The effects of bilateral capsulotomy on neuronal oscillation in treatment-resistant obsessive-compulsive disorder with magnetoencephalogram

Jhin Goo Chang

Department of Medicine

The Graduate School, Yonsei University

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Directed by Professor Chang Hyung Kim

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This certifies that the
Doctoral Dissertation of Jhin Goo Chang
is approved.

Thesis Supervisor: Chan-Hyung Kim

Thesis Committee Member#1: Joong Woo Leem

Thesis Committee Member#2: Se Joo Kim

Thesis Committee Member#3: Daeyoung Roh

Thesis Committee Member#4: Do-Won Kim

The Graduate School
Yonsei University

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ABSTRACT

The effects of bilateral capsulotomy on neuronal oscillation in treatment-resistant obsessive-compulsive disorder with magnetoencephalogram

Jhin Goo Hang

Department of Medicine
The Graduate School, Yonsei University

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Bilateral capsulotomy with magnetic resonance-guided focused ultrasound (MRgFUS) is a novel treatment option for patients with treatment-resistant obsessive-compulsive disorder (OCD). However, no previous study has explored the effect of the procedure on cortical oscillatory activity and electrodynamic connectivity. We investigated changes of cortical oscillation after capsulotomy using resting-state magnetoencephalogram (MEG) along with clinical symptoms. Eight treatment-resistant OCD patients underwent resting state MEG recording repeatedly before, 1 month, and 6 months after the procedure. We compared the clinical symptoms, oscillatory power, and phase coherence among cortical sensors between each recording. Finally, we investigated the relationship between coherence and changes in obsessive-compulsive symptoms. After the procedure, obsessive-compulsive symptoms improved gradually over 6 months of follow-up. Significant decrease in power of high beta (20-35 Hz) band was observed with a tendency to decrease over time, mostly in the frontal and centro-parietal regions. The coherence results showed a gradual decrease in connectivity in all frequency bands, except theta (4-8Hz) band. Obsessive-compulsive symptom change was associated mostly in the regional frontal connectivity change right after the procedure (until 1 month). However, delayed change (between 1 month and 6 months) was associated with interregional connectivity change between the frontal and occipital area. These MEG findings indicate that the effect of bilateral capsulotomy is associated not only with local neuronal activity but also global brain network reorganization. Overall, our results advance the understanding of the neuronal mechanism of capsulotomy on treating OCD.

Key Words: obsessive compulsive disorder, capsulotomy, oscillation, magnetoencephalogram, connectivity

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I. INTRODUCTION

Obsessive-compulsive disorder (OCD) is a brain disorder characterized by recurrent intrusive thoughts and stereotyped behaviors accompanied by defects in cognitive and affective processing.[1] It has a lifetime prevalence of 1–2% worldwide and is associated with poor quality of life, functional impairment, and increased use of health care services.[2,3] Pharmacotherapy with serotonin reuptake inhibitor (SRI) and cognitive behavioral therapy (CBT) are recommended as treatment options for OCD. However, substantial portions of patients did not perceive long-term benefit through these conventional treatments and remained treatment resistant.[4]

Bilateral lesioning in the anterior limb of internal capsule (ALIC) is one of the possible options for treatment-resistant OCD.[5] A recent systemic review of bilateral capsulotomy for treatment-resistant OCD reported that it could reduce Y-BOCS score to 37% and achieve response in 41%. However, it has been selected in very limited situations, due to the risks of unpredictable open neurosurgical or radiation-associated adverse effects and clinician's reluctance to psychosurgery.[6] Recently, a novel surgical technique, named magnetic resonance-guided focused ultrasound (MRgFUS), which uses ultrasound to produce an intra-cranial lesion without risk of radiation, has been introduced.[7,8] Closed-loop monitoring in real time allows for confirmation of lesion size and location during every stage of lesioning, and has been applied safely and widely for the treatment of psychiatric and neurologic disorders, including treatment-resistant OCD.[9,10]. In our previous clinical study, we observed the short-term and long-term efficacy and safety of bilateral thermal lesioning of the ALIC using MRgFUS in patients with treatment-resistant OCD for 2 years.

Identifying functional changes of the brain after treatment is important to identify disease etiology and treatment mechanisms in OCD. Converging functional neuroimaging studies reported that restoration of dysfunctional frontal activity, including OFC and ACC, is the underlying treatment mechanism of SRI or CBT.[11] Moreover, the increased efficacy of global brain connectivity after SRI treatment suggests that distortions occur within large-scale brain networks, rather than from independent brain regions.[12] However, only few studies investigated effect of the bilateral capsulotomy on brain function. Functional brain imaging with [18F]-fluoro-deoxyglucose (18F-FDG) identified normalized glucose metabolism in bilateral prefrontal cortical regions and thalamus after capsulotomy along with symptom improvement.[13] Resting state functional MRI study showed reduced connectivity between the ventral striatum and dorsal anterior cingulate cortex after capsulotomy.[14] Both results suggest that the treatment effect of capsulotomy might be associated with restored dysfunctional fronto-striatal circuit. However, assessing blood flow or metabolism does not directly reflect neuronal change and no study has observed the effect of capsulotomy on the global brain network.

Recording neural oscillations provide new understanding of the direct functionality and electrodynamic connectivity among distant brain regions.[15] Since change of neural oscillation appeared immediately after the neurosurgical or modulation therapy, it could be utilized in real-time treatment feedback. MEG is a non-invasive tool, which measures neural oscillations in the cortex with magnetic fields that are induced by synchronized current flow in neuronal assemblies.[16] Since magnetic fields are not distorted by the different conduction of the skull and other inhomogeneities of the head, it is potentially a more powerful localization tool of cortical brain function than EEG, which measures electric fields. In Parkinson's and Alzheimer's disease, MEG signal changes after treatment have been observed to improve the understanding of treatment mechanisms and diseases.[17,18] However, to the best of our knowledge, no studies have observed changes in neural oscillation after bilateral capsulotomy in OCD.

In this study, we plan to explore the effects of bilateral capsulotomy with MRgFUS on neuronal oscillation utilizing MEG. Conventionally, capsulotomy is performed with open craniotomy, so it has limitation to accurately measure changes in neural oscillation. Since the craniotomy was not performed with MRgFUS, it is possible to assess the exact oscillatory change in our study. Our research goals are: 1) assess changes in cortical oscillatory power and connectivity between global brain regions before and after surgery. 2) examine the relationship between changes in cortical connectivity and changes in OC symptoms.

II. MATERIALS AND METHODS

1. Subjects

Our study is part of MRgFUS for treatment-resistant OCD clinical trial (www.clinicaltrials.gov/ct2/show/NCT01986296?term=OCD001&rank=2). Eleven patients with treatment-resistant OCD underwent bilateral capsulotomy with MRgFUS. Patients were consecutively recruited from the outpatient department of psychiatry at Severance Hospital, Yonsei University Health System, and diagnosed with the Korean version of the Structured Clinical Interview for DSM-IV Axis I Disorders by a trained psychiatrist. Treatment-resistant status was defined as nonresponsive to pharmacological treatment (more than 2 types of serotonin reuptake inhibitor at the maximum tolerated dose for more than 12 weeks) and cognitive behavioral therapy (a minimum of 20 sessions of primarily therapist-guided Exposure and Response Prevention). All participants underwent a MEG recording and other clinical evaluations before, 1 month, and 6 months after the procedure. However, because of poor MEG data quality with three patients (one patient did not follow the experimental protocol, and two patients had low data quality), data from eight patients were finally used for the analysis. The study was approved by the Institutional Review Board of Severance Hospital. Written informed consent was obtained from each subject at the beginning of the study.

2. Clinical outcomes

We measured the severity of obsessive-compulsive symptoms using the Y-BOCS. We also assessed depression and anxiety symptoms using the Hamilton Rating Scale for Depression (HAM-D) and the Hamilton Rating Scale for Anxiety (HAM-A), respectively. Patients were classified as responders when Y-BOCS reduction $\geq$ 35% relative to the baseline score.

3. MEG acquisition

A 152-channel whole-head MEG system (Korea Institute of Standards and Science; KRISS, Daejeon, Korea) was used to measure the magnetic fields induced by the brain activity during a 6-min resting period, during which participants were seated comfortably in a magnetically shielded room at the hospital (Yonsei University Health System, Seoul, Korea) and were instructed to remain awake. The resting-state recording consisted of a 3-min eyes-closed (EC) condition followed by a 3-min eyes-open (EO) condition for all participants. Participants were instructed to look at a small crosshair on the screen in front of them during the EO condition. Magnetic fields were recorded at a sampling rate of 1000 Hz with a bandpass filter between 0.1 and 100 Hz.

Table 1. Individual clinical symptom measures

Pt. no.	Age	YBOCS score			HAM-D			HAM-A		
		Baseline	1M	6M	Baseline	1M	6M	Baseline	1M	6M
1	24	38	35	29	27	5	4	34	6	4
2	29	34	27	18	18	8	11	17	7	7
3	22	35	32	26	25	13	11	31	16	17
4	44	34	22	21	20	6	9	26	7	5
5	37	37	29	27	24	5	15	19	8	5
6	34	35	29	23	19	10	9	21	11	13
7	37	34	18	16	17	5	11	17	9	8
8	40	30	28	27	16	10	9	20	19	8

MRgFUS= magnetic resonance‒guided focused ultrasound; Y-BOCS = Yale–Brown Obsessive Compulsive Scale; HAM-D = Hamilton Rating Scale for Depression; HAM-A = Hamilton Rating Scale for Anxiety;

4. MEG data preprocessing

The EO condition was recorded only to confirm the reliability of data under EC conditions and was not used in further analysis. All preprocessing procedures were done with CURRY 8 (Compumedics, Charlotte, NC, USA) Software. First, the baseline of the recording was corrected by subtracting the overall mean of each channel to themselves. Gross-movement artifact and other muscle related noises were identified by a trained specialist and rejected from further analysis. After the artifact rejection, the data was segmented into 4000 ms epochs and saved separately. No other preprocessing or manipulation was done to the data.

5. MEG data analysis

To investigate the power difference and the connectivity difference before and after the MRgFUS, we compared the relative band power and phase coherence differences between each recording. To permit a balanced comparison, twenty-five epochs (total 100 s of recording) were randomly selected by each participant for both analyses. For each analysis, we used EEGALB toolbox and in-house code based on MATLAB 2018b (The Mathworks, Natick, MA, USA).

For relative band power analysis, we first calculated the power spectrum of each channel using Fast Fourier Transform. The power spectrum was divided into seven distinct frequency bands, delta (1-4 Hz), theta (4-8 Hz), low alpha (8-10 Hz), high alpha (10-13 Hz), low beta (13-20 Hz), high beta (20-35 Hz), and gamma (35-45 Hz). The relative power was calculated by normalizing each band power summation of the channel by the full band power (1-45 Hz). Subsequently, the channels were grouped into regions of interest corresponding to the major cortical areas (frontal, centro-parietal, temporal, and occipital) on the left and right hemisphere. A schematic distribution of these areas is shown in Fig. 1.

To investigate the connectivity changes before and after MRgFUS, the phase coherence between each MEG channel pairs were calculated, which can determine the degree of synchronization between the two-time series. The phase coherence (EPOCOH) was calculated by the following equation:

$$ERPCOH^{a,b}(f,t) = \frac{1}{n}\sum_{k=1}^{n}\frac{F_k^a(f,t)F_k^b(f,t)^*}{\left|F_k^a(f,t)F_k^b(f,t)\right|}$$

where the phase coherence is a function of frequency (f) and time (t). The subscript a and b indicates two distinct channels, and the n is the number of epochs, which will be twenty-five in the current analysis. Fka(f,t) is calculated by the short-time Fourier Transform. The * and | | operator represents the complex conjugate and the complex norm, respectively. The calculated phase coherence is ranging from 0 to 1, which indicates absolute absence to complete synchronization between the two channels, a and b. In this current investigation, the phase coherence was calculated for all electrode pairs ((150×149) /2 = 11,175 pairs) and averaged across time and epochs for each electrode pairs.

6. Statistical analysis

For each clinical symptom, Y-BOCS, HAM-D, and HAM-A, the scores of baseline, 1 month, and 6 months were tested to determine whether there is a significant change over time with the Friedman test. For the scores which were significant, post hoc analysis was done using Wilcoxon signed-rank sum test adjusted for multiple comparison ($\alpha = 0.05/3$).

To investigate the relative power changes before and after MRgFUS, repeated measures analysis of variance (rmANOVA) was performed, with laterality (left and right) and regions (frontal, centro-parietal, temporal, and occipital) as within subjects factors, and time (pre, 1M, 6M), and frequency band (delta, theta, low alpha, high alpha, low beta, high beta, gamma) as between subjects factors. Green-Geisser correction was used when sphericity was violated by Mauchly's test. For any significant effect, we performed a post-hoc analysis adjusting the p values using Bonferroni correction for multiple comparison.

For the phase coherence analysis, the averaged phase coherence of the participants was compared for each electrode pair with respect to time (pre,1M, and 6M) with Friedman test. For the connections that were significant ($p < 0.01$), post-hoc analysis was done using Wilcoxon signed-rank sum test. Multiple comparison was corrected for time ($\alpha = 0.05 / 3$), but not for electrodes pairs.

Lastly, we examined the association between changes of regional or inter-regional mean coherence and changes in YBOCS.

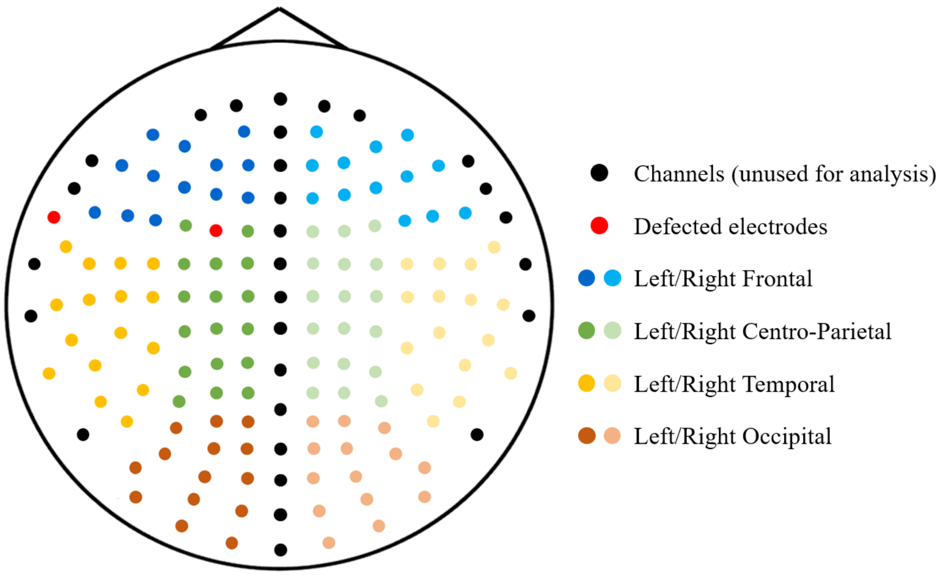

Figure 1. Channel locations and its defined region (frontal, centro-parietal, temporal, and occipital in both hemispheres)

III. RESULTS

1. Clinical response

The statistics with clinical symptoms are represented in Table 2. There were significant reductions in clinical scores of Y-BOCS and HAM-D 6 months after the operation. All clinical symptom assessment had a significant difference in time (Y-BOCS: $p < 0.001$; HAM-A: $p = 0.002$; HAM-D: $p = 0.002$). Compared to baseline scores, Y-BOCS score was reduced significantly not only after 1M but also 6M post-operation ($p = 0.024$). Moreover, there was a significant difference between 1M and 6M after operation ($p = 0.024$). In case of HAM-A and HAM-D score, the symptoms were declined after 1M and 6 M compared to baseline ($p = 0.004$), but both scores did not show any significant difference between 1M and 6M scores. The graphical representation post-hoc results on the clinical scores are represented in Figure 2.

Table 2. Change in Y-BOCS, HAM-A, and HAM-D scores during 6-months.

Clinical scores	Baseline (pre)	1-month (1M)	6-month (6M)	χ2(2)	p
Y-BOCS	34.63 ± 2.39	27.50 ± 5.37	23.38 ± 4.69	16.000	< 0.001
HAM-A	23.13 ± 6.49	10.38 ± 4.72	8.38 ± 4.47	12.968	0.002
HAM-D	20.75 ± 7.06	7.75 ± 3.01	9.88 ± 3.09	12.000	0.002

MRgFUS= magnetic resonance−guided focused ultrasound; Y-BOCS = Yale–Brown Obsessive Compulsive Scale; HAM-A = Hamilton Rating Scale for Anxiety; HAM-D = Hamilton Rating Scale for Depression

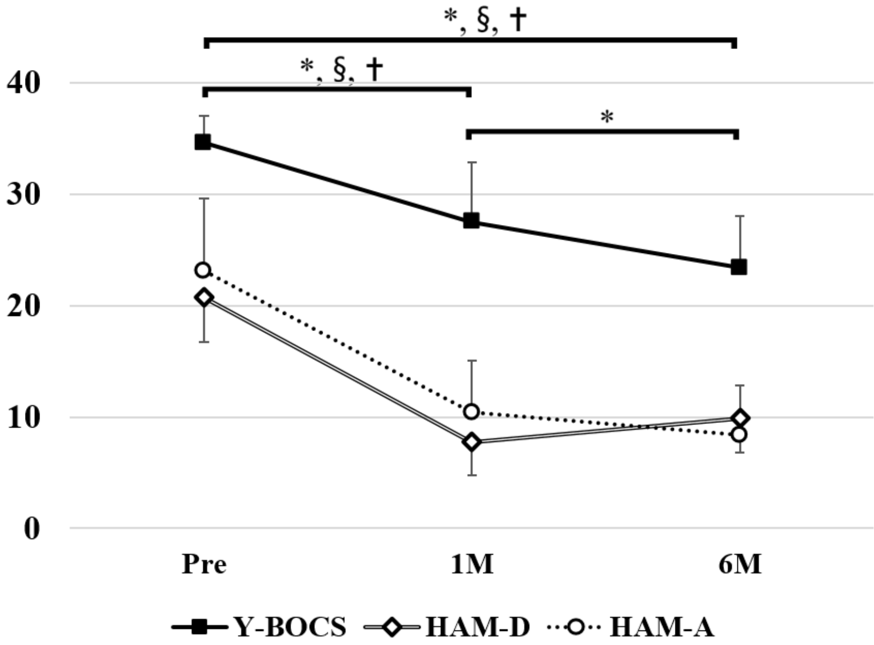

Figure 2. Change in clinical symptoms for before(pre), and 1-month(1M) and 6-month(6M) post bilateral capsulotomy. (Y-BOCS = Yale–Brown Obsessive Compulsive Scale, *: $p < 0.05$; HAM-A = Hamilton Rating Scale for Anxiety, §: $p < 0.05$; HAM-D = Hamilton Rating Scale for Depression, †: $p < 0.05$, all p-values are corrected for multiple correction)

2. Band power analysis

RMANOVA revealed no significant main effect, but significant interaction with frequency bands (time × frequency: $F(12, 980) = 2.140$, $p = 0.021$; laterality × frequency: $F(6, 49) = 2.315$, $p = 0.048$; region × frequency: $F(18, 147) = 23.278$, $p < 0.001$; laterality × region × frequency: $F(18, 147) = 7.369$, $p < 0.001$) and a significant interaction in time × laterality × region × frequency band (F(36,

294) = 1.835, p = 0.004)) was observed.

To further investigate time × laterality × region × frequency band, we have compared the band power for each time over all frequency bands, laterality, and region. The statistical difference only occurred on the high beta frequency with a tendency to decrease over time mostly in frontal and centro-parietal regions (Figure 3). The post hoc comparison showed differences in the left frontal (Pre < 1M, p = 0.017; Pre < 6M, p = 0.008), left centro-parietal (Pre < 1M, p = 0.003; Pre < 6M, p = 0.002), right frontal (Pre < 6M, p = 0.043), right centro-parietal (Pre < 1M, p = 0.007; Pre < 6M, p = 0.001), and right temporal (Pre < 1M, p = 0.022; Pre < 6M, p = 0.022). All comparisons were corrected with Bonferroni correction.

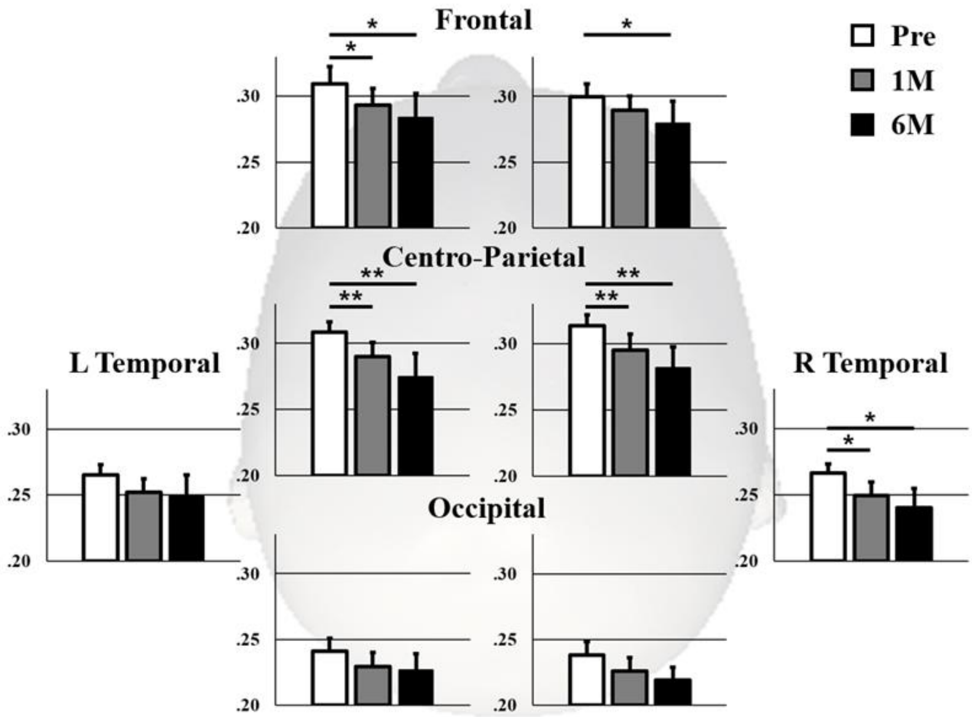

Fig 3. Relative power differences over time of each hemisphere and region

(*: $p < 0.05$; **: $p < 0.01$)

3. Phase coherence analysis

The coherence results between all sensors are presented in figure 3. The statistical test revealed decreased electrodynamic connectivity over time except theta band.

4. Association between connectivity and symptom change

We calculated the correlation coefficient between regional/interregional mean coherence change and Y-BOCS change. Statistically significant results are displayed in Table 3. Negative correlation coefficient means that connectivity increases.

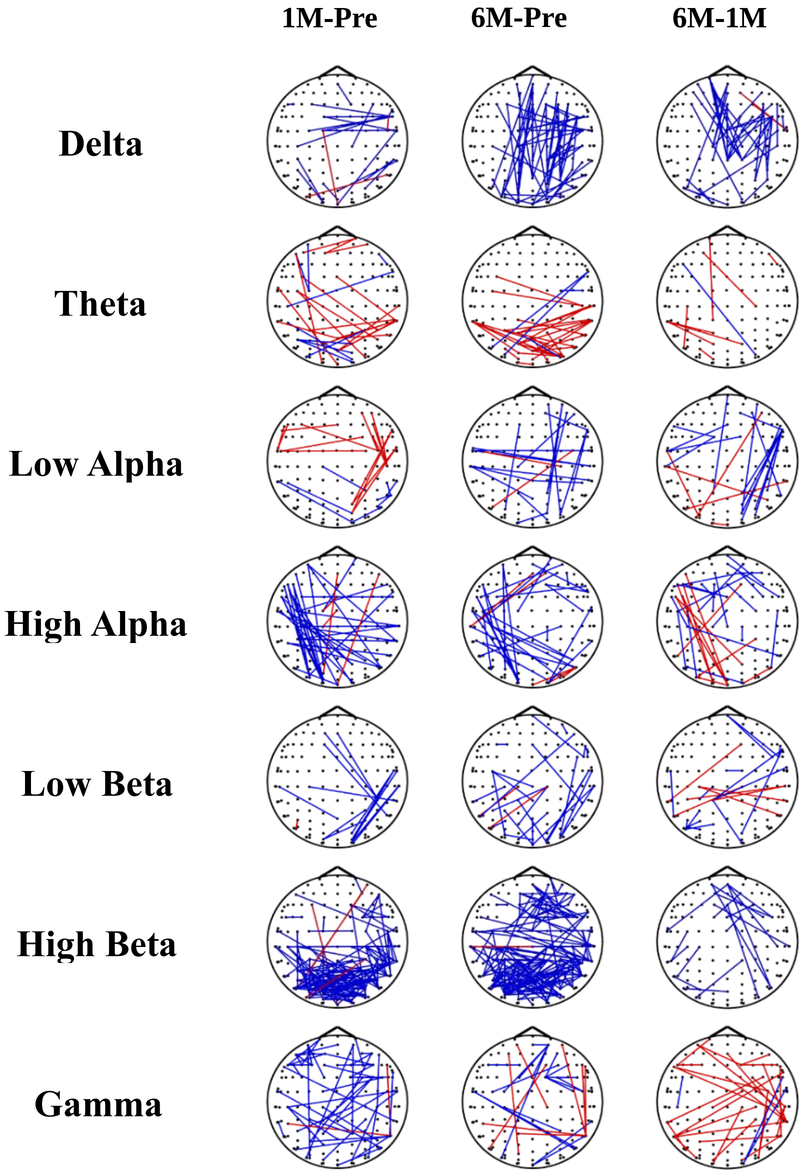

Figure 4. Coherence differences over time between all sensors.

Table 3. Correlation between mean coherence change and YBOCS change

	Y-BOCS 1M-Pre		
	Frequency	**r**	***p***
Regional			
Right frontal	High alpha	-0.7145	0.046
Inter-regional			
Right frontal - right centroparietal	High alpha	0.7785	0.0301
Left frontal - left temporal	High alpha	-0.7545	0.0422
Left frontal - right temporal	High alpha	-0.7545	0.0422
Right occipital - right centroparietal	Low alpha	-0.7306	0.048
Left occipital - right temporal	High alpha	-0.7904	0.025
	Y-BOCS 6M-1M		
	Frequency	**R**	**P**
Regional			
Inter-regional			
Right frontal - right occipital	Low alpha	0.8524	0.011
Left frontal - left occipital	Low beta	0.8648	0.009

Y-BOCS = Yale–Brown Obsessive Compulsive Scale

IV. Discussions

This is the first longitudinal study that investigated effects of bilateral thermal capsulotomy on neural oscillation with OCD symptomatology in patients with treatment-resistant OCD. We found gradual improvement of obsessive–compulsive symptoms over 6 months of follow-up, while improvements of depression and anxiety symptoms improved rapidly, in 1 month. After the procedure, patients showed decreased power of high beta band in bilateral frontal and centroparietal area. Cortical electrodynamic connectivity decreased in most frequency bands, except theta band. Connectivity change between the fronto-occipital region were significantly associated with long-term improvement of OC symptoms.

At 6 months, obsessive compulsive symptoms improved significantly, (mean 34.63 ± 2.39 to 23.38 ± 4.69, $p = 0.024$) and 37.4% (5/8) were reached to response (defined as 35% reduction compared with baseline). In studies of capsulotomy with conventional manner, approximately up to 50% of participants showed response at 12 months.[19,20] Although our data are difficult to compare to studies, since we investigated only for 6 months. 54.6% of patients (6/11) showed response at 12 months.[8] In terms of time course of efficacy, we observed rapid improvements in depression and anxiety symptoms as early as 1 week after, while improvements in obsessive compulsive symptoms occured over 6 months. This trend is similar in other lesioning or deep brain stimulation studies. This result suggests that the effect of MRgFUS capsulotomy is similar to that of other radiofrequency or gamma capsulotomy, and the therapeutic effects of neurosurgical interventions are related to not only functional neuronal interruption, but also reorganization after lesioning. [21]

After the procedure, relative power of high beta band was decreased significantly in bilateral frontal, centroparietal, and right temporal area within 1 month. Prior baseline studies in OCD have found that there is an increased beta current density in the frontal and parietal lobes and an increased rate of MEG activity in the left superior temporal gyrus compared with normal volunteers. [22,23] DBS at anterior limb of internal capsule reduced prefrontal theta activity at symptom provocation[24]. Anatomically, fibers passing the anterior limb of the internal capsule comprises reciprocal projection fibers between the frontal lobe and the medial and anterior thalamic neuclei.[25] When these results are combined, capsulotomy might restore dysfunctional frontal neural activity. FDG-PET study also reported decreased frontal metabolism after treatment which is correlated with clinical improvement.[13] Considering that decrease in frontal activity lasted through 6 months bilateral capsulotomy could produce long-lasting cortical modifications.

Coherence analysis showed that cortical connectivity in high beta and delta band decreased gradually. While connectivity change in high beta band was concentrated in occipital area until 1 month, delta band change was spread over globally including the frontal area during the next 5 months. Findings are proposed to reflect a loss of selectivity in functional networks which may explain inflexible behavior in many mental disorders, e.g., the "automatic" negative cognitions of MDD, the repetitive behaviors of OCD, or the rigid interests of autism[26]. Widge et al[24]. reported that deep brain stimulation of the internal capsule enhances cognitive control in patients with treatment resistant OCD and MDD. It is known that fast rhythms range connectivity link cortico-cortical short regions, while slow rhythm link long-range regions containing subcortical activity.[15] Our results suggest that the network effect of capsulotomy begins in the local area and extends into the global area. However, since we did not investigate graph analysis, we could not confirm whether the decrease in coherence implicate an increase or decrease in efficacy.

Until 1 month after the procedure, obsessive-compulsive symptom change was associated mostly in the regional frontal connectivity change.

However, until 6month it was associated with interregional connectivity change between the frontal and occipital area. In an fMRI study examining the pharmacological treatment effect, improvement of obsessive-compulsive symptoms was associated with decrease in connectivity degree in the right ventral frontal cortex in OCD patients after treatment.[27] Neuroimaging studies have shown that OCD may be caused by distortions within large-scale brain networks rather than from independent brain regions.[28] Pharmacotherapy with SSRI and CBT are known to modify the dysfunctional global network in OCD with symptom improvement.[12,29] Our results suggest that long-term observation and maintaining psychiatric treatment, including medication and CBT treatment, should be performed after the procedure. However, since we did not investigate graph analysis, we could not confirm whether the decrease in coherence implicates an increase or decrease in efficacy.

One of the most important practical implications of the present work is a testable method for translating the success of capsulotomy into new and improved noninvasive treatments. For example, noninvasive brain stimulation methods such as repetitive transcranial magnetic stimulation enables modulating cortical excitability in specific brain regions and molding plasticity at the network level.[30] Up until now, most studies target the supplementary motor area (SMA) or components of the cortico-striato-thalamo-cortical (CSTC) circuits–the dorsolateral PFC (DLPFC) and orbitofrontal cortex (OFC). The promising success of capsulotomy suggests that connectivity result could help refine target selection in the occipital area.

There are several limitations to the current study. First, we did not investigate the baseline oscillatory difference between treatment-resistant OCD and healthy control. Second, we could not explore the association between clinical symptom changes and cortical oscillation since the number of participants in this study was small. Third, 6 months is not enough to observe improvement after the procedure. In our study, only 3 participants fully responded the treatment after 6 months, but symptoms improved continuously after 24months.

Nevertheless, this was the first long-term study of the effects of capsulotomy on electrophysiology in patients with treatment-resistant obsessive-compulsive disorder. Through this study, we could expand our understanding of the cortical electrophysiological change after capsulotomy in treatment-resistant OCD. This understanding could be applicated in using non-invasive treatment methods which could modify cortical oscillation, such as repetitive transcranial magnetic stimulation or transcranial direct current stimulation.

V. CONCLUSION

This is the first study to explore the changes of neuronal oscillations after bilateral capsulotomy with MRgFUS in patients with treatment resistant OCD. After the procedure, frontal high beta band power was decreased instantly in the resting state after the procedure. Further, electrodynamic connectivity change after the procedure was associated with symptom improvements. Overall, the results advance the understanding of the not only clinical pathophysiology of OCD, but also the neuronal mechanism of capsulotomy.

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ABSTRACT(IN KOREAN)

치료저항성 강박증 환자에서 양측 전피막 절제술 후 전기생리학적 변화

<지도교수 김 찬 형>

연세대학교 대학원 의학과

장 진 구

양측 전피막 절제술은 치료저항성 강박증의 안전하고 효과적인 치료법으로 알려져 있지만, 현재까지 시술 전 후 뇌의 전기생리학적 변화를 관찰한 연구는 매우 적다. 본 연구는 고집적 자기공명영상 유도하 초음파를 통한 양측 전피막 절제술 전 후 대뇌 피질 진동의 파워와 연결성의 변화를 확인하는 것에 그 목적이 있다. 양측성 피막절개술 임상연구에 참여하는 환자 8명에게 치료 전 과 시술 후 1개월, 시술 후 6개월에 휴지기 뇌자도를 촬영하고, 촬영 전 강박증상과 우울증상을 평가하였다. 152개의 전극을 위치에 따라 좌우 전두엽, 측두엽, 두정엽, 후두엽으로 분류하고, 시술 전 후 주파수별 파워와 위상 일관성을 시간에 따라 비교하였다. 또한 강박증상의 변화와 위상 일관성 변화의 상관관계를 계산하였다. 주파수별 파워분석 결과 전두엽과 두정엽의 고베타파 (20-35 Hz)의 파워가 수술직후 감소하였고, 이 변화는 6개월의 관찰기간 동안 지속되었다. 위상일관성 분석결과, 쎄타파(4~8 Hz)를 제외한 모든 주파수의 연결성이 시간이 지남에 따라 감소하는 추세를 보였다.

시술 후 1개월 동안 강박증상의 변화는 전두엽 부위의 위상일관성 변화와, 시술 후 1개월부터 6개월사이의 강박증상의 변화는 전두엽과 후두엽 사이의 부위간 연결성의 감소와 연관이 있었다. 양측 전피막 절제술의 치료효과는 전두 피질의 활성을 감소뿐 아니라, 전반적 뇌 연결성의 변화를 통해 나타난다는 것을 시사한다.

핵심되는 말 : 강박증, 전피막 절제술, 뇌자도, 연결성