Correlation analysis between brain network attributes and skin electrical signals in patients with mild cognitive impairment

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Abstract. The aim of the study was to explore the correlation between brain network attributes and skin electrical signals in patients with mild cognitive impairment (MCI) for early diagnosis. Neuropsychological assessment for subjects and the resting-state fMRI data were collected. The brain network was constructed based on the resting-state fMRI data, and its attributes were analyzed by graph theory. Then wavelet transform was used to extract the features of skin electrical signal data. Finally, Pearson correlation method was used to calculate the correlation between brain network attributes and skin electrical signal. The results showed that brain network attributes of aLp, aL, assortativity and synchronization in MCI were higher than those in normal control, while the hierarchical of MCI was lower than that in normal control. There were significant differences between the two groups of skin electrical signals in mean value, maximum value and minimum value. Moreover, the correlation results showed that neuropsychological assessment were correlated not only with brain network attributes but also with skin electrical signals, and there was a correlation between skin electrical signals and brain network attributes. Using skin electrical signals can provide a new early standard to assist in the diagnosis of MCI, with low cost and easy acquisition.

1. Introduction

Mild cognitive impairment (MCI) is an intermediate state between normal aging and Alzheimer's disease. The core symptom of MCI is the decline of cognitive function, and MCI is easily transformed into Alzheimer's disease. Alzheimer's disease (AD) is a neurodegenerative disease characterized by cognitive and behavioral dysfunction. According to the latest research statistics, one person is diagnosed with Alzheimer's disease every three seconds, which has aroused widespread social concern [1]. Therefore, the diagnosis of MCI and early intervention treatment are of great significance to prevent MCI transforming into AD. At present, the early diagnosis methods mainly include: scale examination, cognitive test, biological marker examination, neuroimaging technology examination [2-4]. Among them, it’s a commonly used method to collect functional magnetic resonance imaging (fMRI) data to analyze the brain functional network [5]. Meantime, the graph theory is applied to the analysis of brain
network, which makes brain regions as nodes and the connection strength between brain regions as edges to construct brain network, so we can find the changes of brain cognition function [6-7]. However, due to the fact that subjects are required to lie still in bed and remain awake during the whole process of fMRI data acquisition, the subjects are prone to sleepiness and fatigue, which affects the results of data acquisition. Moreover, the cost of fMRI data acquisition is high, and the analysis results will be different due to different methods.

It has been reported that skin electrical signals can reflect the cognitive changes of the brain [8]. Its advantages are objective, accurate, reliable, and easier to collect than other physiological parameters [9]. Chen found that there was a relationship between skin electrical signal and cognition in lie detection experiment [10]; Du also found that skin electrical signal was affected by cognition level [11]. In this paper, we used graph theory to analyze brain network attributes of fMRI data, wavelet analysis is used to extract the features of skin electrical signals, and Pearson correlation coefficient method to calculate the correlation between brain network attributes and skin electrical signals, so as to achieve the purpose of using skin electrical signals as objective analysis indicators to assist in the diagnosis of MCI.

2. Methods

2.1. Subjects and data acquisition
The subjects were recruited from the First Hospital of Jilin University. There were 15 males and 14 females with an average age of (57.5 ± 6.3) years. FMRI data and skin electrical signal data were collected from 19 MCI subjects and 10 normal control (NC) subjects. The resting fMRI data were collected by 3-T Philips functional magnetic resonance scanner. TR=2500 ms, TE=27 ms, layer number is 42, layer thickness is 2.5 mm, FOV 230 mm × 230 mm, a total of 240 time points. Biopac MP150 physiological signal recorder was used for skin electrical signal acquisition, and the sampling rate was 400 kHz. Neuropsychological cognitive assessment including: Mini Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA), Trail Making Test (TMT), the California Verbal Learning Test (CVLT) and the Boston Naming Test (BNT). All the subjects were right-handed. This study was approved by the ethics committee of The First Hospital of Jilin University. The informed consent was signed by the subjects or their guardians.

2.2. FMRI data processing
SPM 12 software package (http://www.ion.ucl.ac.uk/SPM) was used for fMRI data. Preprocessing steps: remove the images of the first 10 time points; carry out time layer correction; remove the larger head movement; normalize and filter (0.01-0.08 Hz) for smoothing and filtering. The automated anatomical labeling (AAL) in 90 brain regions were used to calculate the brain network attributes by Gretna toolkit. Literature shows that small world network attributes are related to brain cognitive changes [12-13], so they are counted separately for convenience of comparison. Average shortest path length (aLp) to measure global information transmission ability, average clustering coefficient (aCp) to measure the degree of network collectivization, standardized shortest path length (aλ), standardized clustering coefficient (aγ) and small world (aσ, σ = γ / λ); other brain network attributes include: local efficiency (aEloc) represents the average of local efficiency, global efficiency (aEg) reflects global transmission capacity of the network. The assortativity examines whether the nodes with similar degree values tend to connect with each other. The hierarchy represents the large hierarchical network generated by the basic sub network through iteration. The synchronization reflects the similarity of the degree changes of the nodes when the network is disturbed. The above average values are used for statistics.

2.3. Skin electrical signal preprocessing and analysis
Skin electrical signal acquisition process is affected by the external environment and other factors, the sym5 wavelet transform function is used to decompose the skin electrical signal in three scales. Since the skin electrical signal is mainly concentrated in the low frequency band, so the preprocessed skin electrical signal is obtained by denoising the high frequency band and then reconstructing with the low
frequency band together. The features are mean, variance, standard deviation, maximum, minimum, kurtosis, range and skewness values.

2.4. Pearson correlation analysis
SPSS 24.0 statistical analysis software was used. Measurement data were expressed as $(\bar{x} \pm s)$, and cognitive assessment and brain network attributes were tested by inter group t-test, then Pearson correlation analysis was used to calculate the correlation coefficient among cognitive assessment, brain network attributes and skin electrical signals in MCI and NC. Results of $P < 0.05$ was considered significant.

3. Results

3.1. Cognitive assessment and significant differences in brain regions
The results of cognitive assessment between the two groups in table 1. MMSE, MoCA, CVLT and BNT were significantly different, and NC was higher than MCI; TMT had no significant difference. The results of brain area differences are shown in figure 1. The main areas are lingual gyrus, superior occipital gyrus, middle occipital gyrus, precuneus lobe, superior parietal gyrus, angular gyrus, inferior temporal gyrus, middle temporal gyrus, anterior cingulate gyrus and paracingulate gyrus.

|                  | MMSE     | MoCA     | TMT       | CVLT      | BNT       |
|------------------|----------|----------|-----------|-----------|-----------|
| MCI              | 26.24±1.79| 20.82±4.84| 183.12±55.67| 9.24±5.25| 18.71±4.74|
| NC               | 28.14±1.07| 31.86±5.87| 147.14±32.29| 16.57±1.98| 23.57±1.98|
| t                | -2.618   | -4.780   | 1.590     | -3.554    | -3.543    |
| P                | 0.016    | 0.001    | 0.126     | 0.002     | 0.016     |

Table 1. Comparison of cognitive assessment results

![Figure 1. The results of brain area differences](image)

Significant t test, $P < 0.05$; sagittal plane, cross section and coronal plane; red indicates the different brain areas

3.2. Brain network attributes
The results showed that the brain network attributes $aL_p$, $a\lambda$, assortativity and synchronicity in MCI were higher than those in NC, but the hierarchy were lower in NC, as shown in table 2 and table 3.

|                  | $aL_p$    | $aC_p$    | $a\lambda$ | $a\gamma$ | $a\sigma$ |
|------------------|-----------|-----------|------------|-----------|-----------|
| MCI              | 0.95±0.21 | 0.27±0.02 | 0.51±0.04  | 0.84±0.15 | 0.74±0.15 |
| NC               | 0.89±0.05 | 0.27±0.01 | 0.49±0.01  | 0.83±0.12 | 0.73±0.11 |
| t                | 0.806     | 0.068     | 0.956      | 0.241     | 0.053     |
| P                | 0.427     | 0.947     | 0.347      | 0.811     | 0.958     |

Table 2. Comparison of small world network attributes between MCI and NC

|                  | $aE_{loc}$ | $aE_g$     | assortativity | hierarchy | synchronicity |
|------------------|------------|------------|---------------|-----------|--------------|
| MCI              | 0.34±0.03  | 0.25±0.02  | 0.13±0.07     | 0.02±0.05 | 0.03±0.02    |

Table 3. Comparison of other brain network attributes between MCI and NC

T test of two independent samples, $P < 0.05$
3.3. Skin electrical signal
The skin electrical signal is decomposed into three scales by sym5 wavelet function, as shown in figure 2. Results of skin electrical signals between MCI and NC showed that the mean, maximum and minimum values had significant differences, as shown in figure 3.

![Figure 2. A1~A3 is the low frequency band of wavelet decomposition, D1~D3 is the high frequency band of wavelet decomposition](image)

3.4. Pearson correlation analysis
Finally, the results with statistically significant are shown in table below. MMSE was correlated with hierarchy and synchronicity in MCI; MMSE was correlated with aCp and aλ in NC, while MMSE was correlated with hierarchy. There was correlation between assortativity and CVLT in NC, but there was no significant difference in MCI. Kurtosis in NC was correlated with MoCA, kurtosis was negatively correlated with TMT; kurtosis in MCI was correlated with MMSE. The kurtosis of MCI was correlated with aCp and aλ.

|          | NC      | 0.34±0.01 | 0.25±0.01 | 0.09±0.03 | 0.04±0.03 | 0.02±0.01 |
|----------|---------|-----------|-----------|-----------|-----------|-----------|
| t        | -0.574  | -0.670    | 1.592     | -1.227    | 0.862     |
| P        | 0.571   | 0.508     | 0.123     | 0.230     | 0.396     |

T test of two independent samples, P < 0.05
Table 4. Correlation between MMSE and brain network attributes

|       | MCI        |       | NC        |       |
|-------|------------|-------|-----------|-------|
|       | r          | P     | r          | P     |
| aLp   | -0.397     | 0.115 | 0.720     | 0.068 |
| aCp   | -0.420     | 0.094 | 0.812     | 0.027 |
| aλ    | -0.415     | 0.098 | 0.778     | 0.039 |
| ay    | 0.349      | 0.170 | -0.352    | 0.439 |
| aη    | 0.425      | 0.089 | -0.501    | 0.252 |
| aEloc | 0.224      | 0.388 | 0.656     | 0.109 |
| aEg   | 0.443      | 0.075 | -0.685    | 0.089 |
| assortativity | -0.354 | 0.164 | 0.554     | 0.197 |
| hierarchy | 0.565 | **0.018** | -0.790   | **0.034** |
| synchronicity | 0.533 | **0.028** | -0.477   | 0.279 |

Table 5. Correlation between cognitive and assortativity

|       | MCI        |       | NC        |       |
|-------|------------|-------|-----------|-------|
|       | r          | P     | r          | P     |
| MMSE  | -0.229     | 0.376 | 0.554     | 0.197 |
| MoCA  | -0.085     | 0.744 | 0.435     | 0.329 |
| TMT   | 0.068      | 0.797 | 0.049     | 0.917 |
| CVLT  | -0.303     | 0.237 | 0.880     | **0.009** |
| BNT   | -0.346     | 0.174 | -0.620    | 0.137 |

Table 6. Correlation between cognitive assessment and kurtosis

|       | MCI        |       | NC        |       |
|-------|------------|-------|-----------|-------|
|       | r          | P     | r          | P     |
| MMSE  | **0.509**  | **0.037** | 0.347     | 0.445 |
| MoCA  | 0.223      | 0.390 | **0.772**  | **0.042** |
| TMT   | -0.013     | 0.961 | **-0.879** | **0.009** |
| CVLT  | 0.237      | 0.360 | 0.472     | 0.285 |
| BNT   | 0.076      | 0.772 | 0.104     | 0.824 |

Table 7. Correlation between kurtosis and brain network attributes

|       | MCI        |       | NC        |       |
|-------|------------|-------|-----------|-------|
|       | r          | P     | r          | P     |
| aLp   | 0.452      | 0.052 | 0.129     | 0.722 |
| aCp   | **0.522**  | **0.022** | -0.203    | 0.575 |
| aλ    | **0.475**  | **0.040** | 0.253     | 0.481 |
| ay    | -0.269     | 0.265 | 0.530     | 0.115 |
| aη    | -0.380     | 0.109 | 0.490     | 0.151 |
| aEloc | 0.104      | 0.671 | -0.191    | 0.597 |
| aEg   | -0.445     | 0.056 | 0.031     | 0.933 |
| assortativity | 0.370 | 0.119 | 0.056     | 0.878 |
| hierarchy | -0.417 | 0.075 | 0.063     | 0.862 |
| synchronicity | -0.439 | 0.060 | 0.154     | 0.671 |

4. Discussion
Results of cognitive assessment showed that MCI was lower than NC; and that the lingual gyrus is involved in visual memory and logical analysis; the superior occipital gyrus and middle occipital gyrus are related to the cognitive changes of the brain [12]; the angular gyrus can make the visual and auditory images lose contact; the anterior cingulate gyrus and cingulate gyrus are associated with emotional and cognitive functions [13]. From the results, the two groups have changed in terms of cognition.
Results of this study showed that $aLp$ and $a\lambda$ in MCI were higher than NC, and there was no significant difference in $aCp$ and $a\gamma$. $aLp$ reflects the global information transmission efficiency of the network, and $aCp$ reflects the processing efficiency of the local information. It can be seen that the local information processing of MCI is not affected, but the global information processing efficiency is reduced, which is consistent with the literature [14-16]. Studies of skin electrical signal showed that cognitive level was higher and skin electrical response was more obvious [8-11]. Figure 3 showed that there were differences between MCI and NC.

Pearson correlation results showed that MMSE was correlated with hierarchy and synchronicity in MCI; MMSE was correlated with $aCp$ and $a\lambda$ in NC. There was correlation between CVLT and assortativity in NC. CVLT represents speech learning ability, which indicates that the decrease of CVLT in MCI leads to the change of the correlation of brain network attributes. MoCA was positively correlated with kurtosis, while TMT was negatively correlated with kurtosis. MoCA reflected memory and executive ability, while TMT reflected cognitive and executive ability. MoCA in MCI was lower than NC, but TMT was higher than NC, indicating the cognitive level of MCI was decrease. The kurtosis is positively correlated with MoCA and negatively correlated with TMT due to the phenomenon of partial enhancement of brain compensation mechanism. Table 7, kurtosis in MCI is significantly correlated with $aCp$ and $a\lambda$, but there is no significant difference in NC, speculated that perhaps it is belong to healthy subjects. It needs further analysis and exploration.

Above all, there is a correlation between brain network attributes and skin electrical signals. Through the analysis of the correlation between brain network attributes and skin electrical signals, it lays a foundation for skin electrical signals as an objective index for early diagnosis of MCI, and also provides new research ideas and methods for early diagnosis of MCI.

Acknowledgements
This work was supported by the National Natural Science Foundation of China (61773076, 81600923).

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