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Research Article

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Analysis of EEG Complexity in Patients with Mild Cognitive Impairment

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Abstract

Objective: Mild cognitive impairment patients and normal elderly people were selected in this research. EEG complexity (Lempel-Ziv Complexity, LZC) and P300 value of the two groups were compared in two statuses (quiet eyes closed, cognitive load), The brain functional characteristics of different cognitive states were explored, it was expected to construct a simple and objective cognitive function evaluation approach to provide criteria for early diagnosis of cognitive dysfunction and disease evaluation.

Methods: The clinical data was from 50 MCI patients in Neurology department of the 8th People's Hospital. 45 normal elderly people with corresponding sex, age and education level was chosen as control group. 5 minutes EEG signals were recorded and measured with P300 for both groups with quiet eyes closed and cognitive load states. Due to smooth baseline and inconspicuous artifacts, 2048-point EEG (about 8s) were selected to perform LZC analysis and complexity calculation in Mat tab.

Results: 1. Normal elderly people showed higher LZC than MCI patients. Moreover, LZC was higher in those complex brain function areas such as temporal and frontal areas. 2. With the reduction of cognitive function, the value of EEG complexity was reduced accordingly. 3. The cognitive related brain areas showed more obvious degradation than other brain areas. 4. Under the cognitive load status, the complexity value in cognitive related brain areas of MCI patients decreased significantly. 5. The prolongation of P300 latency and LZC decrease of the MCI patients indicated that LZC could reflect the decrease of cognitive function.

Discussion: In this study, P300 latencies of MCI group was delayed, we could deduce that because of the decline in brain function and brain areas of fibers connecting, the reduction in information processing performance could indicate that the delay of P300 latent period. These were identical with another study where the complexity of EEG is testified that. Based on these, we could infer, from the perspective of nonlinearity, EEG complexity reveals the changes of brain function in patients with cognitive impairment.

Conclusion: The brain electrical LZC value in normal elderly people group was higher than that in cognitive impairment group, those brain areas with more complex functions like frontal area and temporal area had highest LZC, which illustrated the degree distribution differences in complex brain regions. The prolonged latency of P300, these results of cognitive impairment in patients could also predict the degree of cognitive decline.

Keywords: Mild Cognitive Impairment (MCI); Complexity of EEG signal; Event related potentials (P300)

Introduction

The global prevalence of dementia, which is characterized by progressive deteriorative cognition, function and behaviour, places a considerable burden on society [1]. The rate of death is 3 to 4 times higher after a diagnosis of AD dementia than the one-third of all deaths attributable to AD dementia [2]. According to statistics, the dementia prevalence rate is 6% to 12% for the people over 60-years-old increasing up to 20% to 48% for those over 85-years-old [3]. Mild cognitive impairment (MCI) is recognized as the transition state between normal aging and dementia [4]. The construct has been extensively used worldwide, both in clinical and research settings, to define the grey area between intact cognitive functioning and clinical dementia [5]. Identifying individuals with MCI at high risk of conversion to AD is clinically important for selecting appropriate subjects to perform therapeutic trials [6]. Subjects with MCI have a high rate of progression to dementia over a relatively short period. Even among subjects who revert to normal cognition at one point in time, the rate of subsequent MCI or dementia is higher than among those who never develop MCI [7]. Because of the clinical symptoms of patients with MCI were mild, and have more intervention factors, it had gradually become a research hotspot. The diagnosis of Alzheimer disease (AD) dementia is based primarily on the clinical history and examination, but advances in understanding the pathophysiology of AD have led to new diagnostic methods [8]. A "marker of disease state" can be used to diagnose AD in patients with MCI, i.e., to predict which patients with MCI will progress to dementia and those who will not [9]. Recently there is an increasing interest in neurophysiologic techniques such as EEG and MEG that are eminently suitable to capture the macroscopic spatial temporal dynamics of the electromagnetic fields of the brain [10]. Among them, different cognitive state of the energy distribution characteristics processes the EEG signals to reveal the working mechanism of the brain, under different time series lead, different mental tasks [11]. Brain is a non-linear system, and its behavior couldn't be simply and linearly considered as decomposition into single neuron behavior [12]. The complexity of EEG is based on nonlinear theory of the further

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revealed EEG information, and when compared to the traditional linear analysis of EEG signals, the complexity could reflect the difference between ages, consciousness states and brain states by individual differences [13-17]. By comparing the MCI patients and normal elderly people in different states and brain regions, this project adopted the calculation of the complexity (Lempel-Ziv degree) to reveal brain nerve electrophysiological changes. The study objects had definite pathological and physiological background, which could be able to relate the complex value to the pathophysiological basis of the subject, and to draw conclusions that are relatively objective and credible.

Subjects

In this study, we only included patients at the Neurology Department of Shanghai Eighth People's Hospital. The patient quantity was fifty (Male 26; female 24; average age 70.13 ± 5.93) and the quantity of normal elderly people was forty-five (Male: 23; female 22; average age 68.61 ± 7.64). There were no significant differences in age, sex and educational level, and all of the subjects were right hand.

The patients in MCI group were selected according to the new MCI diagnostic criteria and process in 2006 European Association [18] and in addition to the above criteria, we also met these criteria: MMSE score is greater than 24 points; or MOCA score is greater than 26 points; CDR score is less than 0.5 points; and patients with cognitive impairment was excluded if it was caused by depression and anxiety in. The number of contrast group of healthy normal elderly volunteers (meet the diagnostic criteria of the Chinese Medical Association) was forty-five, the average MMSE score was 28-30; or MMSE score was greater than 29 points; CDR score was 0.

Research Methods

EEG signal acquisition

The signals were recorded in quiet eyes closed state and cognitive load state (pure tone hearing oddball sequence stimulation, stimulation parameters with P300 parameters): MCI and normal elderly control group EEG signal for about five minutes. We used Shanghai's NCC MEDICAL NCERP series of EEG and evoked potential instrument, the time constant was 0.3S, high pass filter was 45Hz, sampling frequency was 256Hz, the sampling accuracy was 16bit. Using disk electrode to record, unipolar lead, bilateral reference electrodes were settled on the same side of the process; the ground line was settled at the top of the middle of the nose root. The electrodes were placed in an international standard lead 10-20 system (Figure 1), and 16 brain electrical signals of each group in the quiet closed eyes (5 minutes) were recorded.

Determination of event related potentials

By pure tone auditory stimulus sequence, according to the international 10-20 method, the recording electrode was set to Pz, and the reference electrode was set to FP2. P300 from the target and non-target stimuli consisting of pure tone sequences were induced by "oddball" mode. The parameters were set as follows: non-target stimulation frequency:1KHz, the target stimulus frequency: 2KHz, the target stimuli: randomly distributed, the probability: 20%, the stimulation intensity:110dB, the filter bandwidth:1 ~ 50Hz, the superposition:30 ~ 50 times. After recording to the stable P300, the P300 peak latency was determined.

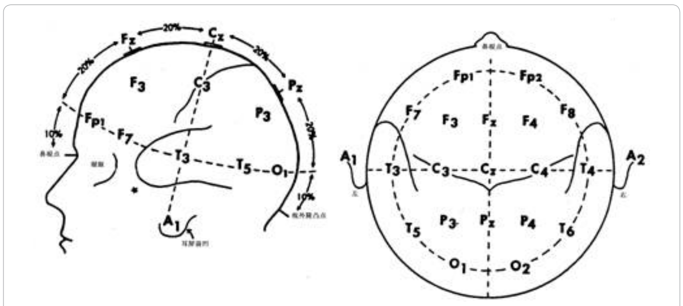

Figure 1: International standard lead 10-20 system.

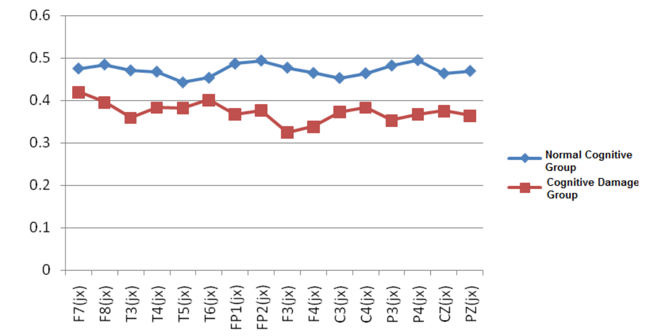

Figure 2: Comparison of LZC values in resting condition.

Selection of EEG signals

First, exclude obvious interference in collected EEG signal, then select those with stable baseline and no obvious artifacts 2048-point data (about 8s) length of egg signal to establish the data file for further analysis. Then, transform the collected EEG signal into the frequency domain signal by the Fourier transform. In filter processing, exclude the EEG data below 0.5Hz and above 45 Hz respectively. Use the IFFT (inverse fast Fourier transform) to process data by the inverse transform. Finally, calculate the Lempel-Ziv of complex degree of the EEG signal upon the processed data.

Statistical analysis

SPSS17.0 statistical software was used for analysis. Measurement data was represented as $\bar{x} \pm s$. The complexity between the two groups was compared with the independent samples t test. And comparison among multiple groups was performed by single factor variance analysis -SNK (q test); comparison between groups used paired samples test; and the difference of p<0.05 was statistically significant.

Results

Comparison of LZC values in two groups in resting condition

In the resting state, the average of EEG signal complex value (LZC) in the different regions of the brain of normal group was higher than the MCI group (P<0.05) (Figure 2 and Table1).

And in MCI group, the complex value in the following brain regions decreased more significantly: i.e., T3 and FP1, FP2, F3, F4, P3, P4 (decreased percentage >20%) (Figure 3 and Table 1).

Comparison of EEG signal complexity in two kinds of normal control group

Paired samples T test and statistical analysis of the LZC value of two kinds of cognitive state in normal elderly group was performed with the results showing no significant difference (Figure 4 and Table 1).

Comparison of the complexity of EEG signal in the two state of cognitive impairment group

In the condition of cognitive load, the LZC value of EEG signals in

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L/ZC Position	Normal group		MCI group		Decreased Percentage (%)
	Resting state	Cognitive load	Resting state	Cognitive load	
F7	0.4756 ± 0.0945	0.4574 ± 0.0951	0.4198 ± 0.0657	0.4177 ± 0.0660	11.75%
F8	0.4850 ± 0.0990	0.4652 ± 0.1134	0.3955 ± 0.0597	0.3930 ± 0.0605	18.44%
T3	0.4713 ± 0.1064	0.4658 ± 0.1090	0.3594 ± 0.0858	0.3545 ± 0.0865	23.74%
T4	0.4682 ± 0.0971	0.4558 ± 0.1051	0.3834 ± 0.0871	0.3790 ± 0.0870	18.10%
T5	0.4430 ± 0.0758	0.4306 ± 0.0839	0.3820 ± 0.0812	0.3827 ± 0.0827	13.78%
T6	0.4538 ± 0.0981	0.4430 ± 0.1023	0.4010 ± 0.1019	0.3994 ± 0.0994	11.62%
FP1	0.4870 ± 0.0917	0.4710 ± 0.0980	0.3671 ± 0.0770	0.3638 ± 0.0753	24.62%
FP2	0.4943 ± 0.0591	0.4941 ± 0.0592	0.3766 ± 0.0860	0.3733 ± 0.0831	23.81%
F3	0.4775 ± 0.0373	0.4769 ± 0.0370	0.3247 ± 0.0513	0.3209 ± 0.0515	32.00%
F4	0.4652 ± 0.0483	0.4626 ± 0.0485	0.3384 ± 0.0585	0.3332 ± 0.0578	27.26%
C3	0.4533 ± 0.0474	0.4520 ± 0.0473	0.3730 ± 0.0993	0.3726 ± 0.0975	17.71%
C4	0.4644 ± 0.0643	0.4640 ± 0.0638	0.3835 ± 0.0570	0.3829 ± 0.0572	17.42%
P3	0.4826 ± 0.0688	0.4827 ± 0.0686	0.3532 ± 0.0844	0.3487 ± 0.0839	26.81%
P4	0.4954 ± 0.0729	0.4910 ± 0.0706	0.3672 ± 0.0842	0.3653 ± 0.0840	25.88%
Cz	0.4642 ± 0.0482	0.4645 ± 0.0476	0.3750 ± 0.0752	0.3741 ± 0.0759	19.21%
Pz	0.4699 ± 0.0632	0.4635 ± 0.0668	0.3644 ± 0.1101	0.3675 ± 0.1123	22.45%

Table 1: LZC values of two groups in different kinds of cognitive state and decreased percentage.

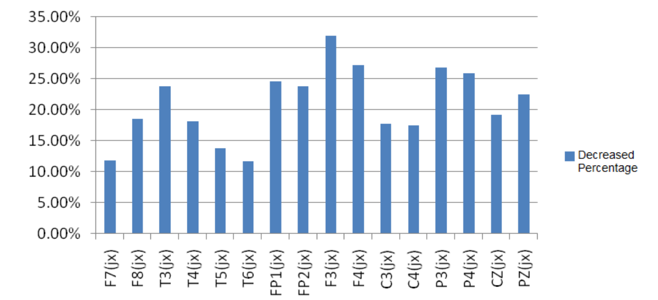

Figure 3: Decreased percentage of each brain region in resting condition for cognitive damage group.

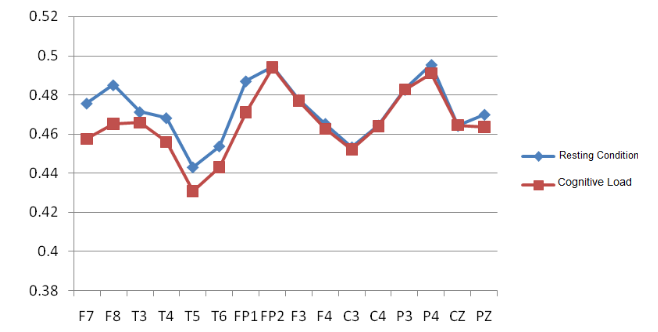

Figure 4: Comparison of LZC values of two kinds of cognitive state in normal group.

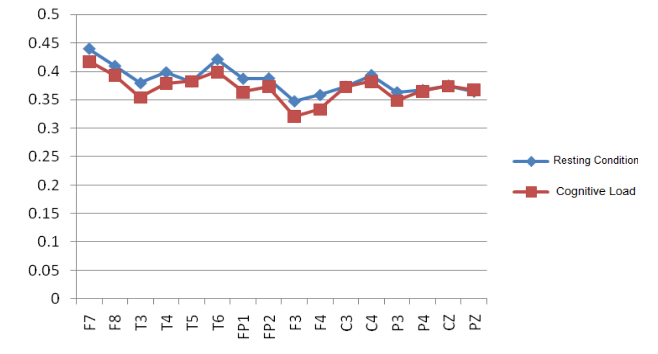

Figure 5: Comparison of LZC values of two kinds of cognitive state in cognitive damage group.

Variables	Group	N	Average	Standard Deviation
P300	1	45	327.24	26.692
	2	50	360.74	24.472
Note: 1 Normal Group; 2 Cognitive Damage Group				

Table 2: P300 comparison between the two groups.

cognitive impairment group was lower than that in resting state. And in this condition, the change of LCZ values of EEG signal complex value in following brain regions had statistical significance: F7, F8, T3, T4, FP1, FP2, F3, F4, P3, the change of lead LZC in the load state had statistical significance ($P<0.05$) (Figure 5 and Table 1).

P300 comparison between the two groups

Comparison of P300 values between the two groups indicated the P300 of the patients with cognitive impairment was significantly higher than that in the control group, and the difference was statistically significant ($P<0.05$) (Table 2).

Discussion

The activity in the brain cortex or scalp surface can be reflected by brain electrical, with nonlinear and non-stable biological characteristics. And brain electrical is sensitive to reflect the brain's pathological and physiological changes. As early as 1999, Jelles et al introduced that the human brain was a complex nonlinear dynamic and self-organized system. People had also found the discharge mode of chaos in a single nerve cell [18]. EEG complex degree is a nonlinear method. It reflects the probability of presence of new model in EEG information, and the higher the value is, the higher the probability of the new model has, which also means the more complicated dynamic behaviours. The determination of the complexity will help further reveal the brain function variance. In this research, we used complexity algorithm and found that the complexity of the whole brain of MCI patients was lower than that of normal counterparts. When compared with normal counterparts, many partitions of the brain atrophy and loss of neurons in MCI patients happened, and the link between levels of neurons was smaller than that in normal people. Because there are fewer neural networks in patients with cognitive impairment, the behavior dynamics is relatively simple. These results can be confirmed by neuroimaging: the researchers had confirmed that there was an abnormal neural network in patients with dementia, which was confirmed by resting state functional MRI: Communication between posterior cingulate cortex and other brain regions in old age [19]. has been reduced gradually. Under the microscope, we could have found that there existed extensive neurons loss and brain pyramidal cells decrease in the brain cortex [20]. Many partitions of the structure of the brain in MCI patients atrophied, and neuronal lost, the function of the whole brain decreased, which indicated cognitive impairment and neurological dysfunction of patients, In perspective of EEG complexity, the whole brain complexity has been reduced. From the view of information science, this result could be further considered as the function of information processing and transmission in the brain of patients with cognitive impairment.

It has been found that EEG signal complex values of MCI patients in frontal and temporal region (T3, FP1, FP2, F3, F4, P3, P4) decreased significantly, which indicated that the brain function of degradation was not identical the cognitive related brain areas such as the frontal and temporal lobes degradation is more serious than that of the other brain areas. It is reported that obvious temporal lobe hippocampus and entorhinal cortex atrophy in MRI of MCI patients has been found [21]. These imaging variances were consistent with our results, which indicated a reduction in the values of the temporal complexity of the region. Left-sided and posterior hippocampal measures were severer for group discrimination than right-sided and anterior measures [22]. Sepsis survivors showed cognitive deficits in verbal learning and memory and had a significant reduction of left hippocampal volume compared to healthy controls [23]. The results showed that the decrease of LZC values of the left temporal lobe was significantly more serious than that of the right side in MCI patients, which may be the main clinical manifestation of cognitive dysfunction. In addition, associated complex reduction of the parietal lobe suggested that cognitive impairment may not only have simple memory loss but other brain functions such as motion and sensation function decline. This result is consistent with Krame et al. [24] research result. According to above, we deduced: in the same time series, EEG signals shows higher rate of new model in normal elderly people than in cognitive impairment patient, and complexity of the brain acceptance and processing are both higher, so that the brain function is relatively intact. Therefore, it has more complex behavior model. While the MCI group of brain function is degrading, with degraded ability of receiving and processing information. At the same time, the complexity degree value of EEG s is reduced with serious degradation of the associated cognitive brain regions, so the main symptom performance is impairment of the cognitive.

From the perspective of how the brain accept and deal with information at different loads and different activate state, to complexity reflected the level of how brain accept and deal with the information. The brain complexity value and resting state had no significant difference in normal elderly people of pure tone hearing oddball stimulus sequence. This result may be related to the type of mental work performed by the subjects. When studying on different mental tasks of normal people, Gu fan et al. [25] found that the complexity of the right frontal top has been greatly reduced while looking pictures, and the complexity of frontal and parietal has been greatly reduced while looking pictures while seeing Chinese characters, but there were no significant changes while looking checkerboard. These indicated that different cognitive tasks will cause different complexity value changes. On the other hand, value of LZC EEG signals for each brain region of MCI patients in cognitive load condition (pure tone hearing oddball sequence stimulation) is lower than that in the resting state. the frontal lobe, temporal lobe, parietal lobe (F7, F8, T3, T4, FP1, FP2, F3, F4, P3 lead) areas of the brain lead LZC values change were statistically significant ($P<0.05$). Information processing and transmission function were damaged in brain of MCI patients, which could be reflected by the reduction of the processing of information rate in the dynamics characteristics of EEG nonlinear system, so in auditory tone oddball stimulus sequence operations, the complexity of the corresponding functional area value decreased. Zhao Li et al. [26] had showed that the brain electrical information transmission in cognitive impairment patients was significantly lower than the normal elderly people, especially sensitive information exchanging between the amount of information exchange were more prominently decreased in the frontal, temporal and other brain areas of. In addition, we also found that the complexity of the parietal lobe of patients with cognitive impairment was also changed. In the study of the relationship between the changes of local cerebral blood flow and in Alzheimer's disease, Cao Lihua et al. [27] found that in dementia patients, there existed reduction of cerebral blood flow in the temporal lobe, parietal lobe and frontal lobe. This kind of cerebral regional low perfusion change was consistent with foreign scholars' studies, who used SPECT performance to indicate low perfusion in the temporal lobe and parietal lobe [28]. The results further revealed other causes of cognitive impairment. With the same psychological operations, these two groups showed different results, so we could have deduced that when under pure tone hearing oddball stimulus sequence operations, the normal group could be more effective to complete the task because of these normal brain function. Therefore, it can be more effective to complete the task; because its functional brain areas decline especially in the frontal and temporal areas, so these could cause the difficulty in completing the loading operation of cognition impairment. In Pijnenburg et al. [29] and Hogan et al. [30] research, they also found that elderly patients with dementia synchronization may be significantly lower than the control group while in the working memory task status.

As a quantitative electrophysiological index, P300has been widely used in the research of cognitive function because of its specificity in cognitive function. For example, when it reflects certain mental activity, such as attention, memory, intelligence and so on. The P300 latency may be more sensitive than neuropsychological tests in the longitudinal follow-up of AD patients when it reflects cognitive decline [31]. The P300 amplitude and latency also distinguished the groups and showed a significant correlation with response speed [32].

In this study, P300 latencies of MCI group was delayed, we could deduce that because of the decline in brain function and brain areas of fibers connecting, the reduction in information processing performance could indicate that the delay of P300 latent period. These were identical with another study where the complexity of EEG is testified that. Based on these, we could infer, from the perspective of nonlinearity, EEG complexity reveals the changes of brain function in patients with cognitive impairment.

Conclusion

The brain electrical LZC value in normal elderly people group was higher than that in cognitive impairment group, those brain areas with more complex functions like frontal area and temporal area had highest LZC, which illustrated the degree distribution differences in complex brain regions. With decreased cognitive function, EEG complexity value also appears consistent changes with it. This also illustrated that EEG complexity value could reflect the change of brain function in certain degree. It is reasonable to consider it as a kind of objective EEG nonlinear detection method for cognitive function. It was not consistent decrease in the degree of cognitive impairment among the complex areas of the brain; under cognitive load synchronization state, complexity the value of cognitive impairment patients in cognitive related brain regions decreased significantly; as same as prolonged latency of P300, this result of cognitive impairment in patients could also predict the degree of cognitive decline.

Lack and Prospects

EEG signal complexity analysis method can quantitatively describe the degree of cognitive dysfunction, to a certain extent, can be used to assess the different stages of cognitive disorders, contribute to clinical progress and prognosis assessment. However, this method uses the binary method of the calculation method, although the method is relatively simple, but slightly rough, to be improved.

In this study, we studied the complexity of EEG-LZC values in two groups of subjects under different cognitive states. However, for the prolongation of time, the two groups were tested the longitudinal change of LZC value of EEG signal needs further study. Due to the limited time and technical conditions, the research indicators adopted in this study are relatively small. In the future, we can increase the sample size and prolong the observation time, which will further reveal the clinical characteristics of patients with dysfunction.

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