Electroencephalogram beta power assay: A promising diagnosis tool of cognitive impairment in early time after cerebral hemorrhage

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Abstract

Background: Cerebral hemorrhage (CH) could affect the cerebral function on specific cognitive abilities and lead to the cognitive decline or cognitive dysfunction. Electroencephalogram (EEG) is a relatively cheap and easy usable tool, which could reflect the cerebral function of the patients. Materials and Methods: A total of 170 patients (patients with and without cognitive impairment) with CH and 120 normal healthy controls were recruited from September 2008 to June 2012 at the Department of Neurology. EEG studies were carried out to analyze the cerebral function in all the subjects. Correlation, clustering and concordance analysis were performed to analyze the relationship between EEG power and Montreal cognitive assessment (MoCA) scores. The effects of EEG analysis were assessed to diagnosis the cognitive impairment. **Results:** The results were showed that patients with cognitive impairment had a significantly decreased EEG beta power (0.771 \pm 0.149 μ V²) compared with the normal cognitive function (1.654 \pm 0.186 μ V², P < 0.01) or normal healthy controls (1.703 \pm 0.216 μV^2 , P < 0.01). Significantly positive correlation (r = 0.90174, P < 0.001) was discovered between relative beta power and hemorrhage type, while significantly negative correlations between the relative beta power and hemorrhage size and amount were also observed (r = -0.81235 and r = -0.90136, respectively, all P < 0.001). There was a better concordance between K-means clustering algorithm calculating of the relative beta power and MoCA scores ($\kappa = 0.913$, P < 0.001). **Conclusion:** The cognitive impairment post hemorrhage was positively correlated to hemorrhage type and negatively correlated with hemorrhage size and amount. The analysis method of EEG beta power abnormality holds a promise to assess the cognitive impairment post CH.

Key words: Beta power, cerebral hemorrhage, cognitive impairment, concordance analysis, electroencephalogram

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Introduction

Cerebral hemorrhage (CH), is a subtype of intracranial hemorrhage that occurs within the brain tissue. [1] CH could affect the cerebral function on specific cognitive abilities and lead to the cognitive decline or cognitive dysfunction. [2] Clinically, cognitive impairment could cause serious social, vocational or other abilities impairment. [3,4] Earlier studies have focused on the

cognitive consequences of some of the degenerative disease^[5,6] but the cognitive impairment or decline in patients with CH has not been well-investigated.^[7]

Electroencephalogram (EEG) is a relatively cheap and easy to use tool. EEG has been used to assess the cognitive function of patients with brain injury or degenerative diseases. [8] In Alzheimer's disease (AD) patients, abnormal EEG recordings could reflect cognitive decline status. [9] Signs of diffuse EEG slowing are useful in differentiating the healthy humans from AD patients. [10] Thus, EEG recordings may provide valuable diagnostic assistance in evaluating patients with cognitive impairment.

EEG beta power was employed to investigate the cognitive impairment after CH. K-means clustering algorithm was used to divide CH patients into cognitive impairment group (CHCI) and congniive normal controls (CHNC). Meanwhile, the normal subjects were also employed as the control group cognitive normal (CN). In present study, the beta power recordings were detected and analyzed and the potential value for cognitive impairment of CH patients was investigated.

Materials and Methods

Subjects

In the present study, 170 CH patients (51 patients with thalamic CH, (84 patients with basal ganglia CH, and 35 patients with both) were recruited from September 2008 to June 2012 at the Department of Neurology of Xinqiao Hospital. Also 120 normal healthy controls (CN) were selected from Physical Examination Center. Informed consent was obtained from either the patients or care givers.

Diagnostic method and criteria

Montreal cognitive assessment (MoCA) scale (Beijing version) was used to assess the cognitive impairment at the time of EEG and at 12 weeks post CH. Of the 170 patients, 105 (61.8%) patients with a MoCA score less than 26 were grouped as cognitive impairment (CHCI) group and 65 (38.2%) patients with MoCA score more than 26 were grouped as cognitive normal (CHNC). All the subjects with MoCA score more than 26 were grouped into CN group.

Some standardized diagnosis scales, such as Hamilton depression rating scale (to exclude the depressive disorder), Hachinski ischemic scale (to exclude AD), instrumental activities of daily living, basic activities of daily living and clinical dementia rating scale were selected to exclude other diseases.

EEG recordings and analysis EEG activity was recorded continuously from 16 channels by using the standard EEG

electrode placement (Jasper 10-20 electrode placement) and positioned according to the 10-20 international systems (Fp1, Fp2, F7, F3, F4, F8, T3, C3, C4, T4, T5, P3, P4, T6, O1 and O2). EEG data were analyzed and fragmented off-line in consecutive epochs of 2 s, with a frequency resolution of 0.5 Hz.[11] The EEG epochs with ocular, muscular and other types of artifacts were preliminary identified by a computerized automatic procedure. EEG epochs with sporadic blinking artifacts were corrected by an autoregressive method validated in Moretti's et al. study. [12] Eight beta bandwidth signals of EEG channels (including Fp1, C3, C4, T4, T5, P3, P4 and O2) were selected for CH patients in this study. Using these 8 channels selected, an eight-dimensional characteristic vector and a characteristic vector array were obtained.

Clustering analysis

In order to classify the characteristic vector array, the K-means clustering algorithm was employed. The K-means clustering algorithm was used to calculate the centroid (mean EEG power) for each category (CHCI group and CHNC group). The value of the centroid was then iteratively adjusted until the differences between data points and the centroid for each group was minimized. The steps in the algorithm were as follows as in the previous report:[13] (1) Choose K initial cluster centers (two centers, CHCI and CHNC, K = 2); (2) Calculate the Euclidean distances between the feature vectors; (3) Find the centroids of the newly created K clusters; (4) Using the centroids of step 3 as cluster centers, repeat step 2 and step 3 until the centroids no longer changed. At this point, the algorithm is assigned to attain "convergence", i.e., they no longer change with subsequent iterations.

Statistical analysis

SPSS (19.0 version) statistical software and *t*-test were used for data analysis in this study. The K-means clustering was performed using MATALAB R20120a software. Both of K-means program algorithm and MATLAB function were applied to determine clusters. The concordance analysis was analyzed by Kappa test.

Results

Basic data

No significant differences for gender, educational level, hypertension, hyperglycemia, disease course were found among all the three groups. There was a significant difference for the location of hemorrhage in CHCI and CHNC groups. The occurrence of the basal ganglia hemorrhage in the CHCI group was significantly higher compared with the CHNC group [Table 1, P = 0.008]. The occurrence of the thalamus hemorrhage in the CHNC group was significantly higher compared with the CHCI group [Table 1, P = 0.006]. The occurrence of both

hemorrhages in the CHCI group was significantly higher compared with the CHNC group [Table 1, P = 0.001].

EEG spectral and relative beta power

The EEG beta relative power in CHCI patients decreased significantly (0.771 \pm 0.149 μ V²) compared with CHNC (1.654 \pm 0.186 μ V²) (P < 0.01) or CN group (1.703 \pm 0.216 μ V²) (both P < 0.01) [Figure 1 and Table 2]. Relative beta power values for CHNC group were closely aligned with CN group suggesting no significant difference between CHNC and CN group (P > 0.05) [Figure 1].

MoCA score at time of EEG and 12 weeks post disease

Table 3 shows the MoCA scores for both at the time of EEG and 12 weeks post disease in the three groups. For the initial EEG, the MoCA scores of CHCI and CHNC patients (15.71 \pm 2.03 and 18.15 \pm 1.85) were significantly lower compared with CN group (29.25 \pm 1.97) (both P < 0.01). The MoCA scores of CHCI patients were also significantly lower compared with the CHNC patients (P < 0.05). For the 12 weeks EEG, the MoCA scores of the CHNC group patients (28.67 \pm 2.68) were significantly improved compared with the initial EEG (18.15 \pm 1.85) (P = 0.021). Although the MoCA scores of CHCI group patients (16.81 \pm 2.03) only indicated a little improvement compared with the initial EEG (15.71 \pm 2.03) (P = 0.073).

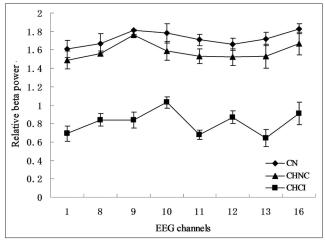


Figure 1: Relative beta power for the three groupsc

Correlation between relative beta power and hemorrhage characteristics

The correlation analysis results indicated that there was a significantly positive correlation between the relative beta power and hemorrhage type [Figure 2a] (r = 0.90174, P < 0.001). At the meantime, the relative beta value were negative correlated with the hemorrhage size (r = -0.81235, P < 0.001) and hemorrhage amount (r = -0.90136, P < 0.001), respectively [Figure 2b and c].

Clustering and concordance analysis

The beta powers of 170 patients on the highest channels (1, 10 and 12) were reflected on the three-dimensional graph of beta power to observe the difference. The results were showed that the relative beta power from 63 cases out of the total cognitive normality post CH (65 cases for MoCA assessment) distributed in the interval I ([0.8, 1.5]); and 102 cases out of the total cognitive impairment post CH (105 cases for assessment) distributed in the interval II ([0, 1.0]) [Table 4 and Figure 3]. Therefore, 2 cognitive normality and 3 cognitive impairment patients distributed in the interval III ([1.0, 1.2]), which were relatively far apart from both convergence center.

Two specific convergence interval I and II were selected and the clustering results and MoCA scorings were compared [Table 4 and Figure 3]. The results illustrated that 63 cognitive normality cases analyzed by EEG were consistent with the MoCA scoring and the sensitivity was 96.9%. 102 cognitive impairment cases analyzed by EEG were consistent with the MoCA scoring and the sensitivity was 97.1%. Kappa analysis results indicated that there was a better concordance between beta power

Table 2: Relative beta power analysis						
Group	Cases	Relative beta power	P ₁	P ₂	P ₃	
CN	120	1.703±0.216	0.009	0.017	0.208	
CHNC	65	1.654±0.186 ^{\$}				
CHCI	105	0.771±0.149** ^{,#}				

** P_1 <0.01 represents the comparison between CHCl and CN group, * P_2 <0.05 represents the comparison between CHNC and CHCl, \$ P_3 >0.05 represents the comparison between CN and CHNC group. CN - Cognitive normal, CHNC - Cerebral hemorrhage cognitive normal group, CHCl - Cerebral hemorrhage cognitive impairment group

Table	1: B	Basic	date	of t	lhe	sub	jects
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	CHCI (cases)	CHNC (cases)	CN (cases)	P ₁	P ₂	P ₃
Age (year)	68.47±9.14	61.18±4.96	59.76±10.5	0.014	0.025	0.26
Male (case, %)	56 (53.3)	36 (55.4)	67 (55.8)	0.251	0.365	0.189
Educational level (year)	7.69±0.93	7.47±0.73	7.47±0.51	0.345	0.219	0.186
Hypertension (case, %)	68 (64.8)	39 (60.0)	73 (60.8)	0.198	0.207	0.412
Hyperglycemia (case, %)	33 (31.4)	20 (30.8)	36 (30)	0.326	0.231	0.146
Course of disease (hour)	8.43±0.98	8.15±1.19	-	0.161	-	-
Basal ganglia area	39 (76.5)	12 (23.5)	-	0.008	-	-
Thalamus area	19 (22.6)	65 (77.4)	-	0.006	-	-
Both areas	31 (88.6)	4 (11.4)		0.001		

P₁ CHCI versus CHNC, P₂ CHCI versus CN, P₃ CHNC versus CN. CN - Cognitive normal, CHNC - be congniive normal controls, CHCI - Cerebral hemorrhage cognitive impairment group

Table 3: MoCA score at time of EEG and 12 weeks post disease

Groups	CN		CHNC		СНСІ	
	Initial EEG	12 weeks EEG	Initial EEG	12 weeks EEG	Initial	12 weeks EEG
MoCA score	29.25±1.97	29.46±2.06	18.15±1.85	28.67±2.68	15.71±2.03	16.81±1.13
P value	0.118		0.021		0.073	

MoCA - Montreal cognitive assessment, EEG - Electroencephalogram, CN - Cognitive normal, CHNC - Cerebral hemorrhage cognitive normal group, CHCI - Cerebral hemorrhage cognitive impairment group

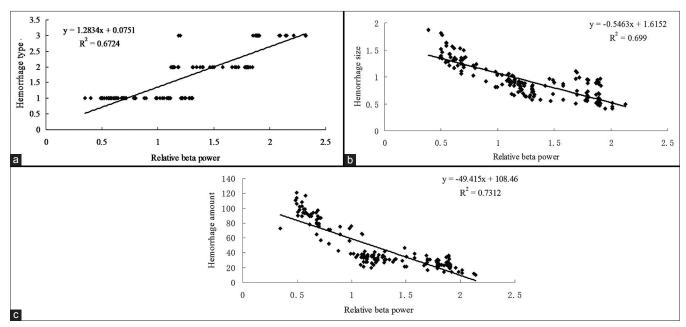


Figure 2: Correlations between relative beta power and cerebral hemorrhage characteristics. (a) Correlation between beta power and hemorrhage type, 1 represents thalamus area, 2 represents basal ganglia area, 3 represents both area (b) Correlation between beta power and hemorrhage size (c) Correlation between beta power and hemorrhage amount

analysis and MoCA scoring method for the cognitive impairment assessment (K =0.913, P < 0.001). Through the McNemar paired Chi-square test, we found that there were no significant differences between beta power analysis and MoCA scoring method for the cognitive impairment post CH [Table 4, P = 0.275].

Discussion

Recently, exploring proper testing methods that could diagnosis the cognitive impairment post CH has become a hot field for the CH study. A series of standardized diagnostic method for cognitive impairment have been utilized. MMSE scale and MoCA scale have been performed to assess the cognitive impairment in some of the acquired diseases. [14-16] In the present study, the MoCA scoring was employed and combined with the EEG beta power to study the cognitive impairment post CH.

In the previous studies, EEG has been used to reflect cognitive impairment status caused by various kinds of diseases, such as cerebral infarcts, AD, Parkinson disease (PD) and others [17,18] Giannakopoulos *et al.* [19] used

EEG analysis identifying the subtle functional changes preceding metabolic deficits in cognitive impairment. The automated pattern recognition techniques of EEG can also identify those mild cognitive impairment progressing to the other diseases.[20] Most of the studies have not investigated the gamma bandwidth because of low power and higher susceptibility to noise. Many investigators also hypothesize that the earliest modifications of the EEG occurs in the beta and theta bands, while changes in the alpha and delta bandwidths appear later in the time course of some brain or neurodegenerative diseases. Meantime, the data regarding EEG changes in patients with brain disease are less readily available. Thus, in the present study, we selected the beta power of EEG to study the cognitive impairment post CH. Correlation analysis results indicated that the beta power was positively related with the hemorrhage type and negatively correlated with hemorrhage size and amount. Our results were consistent with the former study, which explores the cognitive impairment correlating with the hemorrhage characteristics.[21]

CH patients were divided into two subgroups based on their EEG beta power using the K-means clustering

Table 4: The concordance analysis between beta power and MoCA scoring

Relative beta		Total	
power	Normal	Cognitive impairment	
Interval (I)	63	0	63
Interval (II)	0	102	102
Interval (III)	2	3	5
Total	65	105	170

MoCA - Montreal cognitive assessment

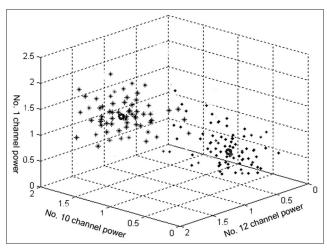


Figure 3: Three-dimensional display of the beta power

technique, including interval I and interval II. The above classification was performed by using the 8 EEG channels exhibiting the largest differences in relative beta power. The beta power of patients was selected on the highest channels (1, 10 and 12) displaying the three-dimensional graph. The Kappa value more than 0.75 was thought to be a better concordance. The K-means clustering analysis shared a better concordance with MoCA scoring (κ = 0.913 for the cognitive impairment assessment, and the sensitivity could achieve 96.9% and 97.1%, respectively).

The previous study showed that the beta power abnormality is effective in modifying CH patients who most likely to progress to cognitive impairment. [13] Our results in present study is consistent with this conclusion. We also found that the analysis of beta power in interval III concerning three patients who were identified as cognitive impairment by MoCA scoring, but who didn't progress to the cognitive impairment in later follow-up diagnosis. While two CH patients in beta power interval III were assessed cognitive normality by MoCA scoring, who developed cognitive impairment in later follow-up diagnose. Hence we concluded that the EEG beta power may exclude the false diagnosis caused by MoCA assessment.

In clinical, it's difficult to identify the cognitive impairment post CH in early time. While the EEG

recordings could be selected within the 24 h post CH. This study demonstrated that EEG can predict cognitive impairment burden at the acute stage of CH.

Conclusion

The analysis method of EEG beta power abnormality holds a promising to assess the cognitive impairment post CH. The cognitive impairment post hemorrhage was positively correlated to hemorrhage type and negatively correlated with hemorrhage size and amount.

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