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ORIGINAL RESEARCH

Resting-State Alpha Activity in the Frontal and Occipital Lobes and Assessment of Cognitive Impairment in Depression Patients

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Background: Major depressive disorder (MDD) becomes one of the psychiatric disorders characteristic of a combination of cognitive, emotional, and somatic symptoms. Additionally, cognitive impairment has the most significant impact on functional results. However, the evaluation of cognitive level is still based on various subjective questionnaires as there is no objective standard assessment yet. This research focuses on resting-state alpha activity to identify cognition in MDD patients using electroencephalography (EEG) signals.

Methods: Ninety-two subjects were recruited: 44 patients with MDD and 48 healthy individuals as controls. Functional outcome and cognition were assessed using standardized instruments, and the EEG resting state signal of open and closed eyes was recorded. The comparison and correlation of cognitive levels with alpha power in the bilateral frontal region, bilateral central region, bilateral occipital region, and middle line was evaluated.

Results: The relative alpha power in MDD group was significantly lower than that in the control group ($P < 0.05$). Through correlation analysis, it was shown that the bilateral frontal and occipital alpha power of MDD patients in the closed-eyes state was positively correlated with information processing rate, verbal learning, working memory, and attention retention. The alpha power of the bilateral frontal region in the open-eyes state was positively correlated with information processing rate, working memory, and attention retention ($P < 0.05$).

Conclusion: The research indicates that the changes in frontal and occipital alpha activities may be a promising neurophysiological indicator of cognitive level to diagnose and treat response prediction.

Keywords: major depressive disorder, MDD, EEG, alpha power, cognition impairment

Introduction

Major depressive disorder (MDD) has been one of the most typical psychological disorders that influences about 5–6% of people all over the world.[1] In accordance with the World Health Organization's (WHO) report, MDD is the second major global cause of disease burden in 2020.[2] One of the main challenges of treating MDD is to prevent relapse of MDD.[3] On account of the essence of MDD as a dynamic disorder, repeated relapses are progressively independent from social and environmental pressures; besides, their probability and frequency gradually increase.[4] The risk of reoccurrence is ascribed to the fact that the MDD patients are different from never-depressed persons in their cognition of vulnerability.[5,6] MDD is related to cognitive deficits; besides, functional impairments are connected with the brain regions, like the frontal and temporal regions.[7] According to recent research, MDD exhibits decreased left frontal activities, which is measured by increased interhemispheric alpha power/amplitude).[8] Transcranial alternating current stimulation (tACS) has been shown to improve symptoms of major depression and is associated with a reduction in alpha oscillation power.[9] Compared to subjects with no MDD, the MDD patients have shown less frontal activities. Hence,

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EEG alpha interhemispheric asymmetry is regarded as a risk marker.[10] In addition to alpha oscillation power,[11] several characteristics of alpha oscillation variation can also be used as potential biomarkers for MDD, including alpha peak frequency,[12] and functional connectivity.[13]

Besides the alpha band, the other bands, like the theta band, have also shown correlation through reported decreased frontal theta activities.[14] Furthermore, hypo-activation in left frontal regions and hyperactivation in right frontal regions have been investigated.[15] Regarding the cognitive level of MDD patients, an in-depth EEC investigation is needed, which involves characteristics like alpha interhemispheric asymmetry and spectral power of different frequency bands. Compared with other researches, EEG alpha interhemispheric asymmetry is significant to evaluate the cognitive level of the depressed patients.[16] For example, it seems that the depressed patients have relatively higher left frontal alpha power compared to non-depressive individuals.[17] Higher alpha power can be determined as active inhibition but not cognitive inertia.[18] Therefore, this evidence increases the validity of the EEG alpha interhemispheric asymmetry feature to assess the cognitive level of individuals with depression. Wang et al had revealed distinct alpha oscillatory patterns in individuals with MDD, characterized by elevated high alpha oscillations and reduced low alpha oscillations compared to healthy controls.[19] However, the integration of EEG and measurement of cognition is less explored, and its differences in brain regions of resting-state alpha activity remain uncertain.

This study fills the gap by evaluating the resting-state alpha activity and cognitive level among depressed patients (spectral power calculations for discrepant EEG frequency bands and EEG alpha interhemispheric asymmetry). We hypothesized that there would be multi-dimensional impairments in the cognitive level of patients with MDD in our research. Furthermore, we speculate a positive correlation between the alpha level in the resting state and the patient's information processing rate, reasoning, problem solving, verbal learning, and working memory, etc., suggesting that the alpha level in the resting state may be used as a biological indicator for cognitive impairment in MDD patients.

Method

Study Sites and Participants

This research was implemented at the 300-bed Mental Disorders Centre of Beijing Anding Hospital from July 2022 to May 2023. In the psychiatric service, the whole patients were successively invited to engage in the investigation. Inclusion criteria included 1) ages between 18 and 60; 2) diagnoses of MDD in accordance with the International Classification of Diseases, Tenth Revision (ICD-10);[20] 3) an aggregate score ≥14 on the 17-item Hamilton Rating Scale for Depression (HAMD-17) and an aggregate score <6 on the Young Mania Rating Scale (YMRS);[21] 4) comprehending the assessment and offering written informed consent. Exclusion criteria included 1) serious medical or surgical history; 2) history of drug or alcohol dependence/abuse; 3) dementia diagnosis or other cognitive impairment. Using advertisements, healthy controls (HCs) were recruited from society. This research protocol was approved by the Biomedical Ethics Board of Beijing Anding Hospital.

Data Collection and Measurements

The fundamental clinical and socio-demographic data were gathered and recorded in a form. Instruments for psychopathology contained the Hamilton Depression Scale (HAMD),[22] evaluating the severity of depression.

Function Assessment

Through the Global Assessment Functioning (GAF) test[23,24] and the Functioning Assessment Short Test (FAST),[24,25] functional status was assessed. Moreover, the GAF score ranged from 1 to 100 and measured psychological, social, and occupational dimensions, with higher scores indicating better functioning.[26] The FAST involved 24 items and covered 6 aspects of functioning, cognitive functioning, occupational functioning, autonomy, interpersonal relationships, financial problem, and free time. Each item score ranged between 0 and 3 with a higher total score, which illustrated the higher severity of functional impairment.

Cognition Assessment

Working memory was measured using the Wechsler memory scale-III ss; the score was figured out through adding forward and backward spatial spans.

The Hopkins Verbal Learning Test-Revised (HVLT-R) is a word list learning test consisting of 12-item word lists presented in three learning tests. The memory score is three times the sum of learning test (0 to 36), on behalf of the learning and working memory.[27] Sustained attention was assessed through the Continuous Performance Test-Identical Pairs version, measuring the capability of identifying and reacting to particular occasional incentives at stochastic intervals and impeding responses to non-target incentives.[28] The rate of processing was determined via the Trail Making Test-Part A,[29] the Category Fluency, the Brief Assessment of Cognition in Schizophrenia, and Symbol Coding subtest items. The verbal fluency score was evaluated via the Animal Naming in Category Fluency.[30] The cognitive testing was performed by a trained neuropsychologist. Aside from the attention, greater performance on cognitive function trials was correlated to higher scores.

EEG Signal Acquisition and Data Processing

The EEG was acquired using a Neuracle ® equipment (Version NSM1FS-200801, Changzhou, Jiangsu province, China), and the 19-channel electroencephalography signals were recorded from the scalp of the participants during the experiment.

The subjects were required to keep themselves emotionally stable for five minutes. When participators seated themselves in a silent room, the resting EEG session was carefully recorded; they were requested to relax and alternate between open and closed eyes every five minutes.

Consistent with the regional division in classical resting-state EEG studies, the average value of the power of electrodes in six regions and the power at three sites in the midline were selected as the indicators of resting-state EEG. The six brain regions included the left frontal region (Fp1, F3, F7), right frontal region (Fp2, F4, F8), left central region (T3, C3), right central region (T4, C4), left occipital region (T5, P3, O1), and right occipital region (T6, P4, O2). The occipital area is generally considered to include the posterior temporal lobe and the parietal lobe, and we mainly collected EEG signals from the posterior temporal lobe.

The three sites on the middle line are Fz, Cz, and Pz. EEG signals were online referenced to the Cz electrode and constantly recorded at a rate of 1000 Hz. In the process of recording, electrode impedance was kept lower than 50 kΩ. All data were analyzed using Matlab (The MathWork, MA, USA) combined with EEGLAB toolbox. First, the channel sequence of the data was corrected using EEGLAB, the data were filtered between 0.1 and 30 Hz to ensure that the data collection method was correct for all participants, and then visual checks are performed to remove any bad channels/trials. Independent component analysis (ICA) was then performed to remove large artifacts such as sustained muscle activity or blinking and side eye movements. Finally, the channels removed in the previous analysis step are replaced with spherical interpolation, and the data are re-referenced as an average across all electrodes.

Statistical Analysis

All analyses were implemented with the SPSS version 21.0. The two groups were compared between demographic and clinical variables using chi-square tests, t-tests, and Mann–Whitney *U*-test accordingly. The effect of electrode location and in eyes open and eyes closed conditions was analyzed using 2-way analysis of variance (ANOVA). Pearson correlation analysis was performed between the alpha power with eyes closed and eyes open and the scores of cognitive constructs in the two groups; besides, p value <0.05 achieved statistical significance (two-tailed).

Results

Basic Demographic and Clinical Characteristics

Forty-four MDD patients and 48 HCs were implicated in this research. Table 1 showed the clinical and socio-demographic features of the samples. The mean HAMD-17 total score for the MDD patients was 22.45 ± 5.49. The total illness duration of the MDD patients was 106.43 ± 100.37 months, while the mean current episode duration was 5.30 ± 6.41 months. By comparison with HCs, the MDD patients might be married ($P < 0.001$), and more likely to maintain current smoking behaviors ($P = 0.002$).

Table 1 Comparison of General Data Between MDD Group and Control Group

Group	Gender (Male/Female)	Married (Yes/No)	Medium Education Level (Yes/No)	Tobacco Use (Yes/No)	Alcohol Use (Yes/No)
MDD(n=44) HC(n=48)	24/20 13/35	26/18 9/39	31/11 32/16	17/27 5/43	21/23 20/28
χ^2 P	7.20 0.07	15.85 <0.001	8.73 0.07	10.05 0.002	0.34 0.56
	Age (years)		**Total Illness Duration(months)**	**Current Episode Duration(months)**	
MDD(n=44) HC(n=38)	36.39±15.88 35.13±10.55		106.43±100.37 –[a]	5.30±6.41 –[a]	
t/Z P	1.50 0.14		–[a] –[a]	–[a] –[a]	

Notes: [a]Mann–Whitney *U*-test; Bolded values, <0.05.
Abbreviations: MDD, major depressive disorder; HC, healthy control.

Cognition and Alpha Levels in MDD Group and Control Group

In contrast to HCs (*all P < 0.05*) in Table 2, the MDD patients might have weaker neuropsychological and functional (GAF and FAST) results, like working memory, sustained attention, verbal fluency, processing rate, etc.

The effect of electrode location and in eyes open and eyes closed conditions was analyzed using 2-way ANOVA pairwise comparison. In terms of the closed-eyes state, the comparative alpha power of bilateral frontal, right central, and bilateral occipital regions in the MDD patients was remarkably lower than that in the HCs (*all P < 0.001*). On the contrary, in terms of the open-eyes state, the comparative alpha power of the bilateral frontal and bilateral central regions in the MDD patients was lower than that of the HCs. As results, the difference achieved statistical significance (*all P < 0.001*) in Table 3 and Figure 1.

Correlation Analysis Between Cognitive Levels and Resting-State Alpha Power

As for the closed-eyes state, the alpha relative power of the bilateral occipital regions was positively correlated with working memory, information processing rate, verbal fluency, and sustained attention ($P < 0.05$, Table 4 and Figure S1); the alpha relative power of the bilateral frontal regions was positively correlated with verbal fluency and sustained attention ($P < 0.05$); the alpha relative power of the right central region was positively correlated with information processing rate ($P < 0.05$). In most brain regions apart from the left central region, there were relations between resting alpha power and scores of GAF and FAST, which reflect patient functional outcomes ($P < 0.05$, Table 4).

In the open-eyes state, the alpha relative power of the right frontal and occipital regions was positively correlated with working memory, information processing rate, verbal fluency, and sustained attention ($P < 0.05$, Table 4 and Figure S1);

Table 2 Comparison of Function and Cognitive Level Between MDD Group and Control Group

Group	GAF	FAST	Working Memory	Verbal Fluency	Information Processing Rate	Sustained Attention
MDD(n=44) HC(n=48)	70.02±19.23 94.46±7.16	16.80±13.62 5.69±8.67	40.95±11.32 47.23±9.49	43.00±9.49 49.21±11.39	31.14±12.67 45.04±9.51	34.45±13.14 41.71±11.23
t/Z P	−8.21 <0.001	–[a] 0.04	−2.99 0.004	−2.83 0.006	−5.99 <0.001	−2.85 0.005

Notes: [a]Mann–Whitney *U*-test; Bolded values, <0.05.
Abbreviations: MDD, major depressive disorder; HC, healthy control.

Table 3 Comparison of Closed and Open-Eyes Alpha Power Between MDD Group and Control Group

Variable	Eye – closed		Univariate Analyses		Eye – open		Univariate Analyses	
	MDD (n=44)	HC (n=48)			MDD (n=44)	HC (n=48)		
	M ±SD	M ±SD	t/Z	P	M (SD)	M (SD)	t/Z	P
LFR	0.62±0.22	0.96±0.04	−10.57	<0.001	0.33±0.14	0.65±0.19	−9.38	<0.001
LCR	0.44±0.09	0.49±0.18	−1.81	0.07	0.30±0.19	0.67±0.14	−10.56	<0.001
LOR	0.18±0.07	0.77±0.10	−32.93	<0.001	0.17±0.07	0.21±0.11	–[a]	0.09
RFR	0.60±0.21	0.83±0.13	−6.59	<0.001	0.36±0.26	0.72±0.16	–[a]	<0.001
RCR	0.38±0.13	0.51±0.06	−5.88	<0.001	0.28±0.16	0.68±0.18	−11.27	<0.001
ROR	0.35±0.10	0.80±0.06	−27.068	<0.001	0.27±0.15	0.25±0.09	1.11	0.27
Fz,	0.45±0.18	0.46±0.20	−0.12	0.90	0.24±0.13	0.26±0.16	–[a]	0.67
Cz,	0.48±0.18	0.47±0.18	−0.21	0.84	0.29±0.11	0.30±0.16	−0.52	0.61
Pz	0.50±0.17	0.54±0.20	−1.03	0.31	0.33±0.17	0.34±0.16	−0.30	0.76

Notes: [a]Mann–Whitney *U*-test.
Abbreviations: MDD, major depressive disorder; HC, healthy control; M, mean; SD, standard deviation; LFR, left frontal region; LCR, left central region; LOR, left occipital region; RFR, right frontal region; RCR, right central region; ROR, right occipital region; bolded values, <0.05.

the alpha relative power of the left frontal region was positively correlated with working memory, information processing rate, and sustained attention (P < 0.05, Table 4 and Figure S1); the alpha relative power of the left central region was proactively connected to information processing rate and working memory (P < 0.05, Table 4). In the bilateral frontal and central region, there was a relation between resting alpha power and scores of GAF and FAST (P < 0.05, Table 4).

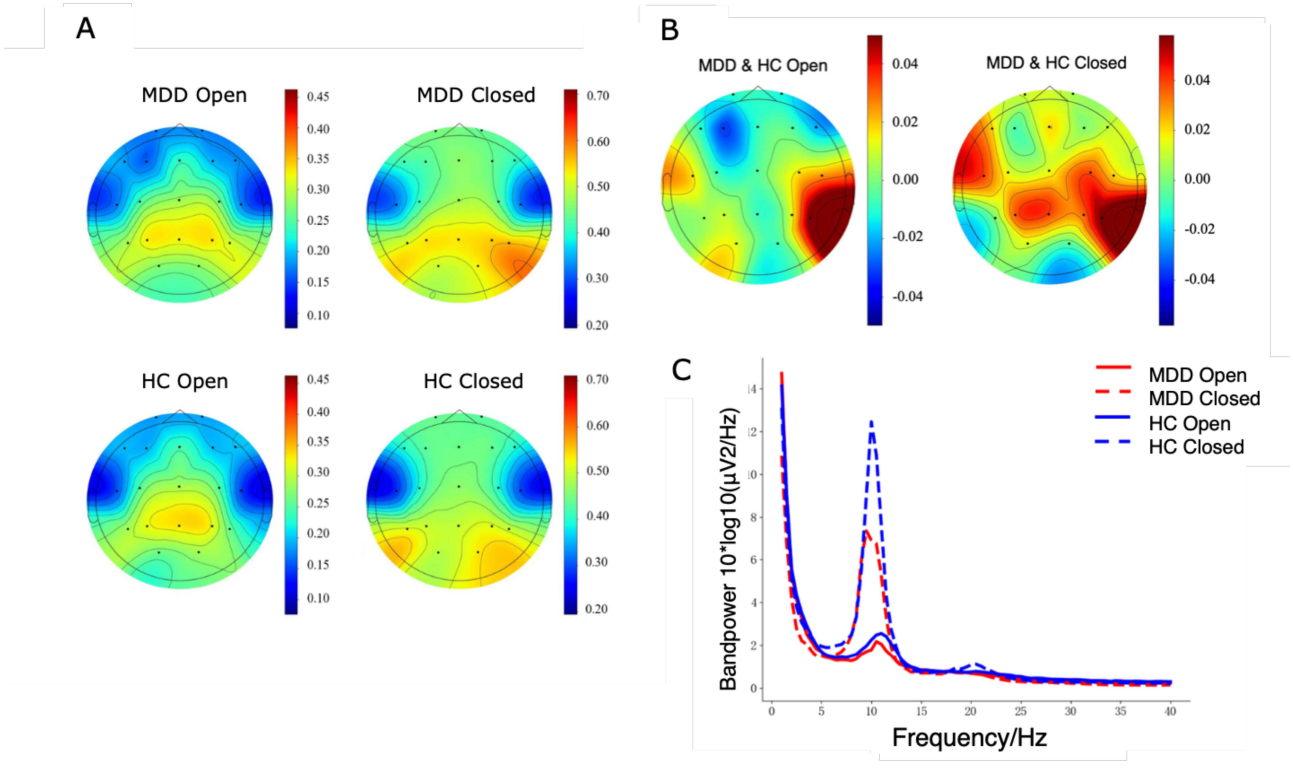

Figure 1 Comparison of resting alpha power between the MDD group and the control group (**A**) alpha power topographic map between the two groups; (**B**) difference map of alpha power between two groups; (**C**) frequency spectrum in resting state of the two groups.
Abbreviations: MDD, major depressive disorder; HC, healthy control.

Table 4 Correlation Analysis Between Alpha Power and Cognitive Dimensions in MDD Patients with Closed and Open Eyes

Eye – Closed Status	GAF	FAST	Working Memory	Verbal Fluency	Information Processing Rate	Sustained Attention
LFR	0.639**	−0.487**	0.197	0.281**	0.515**	0.203
LCR	−0.005	0.106	0.026	0.035	0.023	0.049
LOR	0.636**	−0.441**	0.270**	0.282**	0.519**	0.334**
RFR	0.455**	−0.340**	0.170	0.251*	0.448**	0.224*
RCR	0.435**	−0.273**	−0.062	0.104	0.236*	0.169
ROR	0.680**	−0.490**	0.262*	0.263*	0.494**	0.321*
Eye –open status						
LFR	0.466**	−0.381**	0.291**	0.192	0.351**	0.342**
LCR	0.409**	−0.291**	0.208*	−0.180	0.379**	−0.203
LOR	−0.068	0.02	−0.061	−0.049	−0.020	−0.146
RFR	0.434**	−0.280**	0.366**	0.324**	0.407**	0.445**
RCR	0.406**	−0.298**	0.212*	0.240*	0.420**	0.225*
ROR	0.002	0.105	0.001	−0.008	0.019	0.069

Note: *P <0. 05, **P <0.01.
Abbreviations: LFR, left frontal region; LCR, left central region; LOR, left occipital region; RFR, right frontal region; RCR, right central region; ROR, right occipital region.

Discussion

Commonly, functional and cognitive impairments are related to affective disorders like MDD, which is consistent with most of the literature.[31] Functional impairments are heavily impacted by cognitive impairments as one of the clinical features of MDD, including emotional and somatic symptoms.[32] Perhaps, cognitive impairments exist during the early phases of MDD,[33,34] and during the premorbid stage before the onset of disease.[35] At all stages of MDD, the persistent overreaction of the prelimbic network results in dysfunction and increased vulnerability to emotional dysregulation.[36] Previous studies[37–39] have confirmed the correlation between alpha power and cognition. Studies[40–42] have discovered that event-associated alpha energy is associated with semantic or episodic memory, while performance is associated with working memory. Previous literature have pointed out that individuals with higher resting alpha energy and lower theta energy perform better in cognition and memory, which are potentially helpful indicators of cognitive load.[43]

Alpha power is generally believed to be generated by intercortical interactions driven by thalamic rhythm points. The reduction of alpha power indicates the weakening of cortical inhibition, which enhances the release of subcortical signals and results in impulsive excitability and inattention in behavior.[44,45] Alpha power is connected to both inhibitory function and distant coordination of gamma oscillations.[46,47] Correlation analysis illuminated that in terms of MMD patients, bilateral frontal and occipital alpha power in closed-eyes states was positively correlated with verbal learning, information processing rate, attention retention, and working memory. The results in the open-eyes states further verified the above findings. The alpha power of bilateral frontal regions was positively correlated with information processing rate, working memory, and attention retention, indicating stronger cognitive ability in MDD patients with higher resting alpha power levels.

Recent findings also indicate that reduced alpha power in MDD patients may represent a discontinuity in the function of the fronto-parieto-occipital effective connectivity, which relates to initiating and regulating cognitive control.[48,49] Clinically, MDD patients lack sufficient cognitive control and often suffer from continuously thinking about personal feelings and problems, a process known as emotional rumination.[50] In addition, the EEG pattern of reduced alpha energy may reflect reduced metabolism in the forebrain or thalamus. This implies that the central nervous system is in a state of low arousal, thereby reducing the level and ability to respond to external stimuli,[51] in turn also affecting cognitive function, as manifested in anhedonia in MDD patients.[52] The origin of alpha oscillations is complex and reflects the various mechanisms of cortico-cortical pathways[53] or thalamic-cortical pathways.[54] The dynamic modulation of alpha

oscillations is influenced by the neurotransmitter systems in the thalamus and cortex, and these alterations are reflected in individuals with MDD,[19] where shift toward high alpha oscillations and diminished lower alpha oscillations can be observed in relation to relaxation or cognitive engagement.

This research should be cautiously interpreted due to the following limitations. At the beginning, the sample size was comparatively small. Next, this was a cross-sectional study, not providing more definite conclusions about the progressions of the alpha–cognition relationship. From the viewpoint of the methodology, a bigger sample would be utilized for analysis of all potential combinations among depression, cognition, and their correlation to neural indexes. Third, this study mainly focused on the analysis of the correlation between alpha activity and cognition in MDD patients and did not involve other concussion bands. In future studies, more bands of brain electrical activity should be analyzed in order to more accurately identify the disease characteristics of MDD based on different EEG patterns.

Conclusion

In summary, the MDD patients presented multidimensional cognitive impairment and variation in resting alpha activity. The frontal and occipital changes in alpha activity in MDD patients suggest reduced activation in these regions, which affects emotional and cognitive states, providing promising neurophysiological indicators for diagnosis of MDD and predicting treatment responses, which is advantageous for future clinical practice.

Data Sharing Statement

The data of the investigation will be made publicly available if necessary.

Ethics Approval

This study involving human participants was reviewed and approved by the Human Research and Ethics Committee of Beijing Anding Hospital, Capital Medical University. All the study procedures were carried out in accordance with relevant guidelines. This study was performed in line with the principles of the Declaration of Helsinki.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors have no conflicts of interest to declare in this work.

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