Invest Clin 61(2): 132 - 141, 2020 https://doi.org/10.22209/IC.v61n2a04

Detection of prefrontal lobe blood flow changes in patients with obsessive-compulsive disorder during a verbal fluency task by near-infrared reflectance spectroscopy.

Hong-Ying Yin[1], Fan Jiang[2], Qi-Hua Peng[3] and Yu-Ling Wu[1]

[1]Department of Psychology, Jilin Provincial People'Hospital, Changchun, China.
[2]Department of Psychology, Jilin Normal University,Changchun, China.
[3]Department of Ultrasonic, Changchun Obstetrics and Gynecology Hospital Changchun, China.

Key words: near-infrared reflectance spectroscopy; obsessive-compulsive disorder; verbal fluency; oxygenate hemoglobin; deoxygenate hemoglobin.

Abstract. The purpose of this work was to use near-infrared reflectance spectroscopy (NIRS) to investigate the spectral characteristics and frontal lobe activation in patients with obsessive-compulsive disorder (OCD) during a verbal fluency task. Thirty-seven patients with OCD, who met the diagnostic criteria of International Classification of Diseases 10 (ICD-10), were recruited. The total score of the Symptom Checklist (SCL-90, grade 1-5) was ≥160 points. The total score of the Yale-Brown Obsessive Compulsive Scale was ≥7 points. The changes in frontal lobe blood flow were measured by NIRS when completing a verbal fluency task. Then, the differences between obsessive-compulsive thoughts and obsessive-compulsive behaviors in OCD, and the concentration variation of oxygenate hemoglobin (Oxy-Hb) and deoxygenate hemoglobin (Deoxy-Hb) were investigated. The difference was significant ($P<0.03$) between obsessive-compulsive behaviors and obsessive-compulsive thoughts. Obsessive-compulsive behaviors were positively correlated ($P<0.01$, $P<0.05$) with depression, anxiety, psychosis and other factors in the SCL-90, and significantly positively correlated ($P<0.01$, $P<0.03$) with somatization, hostility and paranoid factor scores in the SCL-90. There was also a trend of partial overlap between the waveform and task period, and the difference was significant ($P<0.01$) between these. Obsessive-compulsive thoughts were negatively correlated ($P<0.05$) with channels 9 and 19. The NIRS monitoring spectrum for patients with OCD has certain spectral characteristics of schizophrenia, but there is a repetitive trend between the recovery period and the task period.

Corresponding author: Qi-Hua Peng, Department of Ultrasonic,Changchun Obstetrics and Gynecology Hospital, Nanguan District, Changchun 130021, China, Tel:0431-82904111, E-mail: pengqh62587@163.com

Detección de cambios en el flujo sanguíneo del lóbulo prefrontal en pacientes con trastorno obsesivo-compulsivo, durante una tarea de fluidez verbal, mediante espectroscopia de reflectancia en el infrarrojo cercano.

Invest Clin 2020; 61 (2): 132-141

Palabras clave: espectroscopía de reflectancia casi infrarroja; trastorno obsesivo compulsivo; fluidez verbal; hemoglobina oxigenada; hemoglobina desoxigenada.

Resumen. El propósito del presente trabajo fue utilizar la espectroscopia de reflectancia en el infrarrojo cercano (NIRS) para investigar las características espectrales y la activación del lóbulo frontal en el trastorno obsesivo compulsivo (TOC) durante una tarea de fluidez verbal. Se reclutaron 37 pacientes con TOC que cumplían los criterios de diagnóstico de la Clasificación Internacional de Enfermedades 10 (CIE-10). La puntuación total de la Lista de Verificación de Síntomas (SCL-90, grado 1-5) fue de 160 puntos. La puntuación total de la Escala Obsesiva-Compulsiva de Yale-Brown fue de ≥7 puntos. Los cambios en el flujo sanguíneo del lóbulo frontal fueron medidos por NIRS al completar la tarea de fluidez verbal. Entonces, se investigaron las diferencias entre los pensamientos obsesivo-compulsivos y los comportamientos obsesivo-compulsivos en TOC, y la variación de las concentraciones de hemoglobina oxigenada (Oxy-Hb) y hemoglobina desoxigenada (Deoxy-Hb). La diferencia fue significativa (P<0,03) entre los comportamientos obsesivo-compulsivos y los pensamientos obsesivo-compulsivos. Los comportamientos obsesivo-compulsivos se correlacionaron positivamente (P<0,01, P<0,05) con depresión, ansiedad, psicosis y otros factores en el SCL-90, y se correlacionaron positivamente de manera significativa (P<0,01, P<0,03) con la somatización, hostilidad y puntuaciones de factor paranoico en el SCL-90. También hubo una tendencia de superposición parcial entre la forma de onda y el período de tarea, y la diferencia fue significativa (P<0,01) entre estos. Los pensamientos obsesivo-compulsivos estaban correlacionados negativamente (P<0,05) con los canales 9 y 19. El espectro de monitoreo NIRS para pacientes con TOC tiene ciertas características espectrales de la esquizofrenia, pero hay una tendencia repetitiva entre el período de recuperación y el período de tarea.

Received: 09-10-2019 Accepted: 04-05-2020

INTRODUCTION

Multi-channel near-infrared reflectance spectroscopy (NIRS) is a painless and noninvasive optical imaging technique (1), which can be used explore the process of internal brain activities in various kinds of human cognitive active procedures as each channel covers a part of the brain area (2-4). The near-infrared light can be absorbed by hemoglobin through the skull within 2-3 cm, and detect the levels of oxygenate hemoglobin (Oxy-Hb) and deoxygenate hemoglobin (Deoxy-Hb) in the venous blood of brain tissues (5-8). Compared with other neuroimaging techniques, its advantage consists of a high time resolution (0.1 second), which can display the dynamic functional changes of the prefrontal cortex in real time (9).

Herrmann *et al.* applied the verbal fluency test (VFT) in the NIRS test, and confirmed that in the frontal lobe, Oxy-Hb was significantly elevated and Deoxy-Hb was significantly decreased, when normal subjects completed the task (10). VFT reflects the complex cognitive activities of subjects, including choosing the right language from memory, remembering a spoken language, suppressing an inappropriate language, and maintaining attention to cognitive activation (11). Most reports have been based on VFT as an activation task, and NIRS has been used to assist in the diagnosis of schizophrenia, depression, biphasic affective disorder and other mental diseases at home and abroad (12). However, few studies have been conducted on obsessive-compulsive disorder. In the present study, the NIRS test was used to investigate the characteristics of the spectrum and frontal lobe activation state in patients with obsessive-compulsive disorder (OCD). The hemodynamic changes of the prefrontal lobe were tested using the 33-lead NIRS system (ETG-4000, Hitachi, Japan) that consisted of 52 channels (14), and the 22 channels that covered the prefrontal lobe were selected as the research area in the current study.

RESEARCH METHOD

Research object

The present study was comprised of outpatients, who were treated in the Outpatient Department of our hospital between January 2016 and December 2016. Inclusion criteria: patients who meet the OCD diagnostic criteria of International Classification of Diseases 10 (ICD-10) (13); patients who were right-handed; patients with a total score of ≥160 points in the Symptom Checklist (SCL-901-5); patients with a total scores of ≥6 points in the Yale-Brown Obsessive Compulsive Scale. Exclusion criteria: patients who suffered from brain organic lesions, mental retardation, drug or alcohol abuse history, and other heart, liver, kidney and serious physical diseases; pregnant or lactating women. A total of 37 patients were enrolled in the present study. Among these patients, 22 patients were male and 15 patients were female, with the average age of these patients was 25.16 ± 0.20 years old. The educational levels of patients were as follow: two patients finished junior high school, nine patients finished senior high school, four patients finished college, 14 patients were undergraduates, and eight patients had an educational background higher than an undergraduate. Marital status: thirty patients were unmarried and seven patients were married. Vocational status: twenty four patients were students, six patients were unemployed, and seven patients had other vocational statuses.

The present study was approved by the Ethics Committee of our hospital, and the patients and guardians were informed. All subjects voluntarily provided a signed informed consent.

METHODS

Yale-Brown Obsessive Compulsive Scale and Symptom Checklist (SCL-90)

The Yale-Brown Obsessive Compulsive Scale and the Symptom Checklist (SCL-90, 1-5) were used to evaluate the psychology of the patients.

Verbal fluency task

The VFT test was carried out in a quiet environment, and the patient was emotionally stable before the test. During the test, the patients were instructed to maintain their head posture and look at the cross on the wall, which was placed in the same horizontal line as the line of sight, located approximately 1 m away. The test was divided into four parts: The first part was the prescanning, and the time was set for 10 seconds. The patient was instructed to sit still and look at the cross in front of them. The second part was the waiting time, and the time was set for 30 seconds. The patient repeated a number from 1 to 5. The third part

was the stimulation time, and the stimulus was induced by presenting three characters: white, heaven and big. Words or idioms were formed using the first given character, and the time for each character to form a word or idiom was 20 seconds. The last part was relaxation, and the time was set for 70 seconds. The patient also repeated a number from 1 to 5.

NIRS data detection and analysis

The hemodynamic changes of the prefrontal lobe were tested using the 33-lead NIRS system (ETG-4000, Hitachi, Japan) during the cognitive activities. The system consisted of 17 optical signal transmitters and 16 detectors, with a total of 52 channels (14). All sensors were fixed to a soft and elastic cloth cover, which was subsequently fixed on the patient's head. In the present study, 22 channels that covered the prefrontal lobe were selected as the research area. Oxy-Hb values, Deoxy-Hb values and analysis data were collected using the Ver1.61 system software attached to the ETG-4000 brain functional quantitative device. The Gravity value was determined by the mean response amplitudes of the changes during time 15-20 seconds of each individual stimulation and coordinates of the channels.

Statistical analysis

Data were processed using SPSS 19.0, and the dose data were expressed as $\bar{x} \pm$ standard deviation (SD). The correlation r-test and paired *t*-test were used, and $P<0.05$ was considered statistically significant.

RESULTS

Correlation analysis of the Yale-Brown Obsessive Compulsive Scale and Symptom Checklist (SCL-90)

There was a significant positive correlation ($P<0.01$) between the total score of the Yale-Brown Obsessive Compulsive Scale (Yale-Brown) and the total score of the Symptom Checklist (SCL-90) in patients with OCD. The difference was statistically significant ($P<0.03$) between obsessive-compulsive behaviors and obsessive-compulsive thoughts ($t=2.40$, $P=0.025$). Obsessive-compulsive behaviors were positively correlated ($P<0.01$, $P<0.05$) with depression, anxiety, psychosis and other factors in the table (SCL-90), and significantly positively correlated ($P<0.01$, $P<0.03$; Table I) with somatization, hostility and paranoid factor scores in the table (SCL-90).

Results for the frontal lobe NIRS data

NIRS spectral characteristics of the frontal lobe in patients with OCD during the verbal fluency task

The score for the verbal fluency task and its integral value in the frontal lobe of patients with OCD were 7.3 ± 0.65 and 6,916 ± 15.97, respectively. The center of gravity (57.44 ± 2.36) was at the last phase. The slope (0.000619 ± 0.000259) suggests that the integral value of the prefrontal lobe was medium in patients with OCD, and that the center of gravity value was at the last phase (the last 20 seconds). The initial activation was slow, while the subsequent wave fluctuation occurred during the task period (Fig. 1).

Spectral comparisons of the concentrations of Oxy-Hb and Deoxy-Hb in patients with OCD during the implementation of the verbal fluency task period and recovery period

When patients with OCD carried out the verbal fluency task, the concentrations of Oxy-Hb and Deoxy-Hb increased again at the end of the task, and this rising trend was slightly higher than the one occurring during the task period. Furthermore, there was an overlapping trend between the waveform and task period of the project, but the difference was significant between these two groups ($P<0.01$, Oxy-Hb task period, compared to the recovery period, $t=15.07$, $P=0.000$; Deoxy-Hb task period, compared to the recovery period, $t=4.52$, $P=0.000$; Figs. 2 and 3).

TABLE I
CORRELATION ANALYSIS OF THE YALE-BROWN OBSESSIVE-COMPULSIVE SCALE AND SYMPTOM CHECKLIST (SCL-90).

Items	$\bar{x}\pm SD$	Yale-Brown total score 19.83±1.40		Obsessive-compulsive behaviors 11.48±0.84		Obsessive-compulsive thoughts 8.43±1.04	
		r	p	r	p	r	p
SCL-90 total score	218.43±10.53	0.62	0.002				
Somatization	22.53±1.70			0.51	0.013	0.26	0.236
Obsessive-compulsiveness	30.27±1.35			0.40	0.061	0.21	0.332
Interpersonal relation	23.30±1.55			0.35	0.104	0.29	0.181
Depression	36.77±1.97			0.10	0.660	0.64	0.001
Anxiety	25.73±1.30			0.29	0.186	0.58	0.004
Hostility	14.40±1.20			0.66	0.001	0.37	0.079
Horror	13.93±1.06			0.01	0.968	0.56	0.005
Bigotry	13.47±0.87			0.46	0.026	0.29	0.176
Psychosis	21.27±1.43			0.29	0.186	0.44	0.035
Others	17.27±1.09			0.33	0.120	0.59	0.003

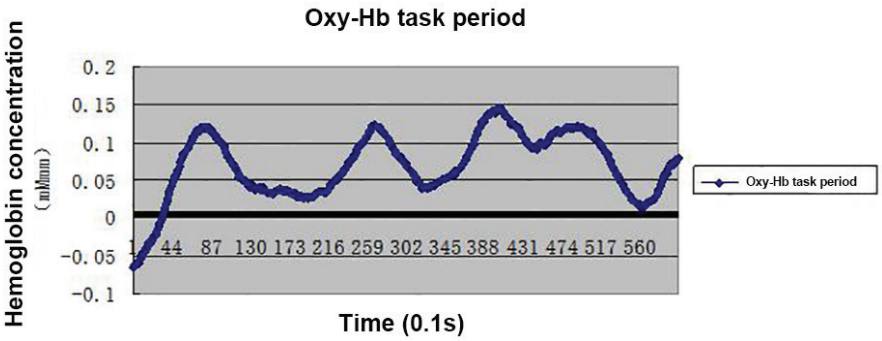

Fig. 1. NIRS spectral characteristics of the frontal lobe in patients with OCD during the verbal fluency task.

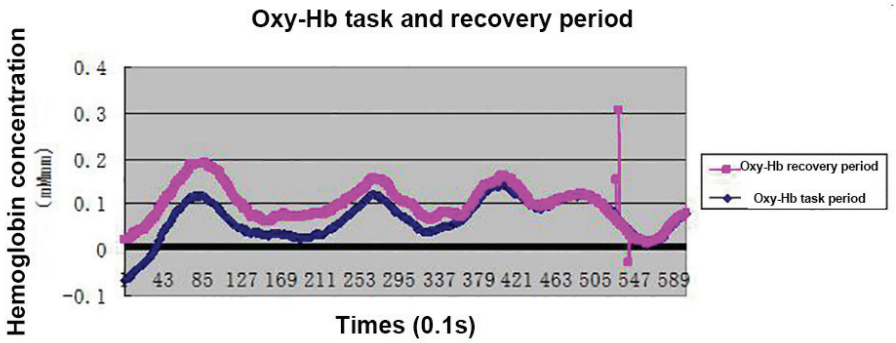

Fig. 2. Changes of the concentrations of Oxy-Hb in patients with OCD during the task period and recovery period.

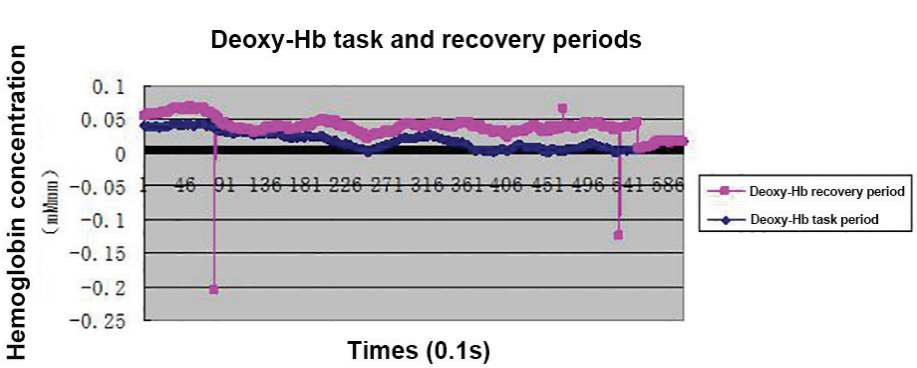

Fig. 3. Changes of the concentrations of Deoxy-Hb in patients with OCD during the task period and recovery period.

The correlation of hemoglobin concentrations among obsessive-compulsive thoughts, obsessive-compulsive behaviors and the data obtained from the 22 channels are shown in Fig. 4. It was found that obsessive-compulsive thoughts were negatively correlated with channels 9 and 19 ($P<0.05$), but there was no correlation ($P>0.05$) between obsessive-compulsive behaviors and channel 22 (Table II).

DISCUSSION

In this Observational-Analytical study, it was found that the mental health of 37 patients with OCD significantly deviated from the normal (SCL-90 total score: 218 points >160 points). Furthermore, there was a difference between obsessive-compulsive behaviors and obsessive-compulsive thoughts. Obsessive-compulsive behaviors often present symptoms of depression, anxiety, psychosis, diet and sleep disorders ($P<0.01$, $P<0.05$), while obsessive-compulsive thoughts often embody somatization, hostility and paranoia ($P<0.01$, $P<0.03$). It has been suggested that obsessive-compulsive behaviors are partially due to emotional traits and obsessive-compulsive thoughts are biased to mental traits, which confirms the view that obsessive-compulsive disorder patients have thinking disorder (15). Therefore, some reference for the selection of antidepressants and antipsychotic drugs in different types of clinical treatments can be provided (16, 17).

The NIRS test was performed in 37 patients with OCD using the verbal fluency method. With respect to the achievements of the verbal fluency task, the average number of words formed by OCD patients within 60 seconds was seven, which was significantly lower than that in normal subjects and schizophrenia patients (18, 19). The integral area of the frontal lobe was medium, and the center of gravity value was at the last phase. The initial activation time was slow and reached the peak again at the end of the task, which was different from the depression integral value area of ≤54, the forward center of gravity value, and the fast-initial activation. Furthermore, this was similar to the late phase of schizophrenia, irregular changes in the task, and the increased reaction at the end of the task, but this did not have the characteristics of the prefrontal lobe of schizophrenia with a small score. This indicates that although depression is present in the syndrome of OCD and antidepressant drugs have been used in the treatment of OCD in clinic, the data of the present study suggests that other significantly different diseases still exists between obsessive-compulsive disorder and depression, which is more like a kind of disease between depres-

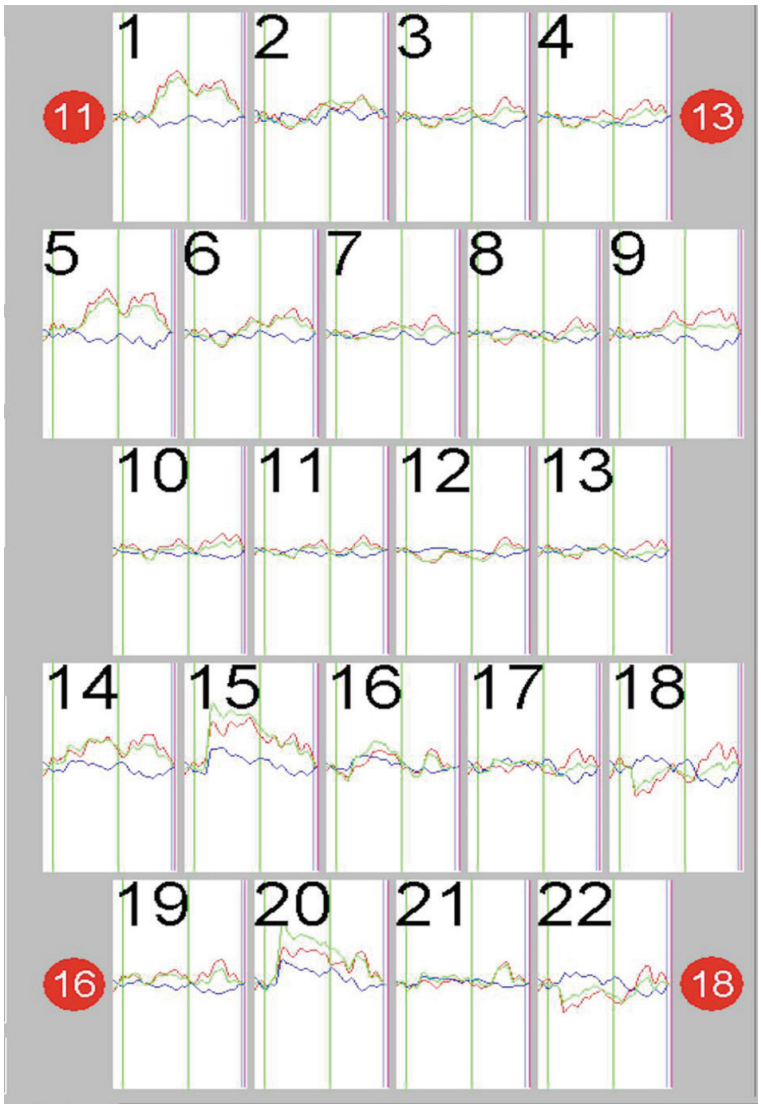

Fig. 4. Data obtained from the 22 channels detected by NIRS.

sion and schizophrenia. This also confirms that OCD is separated from the pedigree of neurotic disorder in the DSM-5 diagnostic criteria and becomes the theoretical basis of an independent diagnostic unit.

It is known that OCD presents with symptoms of repetitive thoughts and behaviors that are not necessary but could not be controlled. OCD has the characteristics of "obsessive-compulsive and counter-obsessive-compulsive" in clinic. Counter-obsessive-compulsive means that although the patients do not want to think about or do the things, their thoughts and behaviors cannot be neglected and the patients cannot help repetitively thinking or doing these things (15). Even when a single thought and behavior ends, OCD patients would continue the "obsessive-compulsive repetition". In the present study, it was found that the atlas of Oxy-Hb and Deoxy-Hb in patients with OCD during VFT task period and recovery period exhibited overlapping signs and characteristics of repeatability. From the point of view of NIRS, this proves that the clinical features of "obsessive-compulsive" repeatability was

TABLE II
CORRELATION OF HEMOGLOBIN CONCENTRATION AMONG OBSESSIVE-COMPULSIVE THOUGHTS, OBSESSIVE-COMPULSIVE BEHAVIORS AND THE 22 CHANNELS.

	Obsessive-compulsive thoughts		Obsessive-compulsive behaviors	
	r	p	r	p
CH1	-0.01	0.975	0.32	0.142
CH2	-0.17	0.452	0.38	0.076
CH3	0.27	0.215	-0.29	0.179
CH4	0.33	0.119	0.24	0.272
CH5	-0.19	0.397	0.13	0.570
CH6	-0.18	0.411	-0.06	0.794
CH7	-0.32	0.132	0.27	0.219
CH8	-0.14	0.511	-0.11	0.623
CH9	-0.43	0.041	0.01	0.980
CH10	-0.11	0.623	-0.01	0.965
CH11	-0.09	0.682	-0.14	0.529
CH12	-0.05	0.810	0.08	0.734
CH13	-0.00	0.984	-0.04	0.874
CH14	-0.26	0.224	-0.01	0.984
CH15	0.09	0.675	-0.09	0.682
CH16	-0.29	0.182	-0.13	0.562
CH17	-0.10	0.657	-0.14	0.521
CH18	0.01	0.976	0.15	0.505
CH19	-0.42	0.047	0.09	0.682
CH20	-0.19	0.374	-0.19	0.384
CH21	-0.36	0.093	-0.22	0.317
CH22	-0.17	0.436	-0.13	0.543

persistent, and that the difference continued to be significant ($P<0.01$) between these.

Obsessive-compulsive thoughts were negatively correlated with channels 9 and 19 of the NIRS. This suggests that the clinical symptoms of obsessive-compulsive thoughts result in the decrease in Oxy-Hb concentration in channels 9 and 19 in a low activation state. This area is part of bilateral dorsolateral frontal lobe cortex and is correlated to continuous attention and working memory. The brain dysfunction of attention and working memory occurs in obsessive-compulsive thoughts during VFT, which is similar to the characteristics of schizophrenia (20).

In summary, the activation time and spectrum tested by NIRS in patients with OCD have certain spectral characteristics of schizophrenia. However, the recovery period and task period of Oxy-Hb and Deoxy-Hb have repetitive characteristics, which is different from the peak of schizophrenia, or even higher than the task period at the end of the task.

In the present study, the frontal lobe blood flow was investigated in patients with

OCD during the completion of the speech fluency task. However, the effect of drugs on this approach has not yet been investigated. In future researches, the characteristics of the mesencephalic blood flow spectrum in the treatment of OCD would be further investigated. Furthermore, there is a need to further expand the sample study and clarify the spectral characteristics of the NIRS test in other mental disorders. This would be an important research direction in the future for the application of the NIRS test to assist in the differential diagnosis of mental illnesses, providing objective and reliable electrophysiological indexes for their diagnosis.

REFERENCES

1. **Yin L, Zhou J, Chen D, Han T, Zheng B, Younis A, Shao Q.** A review of the application of near-infrared spectroscopy to rare traditional Chinese medicine. Spectrochim Acta A Mol Biomol Spectrosc 2019;221:117208.
2. **Rashnavadi T, Macnab A Cheung A, Shadgan A, Kwon BK, Shadgan B.** Monitoring spinal cord hemodynamics and tissue oxygenation: a review of the literature with special focus on the near-infrared spectroscopy technique. Spinal Cord 2019;57:617-625.
3. **AlZubaidi AK, Ethawi Y, Schmölzer GM, Sherif S, Narvey M, Seshia M.** Review of biomedical applications of contactless imaging of neonates using infrared thermography and beyond. Methods Protoc 2018;1(4):39. *doi: 10.3390/mps1040039*.
4. **Hou L, Liu Y, Qian L, Zheng Y, Gao J, Cao W, Shang Y.** Portable near-infrared technologies and devices for noninvasive assessment of tissue hemodynamics. J Health Eng 2019;2019:3750495.
5. **Hoshi Y, Tamura M.** Dynamic multichannel near-infrared optical imaging of human brain activity. J Appl Physiol 1993;75:1842-1846.
6. **Badurdeen S, Roberts C, Blank D, Miller S, Stojanovska V, Davis P, Hooper S, Polglase G.** Haemodynamic instability and brain injury in neonates exposed to hypoxia-ischaemia. Brain Sci 2019;9(3): pii E49.
7. **Tinga AM, de Back TT, Louwerse MM.** Non-invasive neurophysiological measures of learning: a meta-analysis. Neurosci Biobehav Rev 2019;99:59-89.
8. **Andersen AV, Simonsen SA, Schytz HW, Iversen HK.** Assessing low-frequency oscillations in cerebrovascular diseases and related conditions with near-infrared spectroscopy: a plausible method for evaluating cerebral autoregulation? Neurophotonics 2018;5:030901.
9. **Akashi H, Tsujii N, Mikawa W, Adachi T, Kirime E, Shirakawa O.** Prefrontal cortex activation is associated with a discrepancy beween self-and observer-rated depression severities of major depressive disorder: A multichannel near-infrared spectroscopy study. J Affect Disord 2015;174:165-172.
10. **Herrmann MJ, Ehlis AC, Fallgatter AJ.** Frontal activation during a verbal-fluency task as measured by near-infrared spectroscopy. Brain Res Bull 2003;61:51-56.
11. **Henry JD, Crawford JR**. A meta-analytic review of verbal fluency performance following focal cortical lesions. Neuropsychology 2004;18:284-295.
12. **Kinou M, Takizawa R, Marumo K, Kawasaki S, Kawakubo Y, Fukuda M, Kasai K.** Differential spatiotemporal characteristics of the prefrontal hemodynamic response and their association with functional impairment in schizophrenia and major depression. Schizophr Res 2013;150:459-467.
13. **Hon SKH, Siu BWM, Cheng CW, Wong WCW, Foa EB.** Validation of the Chinese Version of Obsessive-Compulsive Inventory-Revised. East Asian Arch Psychiatry 2019;29(4):103-111.
14. **Quan WX, Bai YF, Dong WT, Tian J, Yang SZ.** Normal frontotemporal oxygenated hemoglobin level detection by near-infrared imaging. Journal of China Medical University 2012;41:1044-1046.
15. **Yin HY, Zhao MS, Jiang HB, Yang LH, Zhong YF.** Preliminary Evidences of Obsessive Compulsive Disorder as Thinking Disorder. International Conference on E-Commerce and Contemporary Economic Development (ECED 2014) 2014:343-347.
16. **Gregory ST, Kay B, Riemann BC, Goodman WK, Storch EA.** Cost-effectiveness of treatment alternatives for treatment-

refractory pediatric obsessive-compulsive disorder. J Anxiety Disord 2020;69:102151.

17. **Marazziti D, Mucci F, Avella MT, Dell'Oste V, Baroni S, Dell'Osso L.** Treatment of the obsessive-compulsive and bipolar disorders comorbidity: pharmacodynamic and pharmacokinetic evaluation. Expert Opin Drug Metab Toxicol 2019;15(8):619-631.
18. **Houghton DC, Stein DJ, Cortese BM.** Review. Exteroceptive sensory abnormalities in childhood and adolescent anxiety and obsessive-compulsive disorder: A critical review. J Am Acad Child Adolesc Psychiatry 2020;59(1):78-87.
19. **Tezenas du Montcel C, Pelissolo A, Schürhoff F, Pignon B.** Obsessive-compulsive symptoms in schizophrenia: an up-to-date review of literature. Curr Psychiatry Rep 2019;21(8):64.
20. **de Boer JN, Vingerhoets C, Hirdes M, McAlonan GM, Amelsvoort TV, Zinkstok JR.** Efficacy and tolerability of riluzole in psychiatric disorders: A systematic review and preliminary meta-analysis. Psychiatry Res 2019;278:294-302.