Predictors of response to exposure and response prevention for obsessive-compulsive disorder

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Abstract

Background Cognitive behavioral therapy (CBT), which includes exposure and response prevention (ERP), is effective in improving symptoms of obsessive-compulsive disorder (OCD). However, whether poor cognitive functions and autism spectrum disorder (ASD) traits affect the therapeutic response of patients with OCD to CBT remains unclear. This study aimed to identify factors predictive of the therapeutic response of Japanese patients with OCD to ERP.

Methods Forty-two Japanese outpatients with OCD were assessed using the Wechsler Adult Intelligence Scale-III (WAIS-III), Yale-Brown Obsessive-Compulsive Scale, Patient Health Questionnaire 9-item scale, and Autism Spectrum Quotient (AQ) at pre- and post-treatment. We used multiple regression analyses to estimate the effect on therapeutic response change. The treatment response change was set as a dependent variable in multiple regression analyses.

Results Multiple regression analyses showed that among independent variables, communication skill as an AQ sub-scale and Letter Number Sequencing as a WAIS-III sub-test predict the therapeutic response to ERP.

Conclusions Our results suggest that diminished working memory (Letter Number Sequencing), poor communication skill may undermine responsiveness to ERP among patients with OCD.

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Background

Obsessive-compulsive disorder (OCD) is a psychiatric disorder characterized by repeated compulsive and obsessive behavior, and its 12-month prevalence in the world is 1.1 to 1.8% (DSM-5) [1]. The administration of selective serotonin reuptake inhibitors and cognitive-behavioral therapy (CBT) are first-choice treatments for OCD [2]. With a treatment response change of approximately 45 to 70% [2, 3], the efficacy of the latter has been demonstrated [4–6]. However, about 20% of OCD remains unresponsive to CBT [3]. Numerous studies have been conducted on cognitive functions of individuals to account for their lack of response to CBT [7–10]. Neuropsychological functioning has so far been studied as a predictor of the responsiveness of patients with OCD to CBT, but the results are inconsistent [7–10]. Predictor variables can be classified into eight categories: demographic variables; OCD symptom characteristics such as severity; comorbidities and associated symptom severity; cognitive influences; motivational factors such as treatment expectations; treatment factors such as compliance and therapeutic alliance; biological factors; other factors such as personality, family dysfunction, and treatment-specific characteristic [11, 12].

Previous studies have suggested that responses to CBT are diminished among patients whose symptoms overlap with autism spectrum disorder (ASD) criteria [13, 14]; treatment resistance may thus be attributable the presentation of ASD characteristics. Moreover, a heightened severity of obsessive-compulsive symptoms at the first clinical visit has been associated with poor prognosis [15], and severe major depressive disorder has been shown to inhibit therapeutic response to CBT [16]. It has also been suggested that the severity of obsessive-compulsive symptoms and beliefs may influence the response to CBT treatment [17]. Conversely, several previous studies have concluded that complications such as depression and anxiety do not affect treatment responsiveness to ERP and CBT [18–21]. Therefore, no conclusions have been reached regarding treatment response of CBT for patients with OCD, and further research is needed to identify predictors of response to ERP.

Furthermore, no studies have examined the factors that affect treatment effects including the full-version of the WAIS for patients with OCD. Specifying people that need an adapted treatment strategy is very important, and it is necessary to specify predictors of treatment response. Here, the present study aimed to elucidate factors related to therapeutic responses to CBT, focusing on ASD propensity, cognitive function, OCD severity, and depression severity.

Methods

Study Design

The present study was included patients who visited the Cognitive Behavioral Therapy Center of Chiba University between March 2013 to May 2018; it included 106 patients who were diagnosed with OCD by a psychiatrist using the Structured Clinical Interview for DSM-IV Axis I Disorders [22]. The exclusion criteria were any organic central nervous system disorder, psychosis, intellectual disability, high risk of suicide, substance abuse or dependence, or unstable medical condition; patients for whom cognitive function could not be measured in terms of outcomes and those who did not complete the ERP intervention were also excluded. A total of 66 patients were therefore excluded, so that eventually 42 patients (mean age = 33.2 years, standard deviation = 7.6 years, female = 26, male = 16) with OCD were included in the analysis (Fig. 1).

Intervention

CBT was performed on patients with OCD according to a treatment manual created by our research group designed for adult outpatients with OCD [23]. The modules were derived from previous studies on in-person ERP for OCD in Japan; these modules included psychoeducation, exposure exercises, and homework assignments [6]. Sixteen CBT sessions of 50 minutes in length were scheduled each week. All therapists who participated in this study completed the Improving Access to Psychological Therapies project at Chiba University [24]. The quality of CBT was controlled through weekly group supervisions led by a psychiatrist.

Outcomes

Yale-Brown Obsessive-Compulsive Scale

To assess the severity of the obsessive-compulsive symptoms, we used the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) [25, 26]. This scale consists of 10 items (5 obsessions and 5 compulsive items). The questionnaire items are scored on a 4-point Likert-scale; with 0 = no symptoms to 4 = extreme symptoms. The total score range is 0–40, with individual subtotals for obsessions and severity of obsessions. This scale was used in a semi-structured interview setting.

Obsessive-Compulsive Inventory

The Obsessive-Compulsive Inventory (OCI) consists of 42 items and is a 5-point Likert-scale [27, 28]. It consists of seven subscales (washing, checking, doubting, ordering, obsessions, hoarding, and neutralizing).

Patient Health Questionnaire-9

The presence and severity of symptoms of depression experienced in the previous 2 weeks were evaluated using the Patient Health Questionnaire-9 (PHQ-9) [29, 30]. The self-administered questionnaire items are scored on a 4-point Likert-scale; with 0 = not at all to 3 = almost every day. The total score range is 0–27 (0 to 4 indicates no symptoms, 5 to 9 indicates mild symptoms, 10 to 14 indicates moderate symptoms, 15 to 19 indicates moderate to severe symptoms, and 20 to 27 indicates severe symptoms). The cut-off score for clinically significant symptoms of depression is 10.

Autism-spectrum Quotient

Autism-spectrum Quotient (AQ) is a self-managed instrument that can use any of the dichotomous evaluations to measure autistic characteristics [31, 32]. The total score range is 0–50. It consists of five subscales (social skills, attention switching, attention to detail, communication, and imagination). The cut-off score for clinically significant symptoms of ASD is 33.

Wechsler Adult Intelligence Scale-third edition

The Wechsler Adult Intelligence Scale-third edition (WAIS-III) is a comprehensive test of intellectual functioning [33, 34]. A total of 13 subtests assessing either verbal IQ (VIQ) or performance IQ (PIQ) were administered to patients with OCD. The subtests evaluating VIQ included Vocabulary, Similarities, Information, Comprehension, Arithmetic, Digit Span, and Letter-Number Sequencing; those assessing PIQ included Picture Completion, Block Design, Matrix Reasoning, Visual Puzzles, Digit Symbol Coding, and Symbol Search. The Object Assembly subtest was excluded from the present analysis because it has a lower confidence factor than the other subtests [35]. The aforementioned subtests were grouped into the following four indices: VCI (Vocabulary, Similarities, and Information), POI (Picture Completion, Block Design, Matrix Reasoning), WMI (Digit Span and Arithmetic, and Letter-Number Sequencing), and PSI (Symbol Search and Digit Symbol Coding).

Statistical Analysis

The statistical analysis was performed using SPSS Statistics, version 26.00 (IBM Corp., Armonk, NY, USA). To investigate the predictive effects that patient pretreatment background may have had on the treatment response change post treatment, a series of analyses were performed. First, the treatment response change was obtained in terms of the difference between pre- and post-treatment Y-BOCS scores. Next, Pearson correlation coefficients were used to investigate the factors affecting the CBT response change and to explore the relationships between such changes and other clinical variables including age, sex, severity of obsessive-compulsive symptoms in Y-BOCS at pretreatment, the traits associated with the autistic spectrum in AQ total scores or its sub-scales, intelligence index in WAIS-III or its sub-tests, OCI total score or its sub-scales, and severity of depression in PHQ-9. Finally, forward stepwise regression analysis was performed with the variables that remained significant in the correlation analysis as independent variables and the CBT response change as the dependent variable.

Results

Demographic and clinical characteristics and WAIS scores of patients with OCD are shown in Table 1. The correlations between the CBT response change and other clinical variables in OCD group are presented in Table 2. Significant differences in the CBT response change were observed according to sex ($p = 0.017$), Attention switching ($p = 0.029$), Communication ($p = 0.026$), and Letter Number Sequencing ($p = 0.005$). No significant correlation was found between the CBT response change and any other clinical variable. Multiple regression analysis was performed with sex, communication skill, attention switching, and Letter Number Sequencing as explanatory variables and the CBT response change as the dependent variable. Multiple regression analyses showed that communication skill as an AQ sub-scale and Letter Number Sequencing as a WAIS-III sub-test were significant predictors of CBT response (Table 3).

Table 1
Characteristics and WAIS scores in patients with OCD

	OCD	
	Mean ± SD	N
No. (male/female)	42 (16/26)	
Age [b]	33.19 ± 7.55	42
Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) (pre) Total	26.68 ± 4.49	42
Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) (post) Total	16.00 ± 8.18	42
CBT response change	10.26 ± 7.86	42
Obsessive Compulsive Inventory (OCI)		
Washing	18.59 ± 10.81	39
Checking	16.62 ± 9.14	39
Doubting	7.10 ± 4.08	39
Ordering	6.85 ± 4.62	39
Obsessions	14.26 ± 5.61	39
Hoarding	3.36 ± 3.17	39
Neutralizing	7.62 ± 5.01	39
Total	74.30 ± 26.18	40
Patient Health Questionnaire-9 (PHQ-9)	12.20 ± 5.83	41
Autism Spectrum Quotient (AQ) AQ		
Social skill	5.13 ± 2.60	40
Attention switching	6.20 ± 2.04	40
Attention to detail	5.32 ± 1.82	40
Communication	3.95 ± 2.67	40
Imagination	4.08 ± 2.38	40
Total	24.68 ± 7.76	40
Wechsler Adult Intelligence Scale-III		
Full-scale intelligence quotient (FSIQ)	100.95 ± 10.90	42
Verbal IQ	102.43 ± 11.51	42

	OCD	
Performance IQ	98.88 ± 11.40	42
Indices		
Verbal Comprehension Index (VCI)	100.95 ± 11.77	42
Perceptual Organization Index (POI)	100.45 ± 12.86	42
Working Memory Index (WMI)	98.26 ± 16.30	42
Processing Speed Index (PSI)	91.17 ± 17.13	42
Subtests		
Vocabulary	10.52 ± 2.44	42
Similarities	10.55 ± 2.47	42
Information	9.38 ± 2.47	42
Comprehension	12.10 ± 2.99	42
Arithmetic	9.69 ± 2.67	42
Digit Span	10.99 ± 3.06	42
Letter Number Sequencing	9.86 ± 3.43	42
Visual Puzzles	10.48 ± 2.80	42
Picture Completion	9.67 ± 2.81	42
Block Design	9.67 ± 3.21	42
Matrix Reasoning	11.12 ± 2.60	42
Digit Symbol Coding	8.69 ± 2.97	42
Symbol Search	9.05 ± 2.62	42

Table 2

Correlations between CBT response change and other clinical indices in OCD

	N	r	p-value
Age	42	0.12	0.455
Sex[a]	42	0.37*	0.017
Autism-Spectrum Questionnaire (AQ)			
Social skill	40	-0.08	0.621
Attention switching	40	-0.35*	0.029
Attention to detail	40	0.07	0.674
Communication	40	-0.35*	0.026
Imagination	40	-0.09	0.600
Total	40	-0.25	0.120
Y-BOCS (pre) Total	42	0.18	0.249
Obsessive Compulsive Inventory (OCI)			
Washing	39	0.18	0.264
Checking	39	-0.23	0.161
Doubting	39	-0.17	0.295
Ordering	39	0.00	0.994
Obsessions	39	-0.10	0.529
Hoarding	39	-0.22	0.186
Neutralizing	39	-0.06	0.726
Total	40	-0.09	0.562
PHQ-9	41	-0.23 -0.026	0.142
Full-scale intelligence quotient (FSIQ)	42	0.08	0.621
WAIS-III Subtests			
Vocabulary	42	0.17	0.269
Similarities	42	0.00	0.981
Information	42	-0.01	0.955

	N	r	p-value
Comprehension	42	0.05	0.740
Arithmetic	42	0.13	0.431
Digit Span	42	0.07	0.699
Letter Number Sequencing	42	0.42**	0.005
Visual Puzzles	42	-0.14	0.365
Picture Completion	42	-0.10	0.539
Block Design	42	0.15	0.333
Matrix Reasoning	42	-0.13	0.418
Digit Symbol Coding	42	0.21	0.178
Symbol Search	42	0.04	0.792

*p < 0.01, **p < 0.05
Abbreviations: OCD, obsessive-compulsive disorder; Y-BOCS, Yale-Brown Obsessive-Compulsive Scale; PHQ-9, Patient Health Questionnaire-9; GAD-7, Generalized Anxiety Disorder-7.
[a]Female=1. Male = 0

Table 3
Results of stepwise regression analyses on response to ERP

Dependent variable	Independent variable	Adjusted R^2	β	p-value
Response	Communication skill	0.33	-0.44**	0.002
	Letter Number Sequencing		0.50**	0.001

**p < 0.01

Discussion

Primary Finding

The present study investigated whether clinical symptoms and cognitive functions are predictive of differential therapeutic response to CBT among patients with OCD. We found that the CBT response change was affected by diminished complex working memory and poor communication skills in Japanese participants with OCD.

Comparison with Previous Studies

A retrospective study of randomized control trials assessing 108 obsessive-compulsive patients receiving selective serotonin reuptake inhibitors reported that co-morbidity and low quality of life (QOL) affected treatment response [37]; however, in a study by Matsumoto et al. (2019), QOL, assessed using EQ-5D, was not detected as a predictor of treatment response to psychiatric disorders, including OCD [38]. The results of the present study suggest that depressive mood severity was excluded, but that partial ASD propensity impairs treatment response. Since QOL has not been measured in the present study, it is desirable to set it as an explanatory variable in future studies.

Previous studies have suggested that CBT for obsessive-compulsive disorder with ASD is effective [39], but that the response to ERP is relatively poor [14]. The novelty of this study was that the ability to communicate in AQ predicted treatment response. Without good communication, it is difficult to set appropriate therapeutic goals and exposure tasks. Therefore, it is natural that communication disorder, one of the core disorders in ASD [1], impairs treatment response.

The results of this study do not suggest that OCI's sub-tests predict of response to ERP. A subtype of obsessive-compulsive disorder, the hoarding state, was reported to reduce patient outcomes due to adherence [40]. Additionally, a previous study showed that reductions in obsessive beliefs influenced improvements in patients with OCD [41], which are inconsistent with the results of the present study. Previous studies suggested the importance of focusing on insights into the need for motivation and therapeutic intervention for patients to comply with ERP [42]. Patient consensus on therapeutic goals and tasks is probably also an important factor in implementing ERP [38]. When patients with OCD have poor executive function, they cannot understand their problem or conduct and complete ERP tasks appropriately. The present study did not measure patients' adherence to ERP or the degree of agreement on treatment. Future research should consider these as well.

The results of the present study suggested that a subtest of working memory, "Letter Number Sequencing," predicts treatment response. This suggests that the executive function, including working memory, of obsessive-compulsive patients undergoing CBT or ERP may predict responsiveness. When patients with OCD have poor executive function, they cannot understand their problem or conduct and complete ERP tasks appropriately. A previous brain imaging study showed that abnormalities in the left dorsolateral prefrontal cortex, a region that has been implicated in working memory [43], negatively affect CBT outcomes [14]. Mental flexibility, as measured using the California Verbal Learning Test, was predictive of a good response to CBT; in contrast, it was interesting to note that fluoxetine responsiveness was impaired [44]. Executive function weakness is also known to affect treatment response [44–46]. The present study, for the first time in the world, has found that a WAIS-III full-version subtest, Letter Number Sequencing, predicts the response of ERP treatment in obsessive-compulsive patients. Letter Number Sequencing is a simple test that can be performed in about 5 to 10 minutes. Therefore, clinicians and cognitive behavioral practitioners may be able to estimate response to treatment based on the results of WAIS-III Letter Number Sequencing and AQ communication skills score before conducting ERP in obsessive-compulsive patients.

This study had several limitations. First, while our findings implicate ASD traits as a risk factor affecting the treatment response change, cohort studies have shown that OCD is predicted by beliefs such as intolerance to uncertainty [47]. Since patients with ASD are characterized by intolerance to uncertainty, it remains unclear whether ASD traits itself is a risk factor or whether the intolerance to uncertainty accounts for the lower responsiveness to CBT. To clarify this point, it will be necessary to also use the Obsessive Belief Questionnaire in future investigations. Second, in the future, more detailed assessments, including the Autism Diagnostic Observation Schedule, Second Edition will be needed for the differentiation of ASD [48]. Third, the effects of the participants' medication were not included, because their administration was changed according to their condition during CBT, though we asked the physicians to maintain the medication content and dose constant as much as possible. Research that regulates the content of pharmacotherapy should be conducted in the future.

Conclusions

Our results suggest that diminished working memory (Letter Number Sequencing), and poor communication skills may undermine responsiveness to ERP among patients with OCD. The corresponding predictors (working memory, communication skills) of response to ERP explain 33% of the responsiveness to CBT among patients with OCD. To validate our findings and overcome the limitations of this study, future research should also consider the intolerance to uncertainty and the quality of CBT.

Abbreviations

OCD
Obsessive Compulsive Disorder
CBT
Cognitive Behavioral Therapy
ERP
Exposure and Response Prevention
WAIS-III
Wechsler Adult Intelligence Scale-III
ASD
Autism Spectrum Disorder
Y-BOCS
Yale-Brown Obsessive-Compulsive Scale
PHQ-9
Patient Health Questionnaire-9
AQ
Autism-Spectrum Questionnaire

Declarations

Ethics approval and consent to participants

Written informed consent was obtained from all participants prior to the assessments, and ethical approval for the present study was granted by the ethics committee of Chiba University (study number 2120). The present study was registered (clinical trial number UMIN000024087) with the University Hospital Medical Information Network Center. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and/or analysed during the current study are available in the [OSF] repository, [https://osf.io/m7hxb/]

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

SH designed the study, analyzed the data, and wrote the manuscript. AT conducted the neuropsychological examinations and critically revised the manuscript for intellectual content. MNi conducted neuropsychological examinations. YHa conducted neuropsychological examinations and contributed to the management of the research. TY contributed to the management of the research and conducted neuropsychological examinations. JT contributed to the management of the research. MNa contributed to the funding and administration of the research. SO, HA, and KM critically revised the manuscript for intellectual content. ES discussed the study results and contributed to the final manuscript. YHi contributed to the overall supervision of the study and the development of the conclusions. All authors read and approved the final manuscript.

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Figures

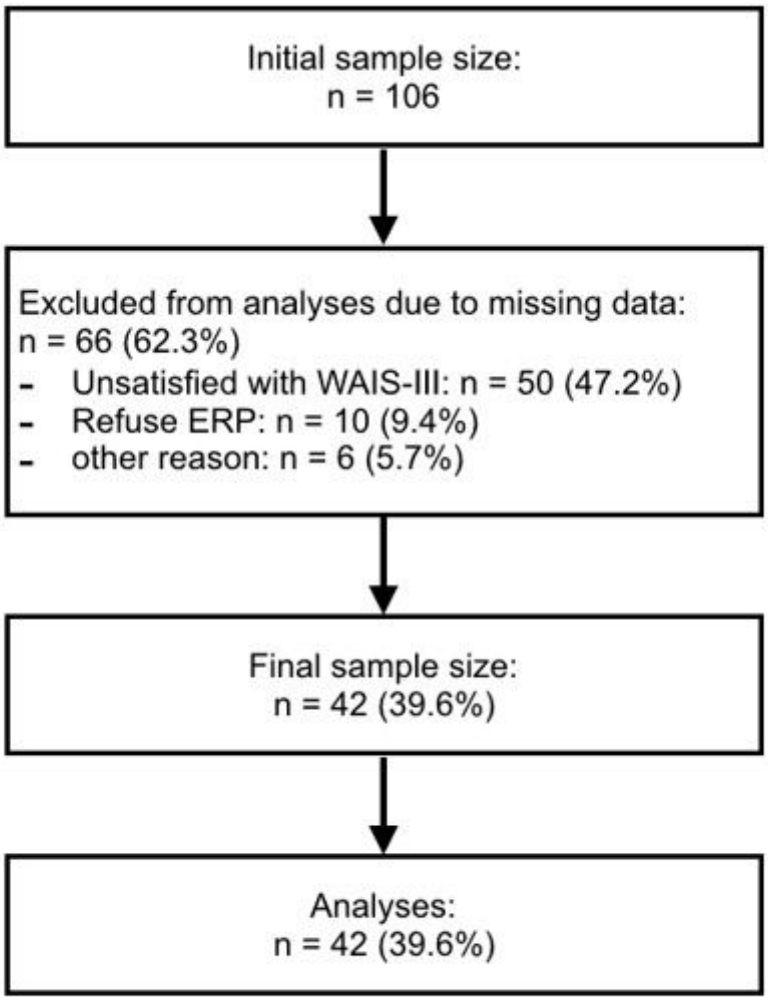

Figure 1

Patient flow