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Preliminary Communication

The influence of personality factors on paroxetine response time in patients with major depression

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ABSTRACT

Background: Determining the factors that predict antidepressant response and offering suitable treatments to people who suffer from major depressive disorder (MDD) is important. We investigated the personality factors that influence paroxetine treatment response by dividing antidepressant responders into two groups.
Methods: We treated 93 patients with MDD using 40 mg/day of paroxetine for six weeks. We used the Cloninger's Temperament and Character Inventory (TCI) to evaluate each participant's personality before the treatment. Of the 93 patients, 75 completed the protocol. The Montgomery Asberg Depression Rating Scale (MADRS) was used to evaluate depressive symptoms before the treatment and at one-, two-, four-, and six-week intervals. We divided the patients into four groups: later responders (LRs), early responders (ERs), nonresponders (NRs), and dropouts (DOs).
Results: Compared with 91 normal control participants, patients with MDD had less novelty seeking and self-directedness and greater harm avoidance. ERs showed less harm avoidance and more self-directedness than the other groups. LRs' TCI scores did not differ from the other groups.
Conclusions: These results suggest that ERs' personality characteristics are different from those of other patients with MDD and that evaluating patients' personality using the TCI at baseline may predict their antidepressant response.
Limitations: Our sample of patients with MDD was small. Some of the patients with severe MDD had difficulty completing the TCI.

1. Introduction

Major depressive disorder (MDD) is one of the most prevalent psychiatric conditions. Selective serotonin re-uptake inhibitors (SSRIs) are frequently used to treat MDD. Although SSRIs are highly effective (Steffens et al., 1997), SSRI response is difficult to predict because response patterns vary between patients. Therefore, determining the factors that predict antidepressant response and offering suitable treatments for people who suffer from MDD is important.

Researchers have been investigating the association between personality and antidepressant response for more than two decades. Cloninger (1987) devised a biosocial model of personality based on 3 independent temperament dimensions: novelty seeking (NS), harm avoidance (HA), and reward dependence (RD). Cloninger postulated that these dimensions are genetically determined and related to the specific activity of neurotransmitter systems such as dopamine, serotonin, or norepinephrine. The Tridimensional Personality Questionnaire (TPQ) was developed to measure NS, HA, and RD. Subsequently, the Temperament and Character Inventory (TCI), a 240-item self-rating questionnaire, was developed to measure 7 dimensions of personality (Cloninger et al., 1993). The TCI consists of four temperament dimensions and the three character dimensions, and it is based on a synthesis of social and cognitive research with personality research from humanistic and transpersonal psychology. Persistence (P), originally thought to be a component of RD, emerged as a distinct fourth temperament factor based on the factor structure of the TPQ.

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Furthermore, the TCI added three character dimensions that are susceptible to self-concept change through social learning: self-directedness (SD), cooperativeness (C), and self-transcendence (ST).

Kampman and Poutanen (in press) reported that an indisputable association existed between TCI scores (particularly HA) and treatment response of patients with MDD in the studies reviewed. Furthermore, several studies have tried to predict clinical response to antidepressants using TCI-measured personality factors (e.g., Hruby et al., 2010; Tome et al., 1997). Tome et al. (1997) showed that a combination of low HA and high RD on the short version of TCI (TCI-125) at baseline predicted better treatment responses in 48 patients with MDD after 6 weeks of a double-blind treatment with paroxetine, an SSRI. Hruby et al. (2010) showed similar results using the TCI with SSRIs or serotonin and noradrenaline reuptake inhibitors (SNRIs). Using the TCI, Sato et al. (1999) showed that high C and SD scores at baseline predicted better responses to a heterocyclic agent, maplotiline, after 8 weeks. Abrams et al. (2004) reported that HA scores at baseline reliably predicted response to sertraline treatment in patients with MDD and dysthymic disorder. However, these previous studies defined "responders" as patients who reacted positively to antidepressants after 6–8 weeks of treatment regardless of their response time.

We sought to determine whether there are personality differences between patients who show immediate improvements to antidepressants and patients who show eventual improvement (e.g., five weeks later). Little research has divided responders into two groups and compared results. Therefore, this study investigated the influence of personality factors in patients with MDD on their paroxetine response, especially with regard to their antidepressant response time.

2. Methods

2.1. Participants

Between December 2004 and September 2008, male and female 18- to 70-year-old patients with an MDD DSM-IV diagnosis from the Hospital of Hirosaki University School of Medicine, Hirosaki-Aiseikai Hospital, Kuroishi-Akebono Hospital, and Ohdate-city Hospital were identified as eligible for participation in this study. In addition, we required that patients score more than 20 points on the Montgomery Asberg Depression Rating Scale (MADRS) (Montgomery and Asberg, 1979). The MADRS consists of 10 items that are scored from 0 to 6. We excluded patients who had taken medications, including psychotropic agents, at least one month before the start of the study as well as those with clinically significant abnormal laboratory or electrocardiography findings, a history of mental illness other than depression (i.e., mania, schizophrenia, epilepsy, alcohol or drug abuse) or clinically significant organic or neurological disease. Out of 93 patients, 18 did not complete the questionnaire. We also recruited 91 19- to 64-year-old healthy people as a control group. Control group participants had no psychiatric history or current psychiatric complaints and scored fewer than 15 points on The Center for Epidemiologic Studies Depression Scale (CES-D) (Radloff, 1977). The majority of healthy controls were medical staff such as nurses, nursing assistants, dieticians, occupational therapists, and psychiatric social workers of Hirosaki-Aiseikai Hospital, Kuroishi-Akebono Hospital, and Huyoukai Hospital.

Table 1 shows the characteristics of the two groups. There was no significant difference in age and sex between patients with MDD and the control group. We conducted the present study after obtaining approval from the Ethics Committee of the Hirosaki University School of Medicine. Participants provided written informed consent after receiving a full description of the study.

2.2. Procedure

We administered a dose of 20 mg/day of paroxetine (Paxil, GlaxoSmithKline, Tokyo, Japan) to patients at 20.00 h during the first week; thereafter, we increased the dose to 40 mg/day. We did not increase the dosage when we observed mild side effects (point 1 in the Udvalg for Kliniske Unders gelser Side Effects Rating Scale (UKU) (Chiba and Takahashi, 2005) or (Lingjaerde et al., 1987); furthermore, we decreased the paroxetine dosage when we observed moderate side effects (point 2 in the UKU) and discontinued the drug in cases of severe side effects (point 3 in the UKU). We also provided diazepam (2–5 mg/day, n = 19) for anxiety, brotizolam (0.25 mg/day, n = 20 and 0.5 mg/day, n = 17) for insomnia, [ME46] and sennoside (12–48 mg/day, n = 12) for constipation. We took blood samples from participants after 1, 2, and 6 weeks of paroxetine treatment. We used the MADRS to evaluate clinical symptoms and used the UKU rating scale to evaluate side effects at 1, 2, 4, and 6 weeks.

All participants completed the Japanese version of the TCI personality evaluation (Kijima et al., 1996) before the treatment. The Japanese version of the MADRS evaluated the

Table 1
Demographic and MADRS scores of healthy controls and participants with major depressive disorders.

	Healthy (n = 91)	Major Depressive Disorders (n = 75)	value	df	p
Age	43.3 ± 11.3	45.7 ± 14.3	t = -1.17	138.861	0.244[a]
Age range	18 - 69	18 - 70			
Sex male / female	29 / 62	28 / 47	$X^2 = 0.545$	1	0.461[b]
Age of onset (years)	-	44.6 ± 14.2			
Duration of illness (months)	-	14.5 ± 25.6			
Paroxetine (mg/day)	-	34.8 ± 9.6			
MADRS 0 weeks	-	39.8 ± 8.7			
MADRS 6 weeks	-	12.6 ± 12.3			

Data show mean ± SD.
[a] t test was used.
[b] chi square was used.