was due to heterogeneity of the subjects. Only a small number of remitted MDD patients without non-remitted ones were enrolled in this study. In short, MDD patients, who were in remission after paroxetine treatment, had significantly increased serum BDNF levels 8 weeks after treatment. The increase of serum BDNF was not paralleled with the reduction of the HAMD17 score. Moreover, serum BDNF level was independent of plasma concentrations of paroxetine. Taking these findings into account, paroxetine significantly increased serum BDNF level in remitted MDD patients whereas the increased serum BDNF by paroxetine might be due to pharmacodynamic mechanism, but not to pharmacokinetic mechanism. This preliminary result is not generalized to other SSRIs. We should undertake further research with larger MDD patients treated with other classes of antidepressant drugs.

CONFLICT OF INTEREST

All authors report no conflicts of interest.

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