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# Temperament and character as predictors of recurrence in remitted patients with major depression: A 4-year prospective follow-up study



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## ABSTRACT

The aim of the present study was to examine whether the specific personality traits, Harm-Avoidance (HA) and Self-Directedness (SD) as measured by the Temperament and Character Inventory (TCI), were predictive for subsequent depressive episodes in remitted patients with major depressive disorders (MDDs) over a 4-year follow-up. A total of 109 inpatients with MDD participated in this study. The subjects completed the TCI when they were assessed to be in remission. They were divided into high or low HA groups and high or low SD groups, as discriminated by the quartile value. A total of 69 patients were followed-up over a 4-year period or until recurrence. Both Kaplan–Meier analysis and Cox's proportional hazards regression analysis indicated that patients with a low SD score had a significantly shorter time to recurrence from remission than patients with a high SD score even when some prognostic predictors were controlled for. In contrast, HA was not found to be a predictor of recurrence for future depressive episodes. A part of MDD patients with low scores in Self-Directedness are likely to develop depression over a subsequent period of time. Interventions that improve SD may help to delay recurrence of depression in MDD patients.

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## 1. Introduction

Previous studies have found some risk factors associated with subsequent relapse in patients with major depressive disorder (MDD), including female gender (Kessing et al., 1998), existence of prior episodes (Kessing and Andersen, 1999; Kessing et al., 2004), presence of dysthymia (Klein et al., 2006), personality disorder (Grilo et al., 2010), and psychopathology comorbidity (Keller et al., 1992). Patients with early onset depression were likely to have more previous depressive episodes, a longer current depressive episode and greater comorbidity than patients with late onset depression (Klein et al., 1999; Rothschild and Zimmerman, 2002).

The ability of personality traits to predict future depression has also been examined in several studies using Cloninger's Temperament and Character Inventory (TCI). The TCI is based on a psychobiological model that describes the structure and development of personality

with four temperament and three character dimensions. Cloninger et al. (1993) postulated that 'temperament' is genetically independent, emerges in early life and influences subsequent perceptual memory and habit formation, and that 'character' is determined by learning about self-concepts, matures in adulthood, and affects personal and social lives over time. The 'temperament' aspect consists of Novelty-Seeking (NS), Harm-Avoidance (HA), Reward-Dependence (RD), and Persistence (P). The three dimensions of 'character' are Self-Directedness (SD), Cooperativeness (C), and Self-Transcendence (ST). In previous studies among individuals sampled from the general population, future depression was predicted by high HA and P scores and low SD scores (Cloninger et al., 2006), high P scores and some facet scales into which HA and RD are subdivided (Elovainio et al., 2004), and only high HA (Farmer and Seeley, 2009). The study in a selected sample of Japanese university students indicated that low SD only emerged as a predictor of future depression (Naito et al., 2000).

A common finding in past research examining remitted patients with MDD was that HA scores remained relatively high (Hirano et al., 2002; Marijnissen et al., 2002; Richter et al., 2000; Smith et al., 2005) and SD scores were still low (Nery et al., 2009; Richter et al., 2000; Smith et al., 2005), although other five dimensions returned to almost the same levels as that of healthy

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controls. Although the association between TCI dimensions and subsequent depression has been identified in subjects from the general population, few studies have investigated it in a long-term follow-up study in clinical subjects with MDD. The aim of the present study was to examine whether temperament and character in remitted patients with MDD predicted the recurrence of depressive episodes over a 4-year follow-up. Thus, we analyzed the patients' HA and SD scores, which were previously indicated as predictors of future depression in the general population. This study is part of the Juntendo University Mood Disorder Project (JUMP).

## 2. Methods

### 2.1. Subjects

A total of 109 inpatients with depression (42 men, 67 women; mean age, 55.3 years; range, 23–83 years) were recruited from Juntendo Koshigaya Hospital between April 2004 and August 2009. The total number of inpatients with mood disorder treated at the hospital during the period of time was 858. All the patients recruited for the study met the criteria for MDD as stipulated in the Diagnostic and Statistical Manual for Mental Disorders, 4th edition (DSM-IV). A structured clinical interview for DSM-IV (SCID) was conducted to diagnose the patients. Patients were excluded if they had a history of other psychiatric disorders including manic episodes, delusions, severe or acute medical illnesses, neurological disorders, or use of drugs that may cause depression. Patients showing clinical evidence of dementia or with Mini-Mental State Examination (MMSE) score < 24 were also excluded. Depressive state was evaluated with the Hamilton Rating Scale for Depression (HAM-D) (Hamilton, 1960), and remission was defined as a score of 7 points or less. All patients were on antidepressant medication when they were confirmed to be in remission. The number of depressive episodes, total duration of depressive phase, and total duration of medication were confirmed via medical records. The Presumed IQ was computed using the Japanese Adult Reading Test (JART) (Matsuoka et al., 2006). The patients were followed-up over a 4-year period or until recurrence. Recurrence was defined as the Clinical Global Impressions-Severity of Illness scale (CGI-S) (Doogan and Caillard, 1992) score greater than or equal to 4.

The study was approved by the Medical Ethics Committee of Juntendo University, and was performed in accordance with the regulations outlined by Juntendo University. All the patients in the study signed an informed consent form.

### 2.2. Measures and procedures

Patients with MDD completed the TCI at the hospital at the time they were confirmed to be in remission. The follow-up of each patient started at this time. The

Japanese 125-item short version of TCI (Kijima et al., 1996) with the true–false response scale was used in the present study. The reliability and validity of the Japanese version in a nonclinical population (Kijima et al., 2000; Takeuchi et al., 2011) and factor validity in outpatients with major depression (Sato et al., 2001) have been reported.

### 2.3. Statistical analysis

Survival analysis was used to estimate time to recurrence during the 4-year follow-up from remission. Patients were divided into two groups by HA and SD scores. The highest quartile was taken as the point of dichotomizing HA and the lowest quartile was taken for SD. The cut-off points in the present study were selected by applying the categorization method using quartile values (Farmer and Seeley, 2009). The Kaplan–Meier method (Kaplan and Meier, 1958) was used to compare the time to relapse of MDD patients with high HA and those with low HA. The cumulative recurrence rates between the high SD and low SD groups were compared likewise. The proportional hazards model of Cox (1972) was applied to evaluate the effect of possible prognostic predictors in the rate of recurrence. A significance level of  $p < 0.05$  was used. Statistical procedures were performed using the Japanese version of SPSS v15 (SPSS Japan Inc., Tokyo, Japan).

## 3. Results

Of the initial 109 participants, the patients who converted to mania or hypomania ( $n=20$ ) or MCI ( $n=1$ ), transferred to another hospital ( $n=8$ ), terminated medication ( $n=6$ ), died ( $n=1$ ) and who were uncertain regarding recurrence/remission due to missing data ( $n=4$ ) were excluded from the data analyses. In total, 69 patients remained in the study and were followed-up for the whole 4-year period. Table 1 presents demographic variables and TCI scores of initial 109 subjects and final 69 ones.

The highest quartile value of the HA scores of the initial 109 participants was 17.0, and the lowest quartile value of the SD scores was 11.0. Patients whose HA scores were above the upper quartile had a significantly shorter time to recurrence following the remission from a depressive episode as compared to patients with HA scores below the upper quartile (log-rank test,  $\chi^2=6.37$ ,  $p=0.01$ ). The median time to recurrence for the former group was 645 days and for the latter 1301 days. Patients whose SD scores were below the lower quartile had a significantly shorter time to recurrence from remission as compared to patients with SD scores above the lower quartile (log-rank test,  $\chi^2=10.95$ ,  $p < 0.01$ ; see

**Table 1**  
Demographic data and TCI scores of initial and final subjects (recurrence or nonrecurrence separately).

	Initial subjects ( $n=109$ ) Mean (S.D.)	Final subjects ( $n=69$ )	
		Recurrence ( $n=39$ ) Mean (S.D.)	Nonrecurrence ( $n=30$ ) Mean (S.D.)
<b>Demographic data</b>			
Age (years)	55.3 (13.9)	50.5 (14.3)	62.5 (11.4)
Gender (M/F)	47/62	16/23	9/21
Education (years)	12.6 (2.6)	12.8 (2.6)	11.8 (2.1)
MMSE score	26.6 (2.3)	26.8 (2.1)	26.7 (2.6)
Presumed IQ	102.2 (11.4)	101.6 (11.2)	99.1 (11.5)
Onset age (years)	49.4 (14.6)	44.4 (14.3)	58.0 (13.6)
Number of depressive episodes	2.0 (1.3)	2.1 (1.3)	1.4 (0.5)
HAM-D score at admission	20.3 (9.5)	19.4 (8.2)	19.7 (7.5)
HAM-D score at remission	4.1 (3.3)	3.2 (2.8)	5.0 (3.6)
Total duration of depressive phase (months)	28.0 (41.0)	37.2 (60.0)	17.0 (14.0)
Total duration of medication (months)	40.3 (62.5)	48.0 (70.5)	25.9 (30.9)
<b>TCI scores</b>			
NS (Novelty Seeking)	7.6 (2.9)	7.4 (2.5)	7.2 (2.4)
HA (Harm Avoidance)	14.1 (3.8)	15.5 (3.5)	14.0 (2.9)
RD (Reward Dependence)	9.1 (2.5)	8.4 (2.8)	9.2 (2.1)
P (Persistence)	2.2 (1.6)	2.4 (1.7)	1.6 (1.4)
SD (Self-Directedness)	14.9 (5.1)	13.3 (4.7)	15.4 (4.2)
C (Cooperativeness)	16.8 (3.3)	16.0 (3.6)	17.1 (3.6)
ST (Self-Transcendence)	4.0 (2.9)	3.6 (2.5)	4.3 (3.3)

MMSE, Mini-Mental State Examination; HAM-D, Hamilton Rating Scale for Depression; TCI, Temperament and Character Inventory.

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