Progress in Neuro-Psychopharmacology & Biological Psychiatry 56 (2015) 109–116

Contents lists available at ScienceDirect

Progress in Neuro-Psychopharmacology & Biological Psychiatry

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

Serum brain-derived neurotrophic factor level in elderly women depression: A community-based study

Masahiro Hashizume [c,*], Mitsugu Hachisu [a], Hideyo Yoshida [b], Miji Kim [b], Hun Kyung Kim [b], Yuichi Amano [a], Chie Hasegawa [c], Takao Suzuki [d], Kazushige Ihara [e]

[a] Division of Clinical Pharmacy, Department of Pharmacotherapeutics, School of Pharmacy, Showa University, Japan
[b] Research Team for Promoting Independence of the Elderly, Tokyo Metropolitan Institute of Gerontology, Japan
[c] Department of Psychiatry, Faculty of Medicine, Dokkyo Medical University, Japan
[d] National Institute for Longevity Sciences, Japan
[e] Division of Public Health, Department of Social Medicine, Faculty of Medicine, Toho University, Japan

ARTICLE INFO

Article history:
Received 24 July 2014
Received in revised form 21 August 2014
Accepted 21 August 2014
Available online 29 August 2014

Keywords:
Brain-derived neurotrophic factor
Community
Depression
Female
Old age

ABSTRACT

Objectives: Serum levels of brain-derived neurotrophic factor (BDNF) have been shown to be lower in patients with major depressive disorder (MDD) than in healthy persons. Although several studies have examined the associations between serum BDNF levels and broader categories of depression identified by psychiatrists or depressive symptoms measured with depression scales among nonpatient populations, some of these studies did not consider possible confounders and included mostly young or middle-aged subjects and nonrepresentative control subjects, such as volunteers and patients' relatives. Therefore, it remains unclear that whether MDD, broader categories of depression, or depressive symptoms in the elderly are associated with BDNF. The present study examined these associations in a community sample and controlled for confounders.
Methods: The subjects were 538 women aged 78 to 88 years who had participated in a follow-up survey of a cohort and had scored 24 or more on the Mini-Mental State Examination. Two depression scales were administered, and, using the Structured Clinical Interview for DSM-IV, psychiatrists identified 53 persons having any mood disorder (AMD) — 8 with MDD and 45 with other types of depression according to the DSM-IV or its research criteria — and 106 healthy controls.
Results: Subjects with MDD had serum BDNF levels lower than did controls but subjects with AMD did not. The severity of depressive symptoms assessed with either of the 2 depression scales was negatively correlated with serum BDNF levels in all subjects and in subjects remaining after persons with MDD or AMD were excluded. These associations were significant after controlling for possible confounders.
Conclusion: We have found an association between MDD and serum BDNF levels in old–old women, as has previously been found in younger patients. Although serum BDNF levels were not found to be associated with the broader category of depression, they were associated with depressive symptoms among subjects without clinical depression.

1. Introduction

Depression is a prevalent psychiatric disorder in the elderly and a risk factor for both functional decline (Bruce et al., 1994a; Penninx et al., 2000; Penninx et al., 1999a) and early death (Bruce et al., 1994b; Penninx et al., 1999b). Early detection of depression allows appropriate treatment and mitigation of its effects, although elderly persons with depression are less likely than younger persons to receive treatment (Charney et al., 2003; Kessler et al., 2010). This difference might be partly attributed to the difficulty of diagnosing depression in the elderly which, in turn, might be due to differences in the phenomenology of depression between older and younger persons (Brodaty et al., 2005; Brown et al., 1984; Gallagher et al., 2010; Hybels et al., 2012). Organic pathology in the brain is often assumed to be an underlying cause of the phenomenological differences of depression in the elderly. To understand the organic pathology of the brain, many studies on the basis of the vascular depression hypothesis (Alexopoulos et al., 1997) have been conducted being driven with development of imaging technologies.

In contrast, few studies on the basis of the neurotrophin hypothesis (Duman et al., 1997), which is one of the main hypotheses of depression at the present day, have been conducted in older persons with depression.

Abbreviation: BDNF, brain-derived neurotrophic factor.

* Corresponding author at: Department of Psychosomatic Medicine, Faculty of Medicine, Toho University School of Medicine, 6-11-1 Omorinishi, Ota-ku, Tokyo 143-8541, Japan.
E-mail addresses: 028704hm@med.toho-u.ac.jp, hashi2@med.toho-u.ac.jp (M. Hashizume).

http://dx.doi.org/10.1016/j.pnpbp.2014.08.012
0278-5846/

The utilization of brain-derived neurotrophic factor (BDNF) in the blood in addition to that in postmortem brain has provided much evidence to support the neurotrophin hypothesis of depression showing that serum levels of BDNF are lower in patients with major depressive disorder (MDD) than in healthy control subjects (Karege et al., 2002; Shimizu et al., 2003) and increase after antidepressant treatment (Aydemir et al., 2005; Gervasoni et al., 2005). Although meta-analyses have confirmed the lower serum levels of BDNF in MDD (Bocchio-Chiavetto et al., 2010; Brunoni et al., 2008; Molendijk et al., 2014; Sen et al., 2008), most studies have included only young or middle-aged subjects.

Few studies have examined the association between serum BDNF and depression in the elderly. To the best of our knowledge, only 1 community-based study (Ziegenhorn et al., 2007) and 1 study in a clinical setting (Diniz et al., 2010) have examined the association exclusively in the elderly, whereas other studies have examined the association in both young subjects and older subjects (Bus et al., 2012; Terracciano et al., 2011). The study of Diniz et al. in elderly subjects found that serum levels of BDNF were lower in patients with MDD than in healthy control subjects, as did studies in younger subjects. The community-based study by Ziegenhorn et al., however, found no such association.

Some researchers have tried to take findings about BDNF levels and depression obtained in patient groups and extend them to nonpatient groups, drawn from the general population or community-dwellers (Bhang et al., 2012; Bus et al., 2012; Elfving et al., 2012; Harvey et al., 2013; Terracciano et al., 2011; Ziegenhorn et al., 2007). However, half of the studies in nonpatient populations, comprising mainly young or middle-aged persons, did not show the same association between serum BDNF and depression (Elfving et al., 2012; Harvey et al., 2013; Ziegenhorn et al., 2007). The failure to confirm the results of previous studies seems partly due to depression in population-based or community-based studies tending to be less severe than MDD in clinical studies (Elfving et al., 2012; Ziegenhorn et al., 2007) or to depression in a population-based study being identified with a depression scale (Harvey et al., 2013). These findings might have been confirmed by community-based studies if they had identified MDD according to standard clinical criteria, as clinical studies do.

Population-based or community-based studies using depression scales, however, can examine a continuous association between depression and serum BDNF in samples comprising both healthy persons and depressed persons (Bhang et al., 2012; Bus et al., 2012; Terracciano et al., 2011), and, therefore, these studies have broader public health implications. Furthermore, population-based studies, regardless whether depression is assessed quantitatively or categorically, can use samples that are more representative than those in clinical studies and can more easily control confounders. Some studies have reported confounders for any association between depression and serum BDNF (Bus et al., 2012; Elfving et al., 2012).

In the present study, we examined the continuous associations of serum BDNF levels with depression, measured with depression scales, among older community-dwellers while considering possible confounders. We also examined the association of serum BDNF with either MDD alone or all mood disorders, including MDD, according to the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) (American Psychiatric Association, 2000), in the same samples. We believe that simultaneous examination of the associations in the community sample would reconcile differences in previous findings between younger patients and older patients and between nonpatient studies and clinical studies.

2. Methods

2.1. Study subjects

The subjects were 575 participants of a survey carried out for 9 days in October 2012. The survey was a follow-up of a cohort of 1289 participants of a 2008 baseline survey that targeted all 10,948 women aged 75 to 84 years in an urban area in Tokyo. The subjects underwent physical and psychological assessments, including hematological examination; the Mini-Mental State Examination (MMSE) (Folstein et al., 1975); and assessment with 2 depression scales. Subjects who were suspected to have depression on 1 of the depression scales (the Depression Scale in Basic Checklist [DSBC]) (Fujisawa et al., 2005), and who scored 24 points or higher on the MMSE were asked to undergo a psychiatric evaluation. Among those who were not suspected to have depression on the basis of the DSBC, consecutive participants on 3.5 days of the survey periods were also asked to undergo psychiatric evaluation.

We assert that all procedures contributing to this study comply with the ethical standards of the relevant national committees on human experimentation. Ethical approval was granted by the ethics committee of the Toho University School of Medicine (Registration Number 24034). Informed consent was obtained before the follow-up survey.

2.2. Depression scales

Symptoms of depression were assessed with the Self-Rating Depression Scale (SDS) (Zung, 1967) and the DSBC. The SDS is composed of 20 items that assess the frequency of symptoms on a 4-point scale from 1 (none or a little of the time) to 4 (most or all of the time) during the past several days. This scale yields a total score of 20 to 80, with higher total scores indicating more severe state of depression. The SDS was self-administered by the subjects but was observed by lay personnel to reduce missing values and adverse ratings for negatively worded items. The DSBC is a 5-item, yes/no question scale that was developed to find depression in the elderly. A yes answer means the presence of a symptom during the last 2 weeks and is given 1 point. The total score ranges 0 to 5, and a total score of 2 or more indicates clinical depression. While psychologists administered the DSBC by reading questions, the test was self-rated and indicated the subjects own responses.

2.3. Psychiatric evaluation

The psychiatric evaluation was carried out within 6 weeks after the survey. Psychiatrists assessed subjects using the A and J modules of the Structured Clinical Interview for DSM-IV (SCID) (First et al., 2003) and identified mood disorders during the past 1 month and over the subjects' lifetime. The SCID enabled us to identify any mood disorders (AMD) during the survey when blood for BDNF and other hematological examinations was drawn. Besides MDD, AMD in the present study could include a major depressive episode in partial remission, dysthymic disorder and bipolar disorder I and II according to DSM-IV, minor depressive disorder, according to the criteria sets for further study in DSM-IV (American Psychiatric Association, 2000), and depression that meets the criteria for minor depressive disorder except that there had never been a major depressive episode. The Grid-Hamilton Depression scale (HAMD) (Tabuse et al., 2007) was administered for all cases of mood disorders identified with the SCID, and those subjects who scored 6 points or less on the HAMD were ultimately judged as not having MDD or AMD. Subjects with no lifetime or current mood disorder comprised a control group. Subjects who were under any treatment for depression were excluded from the depression group and the control group. Before the psychiatric evaluation, psychologists conducted preinterviews, which obtained information on prescribed antidepressants, mainly from prescription notebooks that were given by their family physicians or pharmacists in Japan. Psychiatrists also asked whether the subjects were under treatment.

2.4. Serum BDNF

Blood was withdrawn between 9:00 and 11:00 a.m. or between 1:00 and 4:00 p.m. Soon after being drawn, the samples were centrifuged at 3000 rpm and 4 °C for 15 min, and the sera were transferred to a new