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Research paper

EEG beta and low gamma power correlates with inattention in patients with major depressive disorder

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ABSTRACT

Background: Inattention is a common feature of major depressive disorder (MDD). The aim of this study was to explore the relationship between quantitative electroencephalography (qEEG) power of a specific band and inattention severity in patients with MDD.
Methods: EEG recordings of 73 patients with MDD were collected in during both eyes closed and eyes open conditions. Inattention was assessed by the inattention sub-scale of the Korean version of the Adult ADHD scale (K-AADHD). The severity of symptoms associated with depression and anxiety was assessed with the Hamilton Rating Scale for Anxiety (HAM-A), the Hamilton Rating Scale for Depression (HAM-D), and the Beck Depression Inventory (BDI). Multiple regression and Hayes mediation model were applied for the statistical analysis to verify the effects of clinical variables on inattention score.
Results: The beta (12–30 Hz) and low gamma (30–50 Hz) powers in fronto-central regions were negatively correlated with inattention scores. Symptom severity scores strongly predicted inattention scores; in particular, the BDI accounted for 23.9% of the variance. In mediation analysis, BDI fully mediated the path of anxiety to inattention.
Limitations: The medication effect and comorbidity in our participants were not fully controlled. A subjective assessment tool was hired to measure inattention.
Conclusions: Beta and low gamma power of the fronto-central regions might be a reliable measure of attention deficits in patients with MDD, which in turn, seems to be related to the severity of subjective depressive symptoms. Further work is needed to confirm this finding on larger, drug and comorbidity-free samples, and to test the clinical utility.

1. Introduction

Major depressive disorder (MDD) is a common mental disorder with a lifetime prevalence rate of 17–21% (Iosifescu et al., 2009; Kessler et al., 2005; Savitz and Drevets, 2009), and it is associated with a high degree of subjective distress and psychosocial disability (Judd et al., 2000). The prevalence of comorbidity is very high in MDD in the form of anxiety disorders, personality disorders, substance abuse and medical illnesses, and is costly to individuals and society (Ballenger, 2000).

MDD is characterized by deficits in cognitive domains such as attention, concentration and executive functions, as well as learning and memory (Barabassy et al., 2010; Baune et al., 2006; Jaeger et al., 2006). Executive function, which is involved in the control of memory and attention, is significantly impaired in adults with MDD in acute episode (Rogers et al., 2004). Preiss et al. (2010) suggested that the ability to sustain attention supports various cognitive functions and difficulties in the domain of attention which is one of the earliest signs of MDD. During the past decade, several studies have indicated that cognitive dysfunction is a critical determinant of health outcome in adults with MDD who are otherwise in symptomatic remission (Conradi et al., 2011; Jaeger et al., 2006). It has been reported that functional outcomes in patients with MDD are associated with, or mediated by, cognitive disturbances (McIntyre et al., 2013). Recently, it was revealed that perceived inattention of MDD patients significantly predicted poor workplace performance, as well as a lower quality of life (McIntyre et al., 2015).

The incidence of inattention in patients with MDD has not been systematically evaluated. In one national comorbidity survey, it was reported that 18.6% of the adult patients with MDD met criteria for attention deficit hyperactivity disorder (ADHD) (Kessler et al., 2006). Sustained attention impairment has also been

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reported in adolescents with MDD during the depressed state (Cataldo et al., 2005; Wilkinson and Goodyer, 2006).

QEEG, quantitative methods of analysis, enables the characterization of brain signal oscillations and it has been used as a tool to investigate physiological and pathological cognitive processes (Basar and Guntekin, 2013; Millan et al., 2012). Across decades, high-frequency EEG activity has been repeatedly associated with attentional process in healthy individuals and in a number of different clinical conditions (Barry et al., 2003). Recently, Gola et al. (2013) found that decreased beta band activity during the visual attention task reflects difficulty in activation and deficits in sustaining attentional processes. MacLean et al. (2012) showed that high resting state beta band power is related to high accuracy in the attentional blink task, while increased alpha band power is related to lower performance. In contrast, patients with ADHD had decreased beta and gamma power, in comparison to age-matched healthy controls (Clarke et al., 2001; Matsuura et al., 1993; Roh et al., 2015). However, clinical applications of EEG to ADHD patients still very controversial with the question being whether the knowledge gained from EEG has any practical diagnostic value and clinical utility (Johnstone et al., 2013; Lenartowicz and Loo, 2014; Loo and Makeig, 2012).

In this study we hypothesized that patients with MDD would have symptoms of inattention and these are associated with qEEG changes, especially in beta and low gamma band power. Therefore, the goals of this study were to clarify whether the symptoms of inattention could be reflected by the qEEG band power, and to explore how anxiety and depressive symptom severity affects inattention and qEEG power in patients with MDD.

2. Materials and methods

2.1. Subjects

A total of 73 patients with MDD (mean age=38.71 ± 13.85 years, 33 male) were recruited. Of these, 38 had a comorbidity, such as general anxiety disorder (GAD, n=2), obsessive-compulsive disorder (OCD, n=3), panic disorder (n=11), adjustment disorder (n=12), post-traumatic stress disorder (n=10). All patients were diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria. Symptom severity was assessed with the Hamilton Rating Scale for Anxiety (HAM-A), the Hamilton Rating Scale for Depression (HAM-D) (Hamilton, 1960), and the Beck Depression Inventory (BDI) (Beck et al., 1961). Subjective inattention was measured by the inattention sub-score of the Korean version of the Adult ADHD Scale (K-AADHDS), which was translated and validated (Kim, 2003) from the original adult ADHD scale developed by Murphy and Barkley (1996). The K-AADHDS consists of 18 items investigating behavior and 9 items related to inattention. Only the nine-item inattention scale (Cronbach alpha=.79) was used in our study (Table 1). We obtained written informed consent from all participants before study enrolment. The study was reviewed and approved by the Institutional Review Board of Inje University Ilsan-Paik Hospital.

Table 1
Validated Inattention Scale with 9 items (K-AADHDS).

Scale items for ADHD inattention	Factor Loading
1. Fail to give close attention to details or make careless mistakes in my work or other activities	.528
2. Have difficulty sustaining my attention in tasks or fun activities	.686
3. Don't listen when spoken to directly	.416
4. Don't follow through on instructions and fail to finish work or chores	.615
5. Have difficulty organizing tasks and activities	.619
6. Avoid, dislike, or am reluctant to engage in tasks that require sustained mental effort	.509
7. Lose things necessary for tasks or activities	.411
8. Am easily distracted by extraneous stimuli or irrelevant thoughts	.614
9. Am forgetful in daily activities	.460

Note. K-AADHDS, the Korean version of the Adult ADHD Scale.

2.2. EEG recordings and qEEG analyses

The subjects were seated in a dimly lit, sound-attenuated room, and asked to relax and stay still for 3 min with their eyes open and for 3 min with their eyes closed. Laboratory EEG recordings were collected using a NeuroScan SynAmps 2 amplifier (Compumedics, El Paso, TX) from 62 surface electrodes (FP1, FPZ, FP2, AF3, AF4, F7, F5, F3, F1, FZ, F2, F4, F6, F8, FT7, FC5, FC3, FC1, FCZ, FC2, FC4, FC6, FT8, T7, C5, C3, C1, CZ, C2, C4, C6, T8, TP7, CP5, CP3, CP1, CPZ, CP2, CP4, CP6, TP8, P7, P5, P3, P1, PZ, P2, P4, P6, P8, PO7, PO5, PO3, POZ, PO4, PO6, PO8, CB1, O1, OZ, O2, and CB2) mounted on a Quik-Cap (Compumedics, El Paso, TX) according to the extended international 10–20 placement scheme. The ground electrode was placed on the forehead and the reference electrode was predefined in the cap and positioned at between Cz and CPz. The vertical electrooculogram (EOG) was recorded using bipolar electrodes; one located above and one below the right eye. A horizontal EOG was recorded at the outer canthus of each eye. The impedance of the electrodes was maintained at less than 5 kΩ.

EEG data were recorded with a .1–100-Hz band-pass filter at a sampling rate of 1000 Hz and initially processed using Scan 4.3. Eye movements were visually screened and eliminated by an expert. Only the eyes closed resting state condition was retained for analyses. Signal was segmented using predefined time windows of 2.048 s each. Epoch with signal over the +80 μV or lower than −80 μV on any channel was rejected from the analysis. A total of 30 epochs (~60 s) were prepared for each subject. Spectral density was calculated in each epoch on 62 electrode channels, and averaged 30 epochs by the Fast Fourier Transform. After performing FFT, spectral density averaged into specific frequency ranges, and each frequency band range was composed as follows (Kim et al., 2012): delta (1–4 Hz), theta (4–8 Hz), alpha (8–12 Hz), beta (12–30 Hz), and low gamma (30–50 Hz). Then, the relative power of each channel was calculated by dividing each band power by the total power of the channel. On the basis of previous literature, we considered 6 regions of interest (ROI), of three channels each, and the averaged signal within each region was considered for correlational analyses (Zion-Golumbic et al., 2008) (Fig. 1): left frontal (AF3, F3, and F5), right frontal (AF4, F4, and F6), left central (C3, C5, and CP3), right central (C4, C6, and CP4), left parieto-occipital (P5, P7, and PO7), and right parieto-occipital (P6, P8, and PO8). In addition, the relative global band powers were calculated over 62 electrode channels and then averaged (Gianotti et al., 2007; Jung et al., 2007).

2.3. Statistical analysis

Spearman's correlation analysis was performed to evaluate the relationship between the qEEG and scores on the selected scales in patients with MDD. The bootstrap resampling technique (n=5000) was used to correct multiple correlations. To explore the predicting factors of inattention in patients with MDD, a two-step regression procedure was used. In the first stage, we controlled significant effects of demographic variables on inattention in the regression model. In the second stage, we input HAM-A, HAM-D, and BDI as predictor variables and analyzed the result. To verify the path involved when depression and anxiety affect