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The Effect of Temperament on Neurocognitive Function in the Patients with Obsessive-Compulsive Disorder

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Abstract

The Effect of Temperament on Neurocognitive Function in the Patients with Obsessive-Compulsive Disorder

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Background: Converging evidence revealed impaired cognitive function and distinct temperament pattern in obsessive-compulsive disorder (OCD). However, little is known about the relation between cognitive deficit and temperament in OCD. This study was aimed to

investigate how temperament influences cognitive dysfunction in OCD.

Methods: The participants included 103 patients with OCD and 63 healthy controls. Cognitive functions were measured by the Trail Making Test (TMT), letter fluency, category fluency, and the Wisconsin Card Sorting Test (WCST). Temperament was assessed by Cloninger's Temperament and Character Inventory (TCI).

Results: OCD patients showed poor performance in neuropsychological tests related to psychomotor speed, verbal fluency and set-shifting abilities compared to the healthy controls. Regarding temperaments, the OCD patients showed significantly lower novelty seeking and reward dependence and higher harm avoidance than the healthy controls. Temperament pattern affected impaired neurocognitive functions after controlling symptom severity in the OCD patients. And reward dependence partially mediated group differences between patients and controls in psychomotor speed and verbal fluency performances.

Conclusions: Cognitive impairment was influenced by temperament in the OCD patients regardless of their symptom severity. The

present findings suggest that deficits of cognitive functions may be partially explained by temperamental traits of OCD patients.

Keywords: obsessive-compulsive disorder; cognitive dysfunction; temperament; temperament and character inventory (TCI); executive function; reward dependence

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Introduction

Obsessive-compulsive disorder (OCD) is characterized by intrusive thoughts and repetitive behaviors. Previous neuroimaging studies have documented neurological abnormalities in orbitofrontal striatal circuits in OCD (Saxena, Brody, Schwartz, & Baxter, 1998). Consistently with the findings of brain imaging studies, the numbers of studies have showed neurocognitive dysfunction in patients with OCD. Patients with this disorder have impairment in visuospatial functioning (Shin et al., 2010), verbal fluency (Shin et al., 2008) and executive function (Moritz et al., 2002). However, statistical results across early works have been inconsistent in specific cognitive function such as verbal fluency and set-shifting abilities (see Kuelz, Hohagen, and Voderholzer (2004), for a review). Thus, several literatures have focused to detect clinical factors that influenced neurocognitive function in the patients with OCD (Lawrence et al., 2006). The first line of researches have observed that co-morbid symptoms such as depression (Moritz et al., 2001), tic disorder (Muller et al., 2003) and schizotypal personality disorder (Aycicegi,

Dinn, Harris, & Erkmen, 2003) affect cognitive function in patients with OCD. More recent studies have sought to explore relation between symptom subtypes and neuropsychological dysfunction (Cha et al., 2008). Although these early investigation give some clues for understanding of cognitive function in OCD, no study have investigated how some trait-dependent factors influence cognitive deficit in OCD. Many previous studies have reported weak or no association of symptom severity with cognitive function (Cavedini, Cisima, Riboldi, D'Annucci, & Bellodi, 2001; Deckersbach, Otto, Savage, Baer, & Jenike, 2000; Jurado, Junque, Vallejo, Salgado, & Grafman, 2002). Moreover, there has been studies reporting no improvement or deterioration of specific cognitive function such as verbal fluency and visuospatial memory after medication treatment (M. S. Kim, Park, Shin, & Kwon, 2002). These early null observations indicate that some trait-dependent variables would be associated with cognitive function in OCD.

The biopsychosocial model of personality, developed by Cloninger et al.(1993), demonstrated that temperaments can be defined as heritable, being manifested early in life and stable throughout life, whereas character refers to mature in adulthood and

those of affected by social learning and life experiences. The Cloninger's dimensional model proposed four temperament factors and three character factors. The temperament factors include novelty seeking (NS), harm avoidance (HA), reward dependence (RD) and persistence (P), and the character factors include self-directedness (SD), cooperativeness (C), and self-transcendence (ST). This model has been supported by a number of clinical and neurobiology studies (Hansenne & Ansseau, 1999; Herbst, Zonderman, McCrae, & Costa, 2000). In particular, twin studies have indicated that temperaments factors are homogenous, heritable, and independent of one another (Heath, Cloninger, & Martin, 1994).

The Cloninger's model of personality posits that neurotransmitter systems are related to different temperament dimensions, which imply that serotonin systems are linked to HA, dopamine systems to NS and noradrenalin system to RD. This assumption has been supported by recent studies that showed an association of temperament dimensions with specific brain area and neurotransmitters. A few studies observed that the dopamine D4 receptor (DRD4) gene might be related to measure of NS (Munafo, Yalcin, Willis-Owen, & Flint, 2008). Another study indicated that

serotonin 5-HT2 receptor was related to measure of HA. One of primary pathophysiology of OCD patients is serotonergic and dopaminergic dysfunction (Perani et al., 2008). Clinically, serotonin reuptake inhibitors (SSRIs) are used as the first-line of treatment for OCD patients (See for review Dell' Osso et al.,(2005)), and antipsychotics are known to be effective add-on medication for OCD patients resistant to SSRIs (Cavedini, Bassi, Zorzi, & Bellodi, 2004). Consistently with previous evidence on an association between specific temperament dimensions and serotonin and dopamine, several studies reported greater HA dimension in patients with OCD compared to healthy controls (Alonso et al., 2008; Kusunoki et al., 2000; Lyoo, Lee, Kim, Kong, & Kwon, 2001). Studies also found low NS (Alonso et al., 2008; Kusunoki et al., 2000; Lyoo et al., 2001) and high RD (Pfohl, Black, Noyes, Kelley, & Blum, 1990) in OCD patients.

Early literatures have indicated that neurotransmitters link to cognitive function in clinical and non-clinical populations. In healthy volunteers, serotonergic neurotransmitter affects on performances in executive function and verbal memory (Madsen et al., 2011). Patients with psychiatric disorders such as schizophrenia and OCD,

which involve abnormal serotonergic and/or dopaminergic system, showed aberrant function in various cognitive domains (Kuelz et al., 2004; Simpson, Kellendonk, & Kandel, 2010). These prior findings suggested that cognitive dysfunction in patients with psychiatric disorders is related to the pattern of temperament dimensions, and recently, a few of researches have explored links between temperament and personality dimensions and cognitive functioning in patients with psychiatric disorders. Significant association was found between self-directedness and attentional set shifting in antisocial personality disorder (Bergvall, Nilsson, & Hansen, 2003). In schizophrenia patients, the influences of the various temperament dimensions on executive functions differed from healthy controls (Guillem, Pampoulova, Rinaldi, & Stip, 2008). Some temperament reduced the cognitive function difference between schizophrenia and healthy controls, whereas others reversed cognitive differences. Another study showed that RD dimension was associated with worse performance on implicit learning in bulimia nervosa patients (Galderisi et al., 2011). Regarding OCD, no study has investigated the relationship between temperament and neurocognition in OCD. The investigation of relationship between temperament and cognitive

function in OCD helps understanding the roles of temperament on neurocognitive dysfunction, and to clarify previous mixed results in specific cognitive function.

The primary purpose of this study is to investigate the effect of temperament on cognitive function in the OCD patients. Various neuropsychological tasks that assess executive function and verbal ability were employed and temperaments based on the Cloninger's model were measured. We hypothesized that specific temperament would be related to different cognitive dysfunction in OCD patients independently of symptoms.

Methods

Subjects

One hundred three patients with OCD were recruited from clinic in Seoul National University Hospital. The patients were diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders IV (DSM-IV) criteria using the Structured Clinical Interview for DSM-IV (SCID) (First, Spitzer, Gibbson, & Williams, 1996). Sixty of 103 OCD patients were taking medication selective serotonin reuptake inhibitors (SSRIs) such as fluoxetine, sertraline, clonazepam at the time of experiment. The rest of patients had not taken any medication for their symptoms at least within the previous 4 weeks before the time of assessment.

Sixty-three healthy control subjects were recruited via internet advertisement. They evaluated to exclude any current or life-time Axis I or II disorders using the SCID Non-Patients Version (SCID NP) (First, Spitzer, Gibbson, & Williams, 1998). Exclusion criteria for all of participants were mental retardation, substance abuse, neurological disorder, and a history of head injury. Participants in

this study provided written informed consent prior to experiment. This study had approved by the Institutional Review Board at Seoul National University Hospital.

Clinical Measurement and Personality assessment

The severity of OCD symptoms was assessed using the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) (Goodman et al., 1989). The Korean version of the temperament and character inventory (TCI) was used to assess temperament both patients and healthy subjects. The TCI, self report questionnaire, consisted of 240 items to evaluate 4 basic dimensions of temperament, i.e. NS, HA, RD, and P. The reliability and validity of Korean version of TCI were reasonable using a sample of 550 non-clinical subjects with internal consistency Cronbach α of .77 and test-rest reliability of .81. (Sung, Kim, Yang, Abrams, & Lyoo, 2002)

Neuropsychological Test

The Trail Making Test (TMT) (Reitan & Wolfson, 1985) provided measure of attention, psychomotor speed and speed of mental flexibility. This test is comprised of two parts. The part A

evaluates processing speed and attention and the part B measures set shifting and inhibition. The Wisconsin Card Sorting Test (WCST) (Heaton, Chelune, Talley, Kay, & Curtiss, 1993) is used to assess set shifting ability. The letter and category fluency (Kertesz, 1980; Mattis, 1988) tests are to evaluate the spontaneous oral production of words regarding given letter and specific category within 1min. Phonemic verbal fluency was assessed using the Korean version of the Controlled Oral Word Association (COWA) test (Kang, Chin, Na, & Lee, 2000).

To estimate Intelligence, all participants completed the Vocabulary, Arithmetic, Block Design, and Picture Arrangement, which are subtests of the Korean version of the Wechsler Adult Intelligence Scale (K-WAIS)(Wechsler, 1981). The four-subtest short form has been validated for both healthy subjects and psychiatric patient groups in the Korean version (Lee & Kim, 1995).

Statistical Analysis

Demographic characteristic and temperament dimensions were compared using independent sample *t*-tests between OCD patients and healthy controls. For gender differences, the chi-squared test

was used. Neuropsychological performances were compared using multivariate analysis of covariance (MANCOVA) using IQ as covariate because of significant IQ difference between two groups.

Pearson's correlation coefficients were used to measure the relation between temperaments and neuropsychological test in OCD group.

Multiple regression analysis was used to evaluate the influences of temperament on neuropsychological performances in patients. For independent variable, each temperament dimensions that showed group difference was input, and for dependent variables, TMT A, letter fluency, category fluency and WCST category that showed group difference were entered separately. Finally, Baron and Kenny's Casual Step Test (Baron & Kenny, 1986) was carried out to examine whether temperament dimensions mediated differences in neuropsychological performances between patient and control groups. According to Baron and Kenny, all of following conditions must fulfilled to confirm a mediation effect: a) the independent variable (group) must significantly affect the hypothesized mediator (temperament), b) the independent variable must be significantly related to the dependent variable (cognitive function), and c) after

controlling for the mediator, the mediator must significantly describe the dependent variable in the multiple regression equation, including a reduced effect of the independent variable on the dependent variable.

Results

Demographic characteristics in subjects

As shown in Table 1, demographic and clinical characteristics were no significant difference in gender (χ^2=0.05, df=1, P=0.863), age (t=−0.455, df=164, P=0.650), and education (t=0.984, df=164, P=0.326) between patient and control groups, but OCD patients showed significantly lower IQ than healthy control subjects (t=2.607, df=164, P=0.010).

Comparison between patients and controls in temperament and cognitive function

Independent sample t−tests revealed that OCD patients had significantly higher HA score (t=−8.958, df=164, P<0.005) and lower scores in NS (t=3.855, df=164, P<0.005) and RD (t=3.948, df=164, P<0.005) than healthy controls.

MANCOVA for neuropsychological function yielded that patients poorly performed in TMT part A (F=16.361, P<0.005), letter fluency (F=6.317, P=0.013), category fluency (F=11.555, P=0.001)

and WCST categories completed (F=5.086, P=0.025) than did healthy controls (Table 2).

Relations of temperament with cognitive dysfunction

The correlation analysis between temperament and neuropsychological test in patients revealed that NS was significantly related to category fluency (r=0.204, P=0.039) and RD to TMT part A (r=−0.371, P<0.001) and category fluency (r=0.250, P=0.011).

For the next step, multiple regression analysis was performed to examine predictive role of patterns of temperaments on the cognitive dysfunction in OCD subjects after controlling Y-BOCS score. It was found that RD dimension significantly predicted the category fluency (β=0.286, t=2.153, P=0.034) and TMT part A (β=−1.609, t=−4.187, P<0.001) performances in patients (Table 3).

Lastly, we investigated whether RD dimension would explain cognitive differences in category fluency and the TMT A between OCD and healthy controls. For this, three steps for regression analysis of Baron and Kenny was used. For the TMT A, group had

direct effect on the RD (β =−0.295, P<.001). Second, group had a direct effect on TMT part A (β =0.341, P<0.001). Finally, RD had a significant indirect effect on the TMT part A (β =−0.304, P<0.001) with the effect of group being partially dropped (β=0.249, P=0.001). For category fluency, group had direct effect on the RD (β =−0.295, P<.001). Second, group had a direct effect on category fluency (β =−0.306, P<0.001). Finally, RD had a significant indirect effect on the category fluency (β =0.197, P=0.005) with the effect of group being partially dropped (β =−0.258, P=0.001) (Figure 1).

Discussion

The present study is the first study to investigate the relationship between temperament and cognitive dysfunctions in OCD patients. Large sample of OCD patients exhibited deficits in neuropsychological tasks evaluating psychomotor speed and executive function including verbal fluency and set-shifting abilities. Regarding temperaments, patients had low NS and RD and high HA. Our findings are consistent with previous the results (Kuelz et al., 2004; Lyoo et al., 2001), confirming them in the large patient sample. Moreover, we observed that temperament influenced cognitive dysfunction independently of the symptom severity in the patients with OCD. Specifically, RD was an effective predictor of impaired function in psychomotor speed and verbal fluency abilities of patients. These findings suggest that deficits of cognitive functions may partially explained by temperamental traits of OCD patients.

In our study, RD was the only temperament dimension to predict cognitive function in OCD patients. A similar trend was reported in patients with schizophrenia. A study of Guillem et al.(2008)

observed the association between low RD and executive function in patients with schizophrenia. The schizophrenia patients with low RD showed poor functioning in cognitive flexibility, whereas healthy controls with low RD performed better than controls with high RD. The authors suggested that high RD might protect against the executive dysfunction in patients who are withdrawn affectively and behaviorally. RD has been known to be linked to P300 in frontal region (M. S. Kim, Kim, & Kwon, 2001), which is related to dopaminergic system or motivation, and to striatal projections between the prefrontal cortex (Cohen, Elger, & Weber, 2008). The verbal fluency is related to frontal lobe function, especially set-shifting strategies, as well as verbal memory and verbal expression skills (Alvarez & Emory, 2006). Thus, low RD in OCD patients may be associated with decrease of motivation and abnormal brain activity connected with prefrontal lobe, which probably lead cognitive dysfunction such as set-shifting and psychomotor speed. However, this interpretation is speculative, and so future researches are needed to investigate the relationship between RD and neural and psychological systems in OCD patients.

On the other hand, RD defined as the tendency for a positive

response to signal of reward to maintain or resist behavioral extinctions and tendency to put energy to achieve goal (Hansenne et al., 2000). In our study, OCD have shown deficits in category fluency and TMT part A. Category fluency is measured to oral production and it needs a lot of energy and volition to generate words. Failure of category fluency is also shown in the dementia patients, characterized as avolition and low of energy motivation (Janzing, Naarding, & Eling, 2005). Lack of motivation and low energy might cause poor performance in category fluency. Similarly, TMT part A task is to evaluate psychomotor function. Psychomotor retardation is related to depressive symptom and affected by a lack of motivation (Marazziti, Consoli, Picchetti, Carlini, & Faravelli, 2010). The OCD patients poor performance than healthy control in TMT part A task and this results might affected by low RD in OCD. Low RD in OCD could define as lack of motivation and achievement tendency.

In our study, the patients with OCD displayed low NS and high HA. This pattern of temperamental traits has been consistently reported in both Western (Richter, Summerfeldt, Joffe, & Swinson, 1996) and Asian OCD samples (Kusunoki et al., 2000; Lyoo et al., 2001).

Regarding RD dimension, findings are somewhat confused. Pfohl et al.(1990) reported higher RD in the OCD patients but no dramatic difference from healthy controls. In a study of Lyoo et al.(2001), RD score was lower in patients (13.5±4.8) than in controls (14.9±3.4) with a medium effect size (Cohen's *d*=0.34) but the difference did not reach statistical significance due to the small sample size. More recently, Kim et al.(2009) found lower RD in a large sample of OCD patients (N=130), the finding consistent with that of in the current study. RD represents warm social affiliations, distress in response to social separation and sympathy, and sensitivity to social cues (Cloninger, 1994). Cloninger et al.(1993) presupposed association between obsessive-compulsive personality disorder, one of popular co-morbid conditions of OCD, and low RD.

The present study evaluated three kinds of tasks that are measures of executive function. We found impairments in set-shifting and verbal fluency functions in OCD. Previous studies generally employed specific tasks such as the WCST and verbal fluency to evaluate executive function. And, the results from the studies are far from being consistent in OCD. Some studies observed impaired performances when assessing with those tasks (M. S. Kim

et al., 2002; Schmidtke, Schorb, Winkelmann, & Hohagen, 1998; Sieg, Leplow, & Hand, 1999), whereas other studies found no deficit (Boone, Ananth, Philpott, & Kaur, 1991; Jurado et al., 2002; Martinot et al., 1990). Although there has been no clear explanation for these inconsistent findings, early evidence indicate that several clinical factors such as symptom subtypes, other comorbid psychiatric symptoms and onset point of disorder contribute to cognitive heterogeneity in OCD. However, few studies have examined the influence of trait-dependent factors and inherent features such as temperament and personality on executive function in OCD. The current study found the significant association between temperament patterns and cognitive deficit, indicating that temperament can be an effective factor influencing function in cognitive function in OCD.

This study has limitation in the sense that most patients were medicated at the time of assessment. The medication status may affect temperament patterns (Lyoo, Yoon, Kang, & Kwon, 2003) and cognitive function (Meneses, 1999). Therefore, we compared medicated patients group and unmedicated patients group in our sample, and no difference in neuropsychological performance was

found.

In conclusion, we found that the OCD patients has different pattern of temperament compared to healthy controls and these result may cause of cognitive function impairment in OCD patients This study was conducted to increase the understanding of the effect of temperaments in cognitive functions, so that it may help clinicians to select proper treatment for individual patients according to their treatment traits.

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Tables

Table 1. Demographic Characteristics and Clinical variable of OCD patients and Healthy Controls.

	OCD (n = 103)	Controls (n = 63)	*t or* $\chi 2$	*P*
Male/female	72/31	43/20	0.050	.823
Age (years)	27.83(7.74)	27.29(6.83)	−.455	.650
IQ	110.24 (11.03)	114.74 (10.41)	2.607	.010
Education (years)	14.47 (2.13)	14.83 (2.35)	0.984	.326
Y-BOCS				
Obsession	13.41(3.55)			
Compulsion	12.00(4.55)			
Total	25.35(6.53)			

Note. Data are presented as mean (SD). OCD, Obsessive-Compulsive Disorder; Y-BOCS, Yale-Brown Obsessive Compulsive Scale;

Table 2. Result of Temperament and Neuropsychological test between the OCD patients and Healthy Controls.

	OCD (n = 103)	Controls (n = 63)	*t or* $\chi 2$	*P*
Temperaments				
NS	15.95(5.50)	19.35(5.53)	3.86	<.001
HA	25.43(5.96)	16.61(6.46)	−8.96	<.001
RD	13.62(3.74)	15.92(3.47)	3.95	<.001
P	4.48(1.87)	4.92(1.99)	1.422	.157
Neuropsychological Test				
TMT−A (sec)	39.89(14.76)	39.89(14.76)	16.36	<.001
TMT−B (sec)	81.51(37.31)	66.84(32.30)	2.938	.088
WCST PE	14.99(14.46)	13.02(20.77)	.000	.989
WCST CC	4.74(2.02)	5.59(1.17)	5.086	.025
Category fluency	35.17(8.42)	41.37(10.80)	11.555	.001
Letter fluency	34.72(10.15)	40.95(12.90)	6.317	.013

Note. Data are presented as mean (SD). NS, Novelty Seeking; HA, Harm Avoidance; RD, Reward dependence; P, Persistence; TMT−A, Trail−Making Test, Part A; TMT−B, Trail−Making Test, Part B; WCST, Wisconsin Card Sort Test; PE, Perseverative error; CC, Category completed.

Table 3. Regression Analysis to evaluate the influences of temperament on TMT-A in OCD

	R^2	B	β	t	*P*
Y-BOCS Total	.000	-.227	-.100	-1.038	.302
NS		.159	.059	.579	.564
HA		-.003	-.001	-.012	.990
RD	.152	-1.609	-.408	-4.187	<.001

Note. Y-BOCS, Yale-Brown Obsessive Compulsive Scale; NS, Novelty Seeking; HA, Harm Avoidance; RD, Reward dependence.

Figures

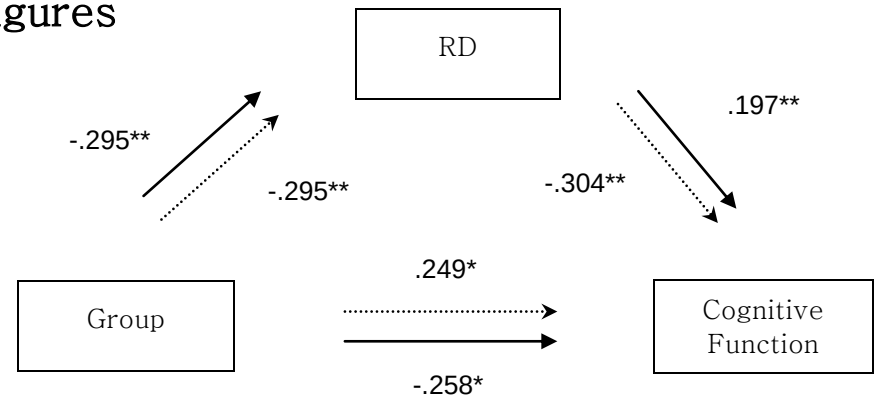

Figure 1. Path diagram of the mediation effect of temperament in cognitive function

—— This line indicated path of the mediation effect of RD in category fluency. The group had a direct effect on category fluency (β =−0.306, P<0.001) which were partially dropped (β =−0.258, P=0.001) after controlled for RD.

····· This line indicated path of the mediation effect of RD in TMT−A. The group had a direct effect on TMT part A (β =0.341, P<0.001) which were partially dropped (β=0.249, P=0.001) after controlled for RD.

Note. Values on paths are standardized β. **P<.001, *P<.01.

국문 초록

배경: 강박장애 환자대상으로 인지기능 손상과 기질적인 측면의 뚜렷한 패턴에 관한 연구 결과들이 그 동안 집중되어 왔다. 그러나 강박장애 환자 내에서 인지기능 결함과 기질적인 측면과의 관련성에 대해 고찰한 연구는 거의 없었다. 이 연구의 목적은 강박장애환자들의 인지적인 결함에 기질적인 측면들이 어떠한 영향을 끼치는지를 알아보고자 하는 것이다.

방법: 강박장애 환자103명과 정상인 63명을 대상으로 Trail Making Test (TMT), 단어 유창성, 범주 유창성 그리고 Wisconsin Card Sorting Test (WCST) 으로 인지기능 측정하였다. 기질적인 측면은 기질 및 특성 (TCI) 사용하여 측정하였다.

결과: 강박장애 환자는 정상인과 비교하여 정신운동성 속도, 언어 유창성, 전환 수행 능력과 관련된 신경심리 검사에서 수행능력이 떨어졌다. 기질적인 측면에서는 강박장애 환자들이 정상인에 비해 자극추구성 (NS), 사회적 민감성 (RD) 낮았고, 위험회피성 (HA)은 높았다. 강박장애 환자들의 증상심각도 통제한 후에도 강박장애 환자들의 기질적인 패턴이 인지기능 손상에 영향을 미치는 것으로 보였다. 그리고 사회적 민감성 (RD)이 부분적으로 정상인과 환자간의 정신운동성 속도와 언어 유창성의 차이를 매개하는 것으로 나타났다.

결론: 강박장애 환자에서 기질적인 측면은 환자의 증상 심각도와 상관없이 인지기능 손상에 영향을 미쳤다. 이 연구에서 강박장애

환자들의 인지기능 손상에 부분적으로 기질적인 측면이 기인하는 것임을 시사해 준다.

주요어: 강박장애, 인지기능 이상, 기질, 기질 및 특성 (TCI), 집행기능, 사회적 민감성(RD)

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