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Altered prefrontal beta oscillatory activity during removal of working memory in obsessive-compulsive disorder

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Altered prefrontal beta oscillatory activity during removal of working memory in obsessive-compulsive disorder

Directed by Professor Se Joo Kim

The Doctoral Dissertation
submitted to the Department of Medicine,
the Graduate School of Yonsei University
in partial fulfillment of the requirements for the degree
of Doctor of Philosophy

Young Jun Boo

June 2022

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ABSTRACT

Altered prefrontal beta oscillatory activity during removal of working memory in obsessive-compulsive disorder

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(Directed by Professor Se Joo Kim)

Obsessive-compulsive disorder (OCD), a chronic illness characterized by recurrent intrusive thoughts and repetitive behaviors, is closely related to working memory impairment. Among the several processes of working memory, the removal process of working memory could be one of the candidates associated with the pathophysiology of OCD. However, little is known about brain activities during the removal process of working memory in OCD. Our goal was to explore the deficit in inhibitory function related to working memory processes in patients with OCD by analyzing differences between patients with OCD and healthy controls in prefrontal alpha and beta oscillatory activities during the multiphase information processes of working memory processes, especially in post-trial period which is presumed to be related to the removal process of working memory. We recruited 16 patients with OCD and 20 healthy controls, and we used magnetoencephalography with a delayed matching-to-sample task (DMST) in this study. The results showed that increases in beta oscillations over the bilateral prefrontal cortex during the post-trial period after the response were significantly reduced in patients with OCD, compared to healthy controls. No significant difference in alpha oscillatory activities during the encoding, retention, retrieval, and post-trial periods was observed. In addition, the change in beta power during post-trial period negatively correlated with the obsessive-compulsive inventory-revised total score in patients with OCD. This finding suggests that inhibitory function related to removal of working memory is altered in the patients with

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OCD. Impairment in the removal of working memory may be a key mechanism to explain why the obsessive thoughts recurrently intrude into mind in patients with OCD.

Key words: obsessive-compulsive disorder, removal of working memory, delayed matching-to-sample task, beta oscillations, magnetoencephalography

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I. Introduction

Obsessive-compulsive disorder (OCD) is characterized by recurrent intrusive thoughts that are hard to ignore or suppress (obsession) and repetitive behaviors that occur as a response to the obsessive thoughts (compulsion).[1] Impaired working memory has been considered as one of the possible candidates related to the pathophysiology of OCD.[2] Working memory is a temporary storage system of information that operates while actively thinking so that working memory process reflects the thought process currently working in the mind.[3] Although previous neuropsychological studies of encoding, retention and retrieval of working memory processes have suggested some working memory deficits in OCD, the findings are controversial.[4-6] Electroencephalography (EEG) study on the encoding of working memory showed differences in alpha changes between patients with OCD and healthy controls.[6] In contrast, a magnetoencephalography (MEG) study using the delayed matching-to-sample task (DMST) showed no difference in alpha power change during the encoding process of working memory.[4] Instead, the study showed that modulation of alpha power in the prefrontal area after distractor presentation was significantly reduced in the patients with OCD than in the controls, suggesting difficulty in inhibiting irrelevant or distracting information in OCD.[4]

In addition to encoding, retention, and retrieval processes, removal of encoded

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working memory has emerged as one of the working memory processes of interest.[7-10] Removal of working memory is defined as the clearing of information when it becomes no longer needed.[10,11] Impaired removal of working memory information is related to the failure to remove negative information that is source of negative thoughts.[12,13] Therefore, deficits in working memory removal cause the rumination on negative thoughts which patients with OCD commonly suffer.[12-14] In patients with OCD, a few studies have reported for removal of working memory.[15-19] However, these findings were inconclusive. Moreover, previous studies focused on the removal of encoded working memory in patients with OCD were based mostly on behavioral tasks without an evaluation of brain activities during removal. Since analyzing brain activities with psychological tasks has been considered more objective than behavioral studies performed only with tasks, evaluating brain activities during the removal of working memory might be meaningful.[20]

In working memory removal, the prefrontal cortex plays an important role in its function of control during working memory processing.[3,21,22] Recently, the inhibitory function of prefrontal beta oscillatory activity in working memory removal have been reported.[22] The prefrontal beta power increased to remove working memory at the end of the trial in working memory task as the encoded information became no longer needed after response.[22] In contrast to the prefrontal cortex, associations of other brain regions with working memory removal have not been reported yet, although other regions including parietal cortex and sensory cortices are known to have function in working memory.[3] In addition, the prefrontal cortex has been suggested to be related to the pathophysiology of OCD,[23] especially with working memory impairment in patients with OCD.[24] Therefore, evaluating prefrontal activities during working memory removal might be helpful for expanding our understanding of the pathophysiology of OCD.

Magnetoencephalography (MEG) has advantages in temporal resolution

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compared to functional magnetic resonance imaging (fMRI), and MEG reflects brain electrical activity and thus MEG could record more precise brain activity than fMRI since fMRI only records hemodynamics.[25] MEG also has greater spatial resolution than EEG, therefore MEG makes it possible to set the regions of interest more precisely. Therefore, recording prefrontal activities with MEG is advantageous compared with other brain evaluation methods.

The present study aimed to examine prefrontal alpha and beta oscillatory activities using MEG during the multiphase information processes of working memory with a case-control design of OCD. In particular, we analyzed the post-trial period, which could represent working memory removal, in addition to three distinct phases of encoding, retention, and retrieval during DMST, a working memory task. We hypothesized that the prefrontal alpha and beta power increases during the post-trial period would be altered in patients with OCD compared to healthy controls.

II. Materials and methods

1. Study participants

We recruited 16 patients with OCD (mean age = 23.56 years, SD 2.37 years, 16 men) from the Psychiatry Department of Severance Hospital in Seoul, South Korea and 20 healthy controls (mean age = 22.50 years, SD = 2.40 years, 20 men) through internet advertising. We included only young male participants to control for any effects due to sex and age. All of the participants were right-handed, and their ages ranged from 20 to 29. The diagnosis was made according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) by a trained psychiatrist to determine if the participants were qualified to enroll in this study. Patients with psychotic disorders, substance-related disorders, cognitive impairment, or severe neurological/medical illnesses were excluded. We obtained written informed consent under the ethics guidelines of the Institutional Review

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Board of Yonsei University (IRB number: 1-2011-0088) and the Declaration of Helsinki.

2. Clinical assessment

A. Montgomery-Åsberg depression rating scale (MADRS)

We used the Korean validated version of the Montgomery-Åsberg depression rating scale (MADRS) to assess the severity of depressive symptoms in all of the participants.[26,27] The MADRS consists of clinician-administered 10 diagnostic items including various depressive symptoms.

B. Yale-Brown obsessive compulsive scale (Y-BOCS)

The Yale-Brown obsessive compulsive scale (Y-BOCS) has been used to evaluate obsessive-compulsive symptoms in patients with OCD.[28,29] The Y-BOCS is a validated clinician-administered scale which consists of 10 items used to assess the severity of obsessive and compulsive symptoms.

C. Korean version of the obsessive-compulsive inventory-revised (OCI-R-K)

We used the Korean version of the obsessive-compulsive inventory-revised to evaluate obsessive-compulsive symptoms in patients with OCD and healthy controls.[30] This self-report scale includes 18 items to assess distress related to obsessions and compulsions.

3. Delayed matching-to-sample task (DMST)

The DMST, a working memory task, was conducted [Figure 1]. It has advantages in evaluating brain activities during working memory processing

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since working memory processing mechanisms, including encoding, retention, and retrieval, could be separated in the task.[22] The task consists of two sets of objects presented separately, and subjects are asked to respond whether the delayed presented object matches the previously presented object.[31] As reported in a previous EEG study,[22] analyzing the post-trial period of the DMST will inform its ability to remove memory information that is no longer needed after working memory retrieval.

Task cue design referred to a previous OCD study in visuospatial working memory using MEG.[4,5] The task consisted of 120 pseudo-randomly presented trials. Each trial started with a small red cross for 2000 ms. After that, a 5×5 square with 3 black-colored squares was shown for 1000 ms. Then 3000 ms delay period was given. The probe consonant was shown for 2000 ms. Participants were asked to respond as quickly and accurately as possible whether the probe shows one of the black squares previously shown or not. Feedback on the answer and accuracy rate was presented for 1000 ms at the end of each trial. The participants performed 10 practice trials before the task.

Accuracy and reaction time were obtained from the DMST to evaluate the behavioral performances of the participants.

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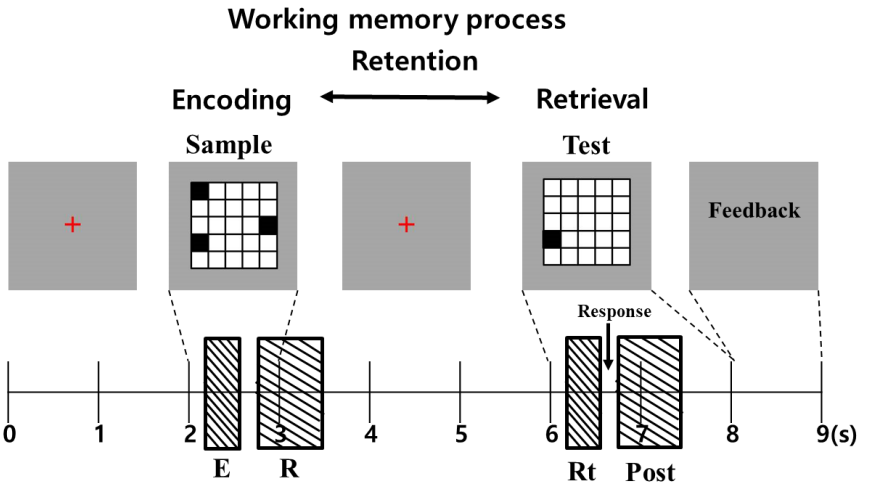

Figure 1. Delayed matching-to-sample task used in the study. The boxes indicate the time window of interest related to each period of working memory processing (E, encoding period; R, retention period; Rt, retrieval period; Post, post-trial period).

4. MEG recordings

A 152-channel whole-head MEG (Korea Institute of Standards and Science; KRISS, Daejeon, Korea) was used to record magnetic fields induced by brain electrical activities. Participants were asked to sit in a magnetically shielded room (Yonsei University Health System, Seoul, Korea). Resting-state recordings were taken under 3 min eyes-closed conditions and 3 min eyes-opened conditions. After that, all participants were asked to perform the DMST with MEG recordings. Magnetic fields were recorded at a sampling rate of 1000 Hz with a bandpass filter between 0.1 and 100 Hz.

5. MEG data preprocessing

Resting-state recordings were taken only to confirm the reliability of the data and were not used in further analysis. All preprocessing procedures were performed with CURRY 8 (Compumedics, Charlotte, NC, USA) software. First,

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the baseline of the recording was corrected by subtracting the overall mean of each channel from itself. Gross-movement artifacts and other muscle related noises were identified by a trained specialist and rejected from further analysis. Epochs were extracted for -300~1500 ms from each sample cue and testing cue. Only trials with correct answers were included in the analysis.

6. MEG data analysis

A. Spectral analysis

To measure the spectral power, an event-related spectral perturbation (ERSP) analysis was applied to the recorded MEG signals. ERSP was calculated using functions implemented in EEGLAB.[32] Spectral power was calculated using the short time Fourier transform every 5 ms with a Hanning window size of 250 ms for each trial. No smoothing or filtering process was applied when generating the resultant ERSP maps. The power spectrum of each trial was then normalized against the average power of the partial baseline period (-300 to -100 ms before the sample cue and test cue) and to probe for changes in the spectral power values after the onset of the sample cue and test cue. The normalized spectral power was then averaged over the trials, and baseline-normalized ERSP maps for each group of participants were created.

B. Oscillations of interest determination

Alpha and beta power for each condition were estimated for a frequency range of 8 to 13 Hz for the alpha based on previous studies on encoding, retention, and retrieval of working memory in patients with OCD,[4,6] and 20 to 35Hz for the beta frequency bands based on a previous report on working memory removal in DMST.[22]

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C. Time window of interest determination

The time window of the post-trial period was based on the response time of the participants [Table 2]. In a study on brain activities during working memory processing, beta bursts related to working memory removal started to increase around the response.[22] Other periods except the post-trial period were analyzed to confirm their consistency with a previous study on brain activities during working memory processing.

From the sample cue, the encoding period (300~600 ms) and retention period (650~1500 ms) were set. From the test cue, retrieval period (300~600 ms) was set. We set 650~1500ms after test cue as post-trial period [Figure 1].

D. Region of interest determination

We included 20 sensors each in the bilateral prefrontal area and set the left/right prefrontal region of interest (ROI) [Figure 2]. Since beta oscillation is related to motor planning extinction in the motor cortex, we tried not to include sensors near the premotor area.[21] Among the sensors in the left prefrontal ROI, 2 sensors in the left prefrontal ROI were highly affected by eye movements and 1 sensor was defective. Among the sensors in right prefrontal ROI, 3 sensors were highly affected by eye movements. These sensors were excluded from the analysis.

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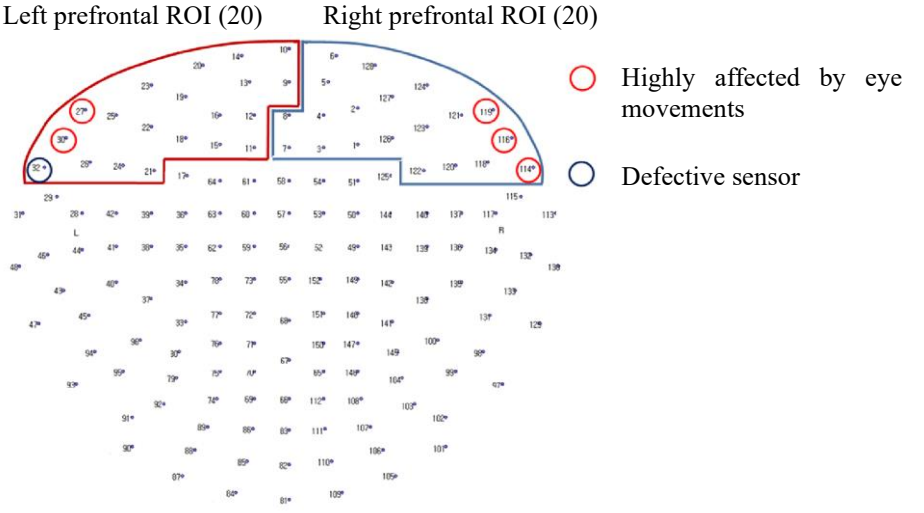

Figure 2. Channel locations and defined regions of interest (left/right prefrontal regions). ROI, region of interest.

7. Statistical analysis

All statistical analyses were performed with SPSS (version 26.0). Demographic and clinical data, including age, Y-BOCS and MADRS scores, were tested with independent sample t-tests to compare patients with OCD and healthy controls. The behavioral performance data of the DMST, including the accuracy of the response, and the reaction time, were also tested with independent sample t-tests to compare patients with OCD and healthy controls. If the demographic, clinical, or behavioral performance variables were not normally distributed, demographic and clinical variables of patients with OCD and healthy control were compared using with two-tailed Mann-Whitney U test. The statistical threshold was set at $p < 0.05$.

For spectral analysis, repeated-measures multivariate analysis of covariance (MANCOVA) was performed to compare the mean power changes in decibel (dB) between the patients with OCD and healthy controls, with hemisphere (left prefrontal ROI vs. right prefrontal ROI) as the repeated factor, group (patients

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with OCD vs. healthy controls) as the between-subjects factor, and period (E, encoding; R, retention; Rt, retrieval; Post, post-trial) for each oscillation (alpha, beta) as the within-subjects factor. The MADRS score was included in the analysis as a covariate to control for the effects of depressive symptoms. For the significant results from MANCOVA, post-hoc analysis of covariance (ANCOVA) was performed. For post-hoc ANCOVA, we adjusted the significance threshold with the Bonferroni approach at $p < 0.00625$ (i.e., 0.05/8 for alpha, and beta oscillations in 4 periods). We calculated values of partial eta squared as the effect size, and the values were interpreted according to Cohen's proposal about partial eta squared: small ($\eta_p^2 = 0.01$), medium ($\eta_p^2 = 0.06$), and large ($\eta_p^2 = 0.14$).[33] In addition, partial correlation coefficients (r) controlling for MADRS scores were calculated between significant results from post-hoc ANCOVA and obsessive-compulsive symptom severity scores (Y-BOCS and OCI-R-K) in patients with OCD. Scattered plots of partial correlation analysis were created.

III. Results

1. Demographic and behavioral data

The demographic data are presented in Table 1. Age differences between the patients with OCD and healthy controls (HC) were not statistically significant (OCD = 23.56 vs. HC = 22.50; $p = 0.192$). The MADRS score was significantly higher in the patients with OCD (OCD = 14.56 vs. HC = 2.95; $p < 0.001$).

The behavioral performance results of the DMST are presented in Table 2. The accuracy rate was not different between the patients with OCD and healthy controls (OCD = 91.81 vs. HC = 94.00; $p = 0.128$). The reaction time was significantly longer in the patients with OCD (OCD = 765.91 vs. HC = 662.03; $p = 0.027$).

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Table 1. Demographic and clinical characteristics of patients with OCD and healthy controls (mean±standard deviation)

	OCD (n = 16)	HC (n = 20)	t(z)	p
Age (years)	23.56±2.37	22.50±2.40	1.330[a]	0.192
MADRS	14.56±8.97	2.95±4.12	4.055[b]	<0.001***
OCI-R-K	38.50±18.63	16.85±12.09	4.213[a]	<0.001***
Y-BOCS	17.69±7.85			
Use of SSRI, n (%)	15/16 (94%)			
Use of Benzodiazepine, n (%)	8/16 (50%)			

OCD, obsessive-compulsive disorder; HC, healthy controls; MADRS, Montgomery-Åsberg depression rating scale; OCI-R-K, Korean version of obsessive-compulsive inventory-revised; Y-BOCS, Yale-Brown obsessive compulsive scale; SSRI, selective serotonin reuptake inhibitor.
[a] t of independent sample t-tests, [b] z of Mann-Whitney U test
* significant at $p < 0.05$, ** significant at $p < 0.01$, *** significant at $p<0.001$

Table 2. Behavioral performance data of the delayed matching-to-sample task (mean±standard deviation)

	OCD	HC	t(z)	p
Accuracy (%)	91.81±4.69	94.00±3.36	- 1.571[b]	0.200
Reaction time (ms)	765.91±154.66	662.03±95.66	2.351[a]	0.027*

OCD, obsessive-compulsive disorder; HC, healthy controls.
[a] t of independent sample t-tests, [b] z of Mann-Whitney U test
* significant at $p < 0.05$

2. Spectral-power analysis of alpha and beta oscillations in prefrontal cortex

The event-related spectral perturbation (ERSP) map during the delayed matching-to-sample task is shown in Figure 3. Repeated-measures MANCOVA with hemisphere as the repeated factor, group (OCD and healthy controls) as a between-subjective factor, MADRS score as a covariate, and period (encoding, retention, retrieval, and post-trial) for each alpha, and beta oscillation as a within-subjects factor showed significant differences between the patients with OCD and healthy controls ($F_{8,26} = 2.509$; $p = 0.036$; $\eta_p^2 = 0.463$). There was no significant main effect of hemisphere ($F_{8,26} = 2.309$; $p = 0.051$). We also found no significant

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interaction effects between the MADRS score and hemisphere ($F_{8,26}$ = 0.222; p = 0.984), or group and hemisphere ($F_{8,26}$ = 0.797; p = 0.611). In the post-hoc comparison between-group ANCOVA, patients with OCD showed a significantly reduced increase in beta oscillatory activities during the post-trial period with a large effect size (F_1 = 10.178; p = 0.003; η_p^2 = 0.236) [Figure 4]. We did not find significant between-group differences in the changes in beta oscillatory activities during the encoding (F_1 = 0.378; p = 0.543), retention (F_1 = 0.856; p = 0.359), or retrieval (F_1 = 0.147; p = 0.704) periods [Figure 4]. We also observed no significant differences in the changes in alpha oscillatory activities during the encoding (F_1 = 0.299; p = 0.588), retention (F_1 = 0.846; p = 0.364), retrieval (F_1 = 4.717; p = 0.037), or post-trial periods (F_1 = 1.149; p = 0.292) between the groups [Figure 5].

3. Partial correlation between prefrontal beta power change during post-trial period and obsessive-compulsive symptom severity score.

In patients with OCD, partial correlation analyses controlling for depressive symptoms were conducted between the obsessive-compulsive symptom severity score and prefrontal beta power change in the post-trial period which showed significant difference in post-hoc ANCOVA. The prefrontal post-trial beta power change showed a statistically significant negative correlation with the OCI-R-K total score in patients with OCD (r = - 0.521; p = 0.046). No association was found between the prefrontal beta power change and Y-BOCS score (r = - 0.108; p = 0.701) [Table 3]. Scattered plots of partial correlations between post-trial beta power change and each obsessive-compulsive symptom severity scores are presented in Figure 6.

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Table 3. Partial correlation between prefrontal post-trial beta power change and obsessive-compulsive symptom severity scores in patients with OCD (n = 16)

		Beta power change (dB)	
Control factor	Symptom severity scores	*r*	p
MADRS	Y-BOCS	- 0.108	0.701
	OCI-R-K	- 0.521	0.046*

OCD, Obsessive-compulsive disorder; MADRS, Montgomery-Åsberg depression rating scale; Y-BOCS, Yale-Brown obsessive compulsive scale; OCI-R-K, Korean version of obsessive-compulsive inventory-revised.
* significant at $p < 0.05$

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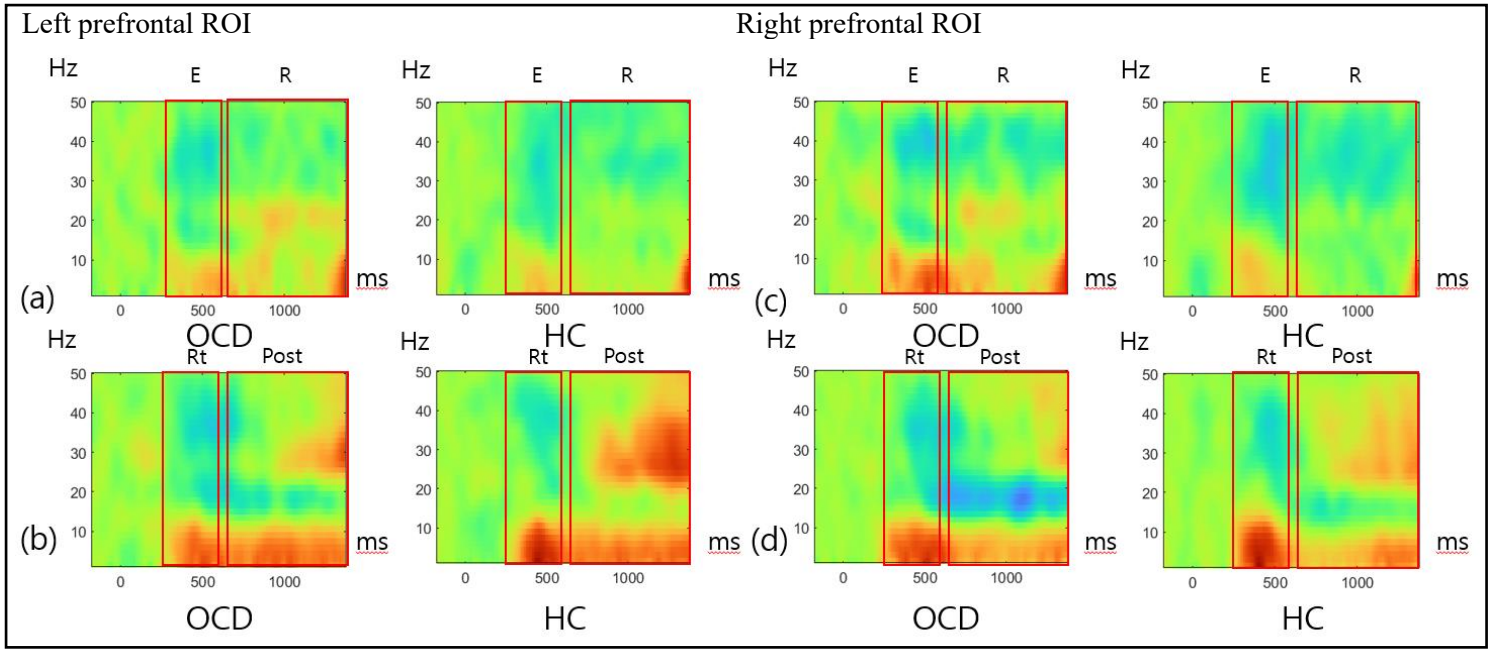

Figure 3. Event-related spectral perturbation (ERSP) map during the delayed matching-to-sample task on prefrontal regions of interest. Red color indicates an increase in power, and blue color indicates a decrease in power. (a) Left prefrontal sample cue, (b) left prefrontal test cue, (c) right prefrontal sample cue, (d) right prefrontal test cue. Red squares indicate the time windows of interest. ROI, region of interest; OCD, obsessive-compulsive disorder; HC, healthy controls; E, encoding period; R, retention period; Rt, retrieval period; Post, post-trial period.

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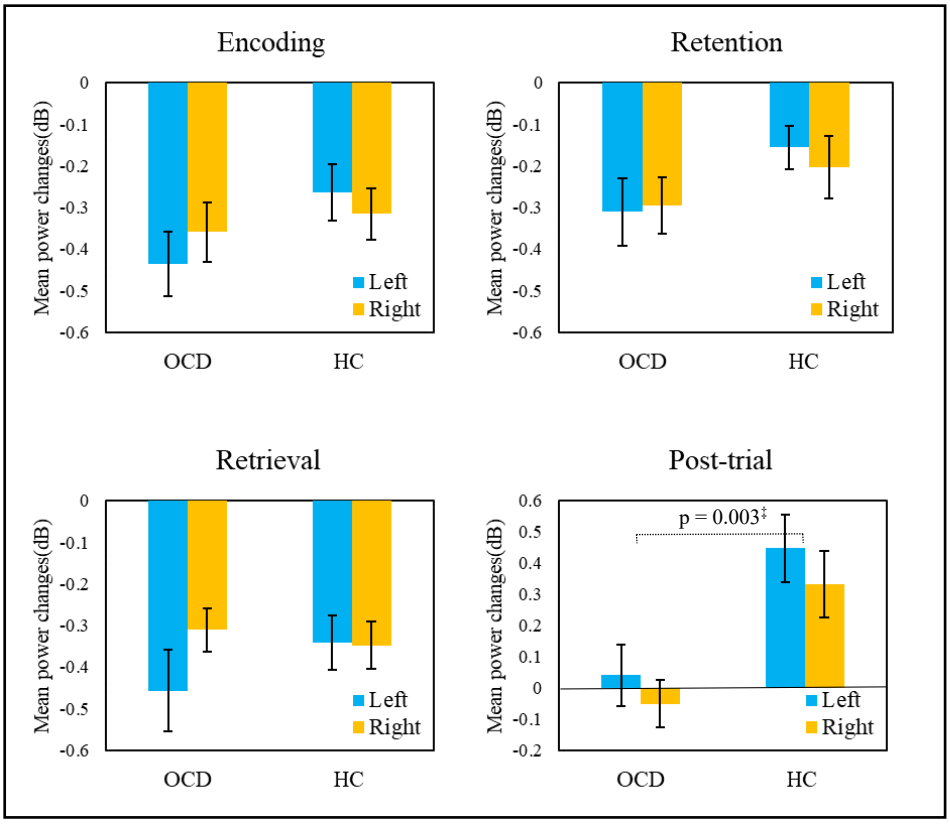

Figure 4. Beta oscillatory changes in patients with OCD and healthy controls by each period in the prefrontal regions of interest. The graphs represent the mean values of the changes in power (dB) in the patients with OCD (n = 16) and healthy controls (n = 20). The error bar shows ±1 standard error of the mean value. OCD, obsessive-compulsive disorder; HC, healthy controls.
‡ Significant at $p < 0.00625$.

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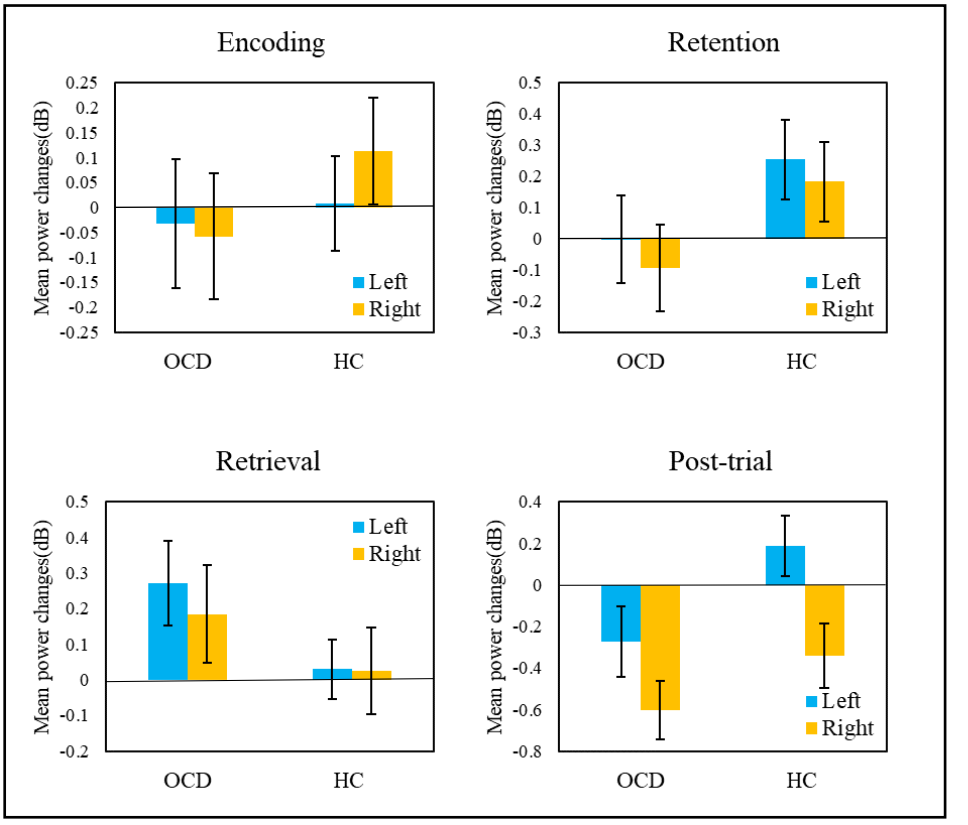

Figure 5. Alpha oscillatory changes in patients with OCD and healthy controls by each period in the prefrontal regions of interest. The graphs represent the mean values of the changes in power (dB) in the patients with OCD (n = 16) and healthy controls (n = 20). The error bar shows ±1 standard error of the mean value. OCD, obsessive-compulsive disorder; HC, healthy controls.
‡ Significant at $p < 0.00625$.

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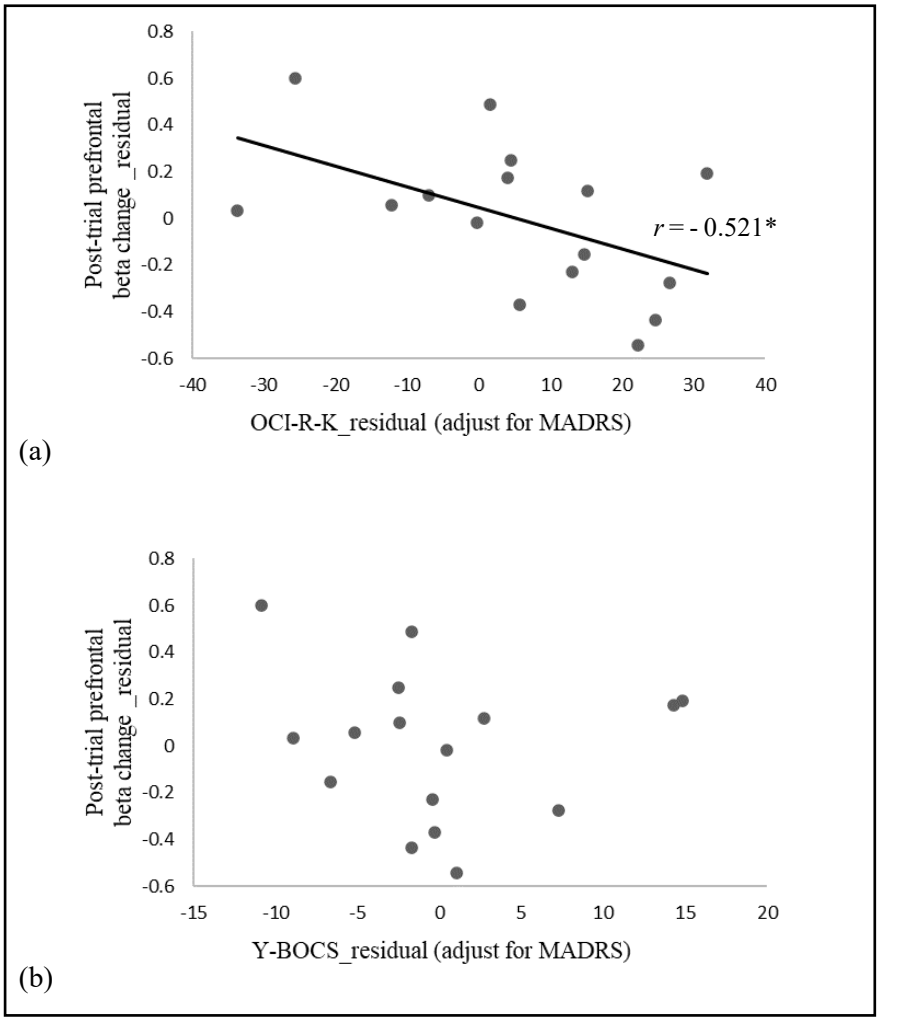

Figure 6. Scattered plots of partial correlations between post-trial beta power change and obsessive-compulsive symptom severity scores in patients with OCD after controlling for depressive symptoms. The x-axis and y-axis indicate unstandardized residual values from a linear regression analysis of obsessive-compulsive symptom scores and prefrontal beta power change during post-trial period after adjusting for MADRS score, respectively. (a) post-trial prefrontal beta change and OCI-R-K score, (b) post-trial prefrontal beta change and Y-BOCS score. MADRS, Montgomery-Åsberg depression rating scale; Y-BOCS, Yale-Brown obsessive compulsive scale; OCI-R-K, Korean version of obsessive-compulsive inventory-revised.
* significant at $p < 0.05$

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IV. Discussion

This study examined changes in prefrontal alpha and beta activities during the multiphase information process of working memory between patients with OCD and healthy controls by using MEG. The main finding of the present study is that the increase in beta power in the bilateral prefrontal regions during the post-trial period of the working memory task was significantly reduced in patients with OCD compared to healthy controls. No between-group difference in prefrontal alpha and beta oscillatory activity was found in the encoding, retention, and retrieval period of working memory information. These results suggest that the post-trial period of working memory may be more strongly linked to the OCD pathophysiology than the other processes of working memory.

The reduced prefrontal beta activity shown in OCD during the post-trial period may reflect failures in the removal of working memory. In the post-trial period of DMST, removal of working memory occurs because the encoded information becomes no longer needed after the response.[22] The beta power increase during the post-trial period correlates with successful inhibition of the unnecessary information.[3,22] Meanwhile, failure to remove unwanted working memory is known to be related to rumination on negative thoughts since the information that is the basis of the negative thought cannot be removed.[12,13] Based on the idea, a randomized controlled trial on working memory training designed to train the removal of negative information reported reduction in the rumination of negative thoughts.[12] Rumination which is characterized by repetitive thinking about their own disturbing problems, is common in patients with OCD.[14] Impairment in removal of working memory may be closely related to difficulties in preventing the rumination of obsessive thoughts in patients with OCD. This can be supported by our finding of the inverse relationship between the beta power change in post-trial period and obsessive-compulsive symptom severity assessed by the OCI-R-K in patients with OCD. Therefore, these findings of a reduced function in removal of working memory during the post-trial period of the DMST in patients

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with OCD provide a possible explanation for why patients with OCD suffer from the recurrent and intrusive obsessive thoughts.

Contrary to the results in the post-trial period, the prefrontal beta oscillatory power changes in the encoding, retention, and retrieval periods were not significantly different between patients with OCD and healthy controls. The prefrontal beta has been proposed to have a role in inhibitory control during working memory processes in the previous EEG studies, in which the beta power decreased during the encoding phase to allow for the encoding of working memory, then slightly increased in the retention phase compared to the encoding phase to inhibit irrelevant working memory from being encoded, and finally decreased during the retrieval phase to permit the retrieval of encoded working memory.[21,22] The patterns of beta oscillatory activities according to the phases were similar to those found in both patients with OCD and healthy controls in the present study [Figure 4]. Although the role of beta oscillation as an inhibitory filter did not seem to be impaired in the present OCD sample during encoding, retention, and retrieval phases, some evidence based on neuroimaging studies of OCD suggests abnormality of prefrontal function during working memory processing. An MEG study on cortical excitability showed abnormal cortical activation specific to the phases using a DMST in patients with OCD; while MEG signal was shown to be reduced in several regions including dorsolateral prefrontal cortex during retention phase, it was shown to be increased in several regions including right anterior insula during encoding and retrieval phases.[5] In a positron emission tomography study, patients with OCD showed activations in the right caudate and superior parietal cortex during a visual working memory task without activations in the right dorsolateral prefrontal and orbitofrontal cortices shown in healthy subjects.[34] In addition, with obsessive-compulsive symptom provocation, the patients showed altered connectivity between orbitofrontal cortex and the caudate for working memory, suggesting an interaction between provoked obsessive-compulsive symptom and working memory occurring in the

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frontostriatal system.[34] Further research is needed to demonstrate the impairment of inhibitory control and alteration in brain activities of various regions during working memory processing in OCD psychopathology.

For alpha activity, there were no differences during the encoding, retention, retrieval, and post-trial periods between patients with OCD and healthy controls. Although little is known about alpha activities in the post-trial period of working memory tasks, it could be suggested that prefrontal alpha activities during the post-trial period are not related to impairment in working memory removal in OCD. Alpha oscillation also has an inhibitory function in working memory, but the inhibitory function of alpha is known to be related to the inhibition of sensory information in visual cortex rather than the prefrontal cortex.[3] Therefore, further study on the function of alpha oscillation in the visual cortex during the post-trial period might be helpful to confirm whether alpha oscillation is related to the working memory removal process. On the other hand, no differences in alpha power changes in the encoding, retention, and retrieval phases are consistent with a previous study using DMST that reported no significant differences between patients with OCD and healthy controls in changes in prefrontal alpha power during the encoding, retention, and retrieval phases.[4] Meanwhile, this study also repeated the same experiment using a DMST with distractors.[4] Patients with OCD showed reduced modulation of alpha power in the prefrontal area compared to healthy controls after the distractors were presented during the retention phase.[4] This study suggested that patients with OCD have alterations in prefrontal inhibitory alpha function so that it is difficult to prevent encoding irrelevant information (distractor). Based on the results of the DMST study with distractors and the present study, it could be suggested that prefrontal alpha oscillatory activities have inhibitory functions related to the suppression of distractors rather than the removal of encoded working memory. In addition, another study using the Sternberg task, a working memory task, found a greater decrease in frontal alpha amplitude during the encoding phase in patients with OCD than in healthy

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controls.[6] The studies reporting altered prefrontal alpha oscillation during the working memory processes used different working memory task paradigms such as distractors or more difficult tasks. These differences might have resulted in different findings from ours. However, considering the present limited sample size, it would be difficult to draw definitive conclusions about the present negative or positive findings for alpha or beta in a certain phase during the DMST. Therefore, further study with various working memory paradigms in a larger sample would be helpful to confirm whether there is an alteration of alpha or beta oscillation in patients with OCD according to certain phase of working memory processes.

In the present behavioral performance on the DMST, while there was no between-group difference in accuracy, the mean reaction time was significantly longer in patients with OCD than in healthy controls. Previous behavioral studies have reported various findings on working memory performance during DMST; lower accuracy[35] or longer reaction times[4,5] in patients with OCD than in healthy controls, and no between-group difference in reaction time and accuracy.[36] The inconsistent findings could be explained by task difficulty and complexity.[37] Considering that the accuracy of the present subjects exceeded 90 percent, no between-group difference in accuracy might be caused by the low difficulty of the DMST used in this study. The fact that the present patients with OCD had longer reaction times suggests that working memory impairments in OCD patients during DMST may be behaviorally compensated by delayed responses.[4] A possible explanation for an accurate but slower performance might be that patients with OCD prefer control to prevent mistakes as a cognitive control strategy than react to stimuli with automatic responses.[38,39]

There are several limitations of this study. First, the present sample size was relatively small. In this study, the estimated effect size using with G * Power version 3.1.9.7[40] with 36 participants, a power of 0.8, and 4 response variables was $f^2(V)=0.39$. Although the assumption of the effect size was consistent with

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the previous MEG and EEG studies from which the effect sizes f^2 generally ranged from 0.31 to 0.48,[6,41,42] the sample size may not be enough to detect differences of some variables with a small effect size. Therefore, the results of the present study require replication in a study with a larger sample size. Second, we cannot entirely exclude the possible effects of psychotropic medication on altered neural oscillations. Most patients in the present study were taking selective serotonin reuptake inhibitors, and nearly half of them were on concomitant benzodiazepines. Alterations in neural oscillations affected by psychotropic medication have been reported to be complex depending on the drug class, individual drugs, and duration of treatment.[43-46] Although the between-group difference in post-trial prefrontal beta power change remained meaningful with large effect sizes when the use of benzodiazepines was included in the analysis as a covariate ($F_1 = 6.961$; $p = 0.013$; $\eta_p^2 = 0.179$), the present findings should be confirmed in further studies of drug-naïve patients. Third, our analyses were based on the sensor level; therefore, the brain regions with differences could not be specifically identified. Further source analysis will provide brain region-based information about the pathophysiology of OCD. Fourth, anticipation of feedback might affect brain activities during the post-trial period. However, brain electrical activities related to anticipation of feedback represented by pre-feedback stimulus preceding negativity (pre-feedback SPN) were not remarkable in the prefrontal area.[47] In addition, we used an easy task with more than 90 percent accuracy in patients with OCD and included only correct trials in the analysis. Therefore, these results are unlikely to be affected by feedback. Finally, the study included only young men. Further study including men and women in various age groups will need to be performed to generalize the results. Despite the limitations mentioned above, this study is the first to report the altered brain activities of patients with OCD in working memory removal.

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V. Conclusion

In this study, the beta power increase during the post-trial period of the DMST in patients with OCD was reduced compared to that in healthy controls in the prefrontal region. In addition, the beta power change in patients with OCD during post-trial period negatively correlated with the OCI-R-K score. These results suggest that the inhibitory function related to working memory removal is altered in patients with OCD. The findings may imply that information clearing regarding intrusive thoughts is impaired in patients with OCD. This could be a possible explanation for why obsessive thoughts recurrently intrude into mind in patients with OCD. Additional studies are required to explore how the impairment in working memory removal is associated with the pathophysiology of OCD.

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ABSTRACT (IN KOREAN)

강박장애 환자의 작업기억 제거 과정 중 전전두엽 베타파 활동 변화

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부 영 준

강박장애는 반복적이고 침습적인 생각과 저항하기 어려운 반복적인 행동을 특징으로 하는 만성질환이며, 작업기억 기능 손상과 연관되어 있다. 여러가지의 작업기억 처리 과정 중 작업기억을 삭제하는 기능이 강박장애의 병태생리와 연관이 있는 후보 중 하나가 될 수 있다. 하지만 강박장애 환자에서 작업기억 삭제 과정이 일어나는 중의 뇌활동에 대한 연관된 연구는 부족하다. 본 연구에서는 작업기억 처리 과정 중 전전두엽의 알파파와 베타파 활동을 분석함으로서, 강박장애 환자에서 작업기억 처리와 관련된 억제기능에 저하가 있는지를 확인하였으며, 특히 작업기억 삭제와 관련될 것으로 추정되는 과제 수행 후 기간 동안에 집중하여 연구를 진행하였다. 본 연구에서는 16 명의 강박장애 환자와 20 명의 건강한 대조군을 모집하였으며, 뇌자도와 지연 표본 대응 과제를 활용하였다. 본 연구에서는 과제 수행 후 기간 동안 양측 전전두엽에서 나타나는 베타파 상승이 강박장애 환자에서 대조군에 비해 유의미하게 줄어드는 것을 확인하였다. 작업 기억 처리 과정 중 알파파의 변화는 관찰되지 않았다. 또한, 과제 수행 후 기간 동안의 베타파 변화는 환자군에서 한국어판 단축형 강박증상목록 점수와 유의미한 부적

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상관관계를 보였다. 이러한 결과는 작업기억 삭제와 관련된 억제 기능이 강박장애 환자에서 변화되어 있다는 것을 시사한다. 강박장애 환자에서 작업기억 제거의 결손은 침습적으로 떠오르는 반복적인 강박사고를 설명할 수 있는 중요한 기전일 수 있겠다.

핵심되는 말: 강박장애, 작업기억 제거, 지연 표본 대응 과제, 베타파, 뇌자도