Research report

Neural complexity in patients with poststroke depression: A resting EEG study

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A B S T R A C T

Background: Poststroke depression (PSD) is one of the most common emotional disorders affecting poststroke patients. However, the neurophysiological mechanism remains elusive. This study was aimed to study the relationship between complexity of neural electrical activity and PSD.

Methods: Resting state eye-closed electroencephalogram (EEG) signals of 16 electrodes were recorded in 21 ischemic poststroke depression (PSD) patients, 22 ischemic poststroke non-depression (PSND) patients and 15 healthy controls (CONT). Lempel–Ziv Complexity (LZC) was used to evaluate changes in EEG complexity in PSD patients. Statistical analysis was performed to explore difference among different groups and electrodes. Correlation between the severity of depression (HDRS) and EEG complexity was determined with pearson correlation coefficients. Receiver operating characteristic (ROC) and binary logistic regression analysis were conducted to estimate the discriminating ability of LZC for PSD in specificity, sensitivity and accuracy.

Results: PSD patients showed lower neural complexity compared with PSND and CONT subjects in the whole brain regions. There was no significant difference among different brain regions, and no interactions between group and electrodes. None of the LZC significantly correlated with overall depression severity or differentiated symptom severity of 7 items in PSD patients, but in stroke patients, significant correlation was found between HDRS and LZC in the whole brain regions, especially in frontal and temporal. LZC parameters used for PSD recognition possessed more than 85% in specificity, sensitivity and accuracy, suggesting the feasibility of LZC to serve as screening indicators for PSD. Increased slow wave rhythms were found in PSD patients and clearly correlation was confirmed between neuronal complexity and spectral power of the four EEG rhythms.

Conclusions: Compared with conventional spectral analysis, complexity of neural activity using LZC was more sensitive and stationary in the measurement of abnormal brain activity in PSD patients and may offer a potential approach to facilitate clinical screening of this disease.

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1. Introduction

Poststroke depression (PSD), referred as emotional disorders with main symptoms of dropped interest and depression, is one of the most common emotional disorders afflicting stroke sufferers (Dafer et al., 2008; Gaete and Bogousslavsky, 2008). About one-third of stroke survivors experienced an early or later onset of depression, which impede the rehabilitation and recovery process, jeopardizes quality of life and increases mortality (Angelelli et al., 2004; Gaete and Bogousslavsky, 2008). Diagnostic and Statistical annual of Mental Disorders, 4th edition (DSM-IV) diagnostic criteria (American Psychiatric Association, 1994b) are conventionally used for diagnosing PSD. Some depression assessment scales like Hamilton Depression Rating Scale (HDRS) and the Beck Depression Inventory (BDI) are used for screening and evaluating the severity of PSD commonly (Aben et al., 2002; Agrell and Dehlin, 1989; Kang et al., 2013). However, there have been concerns raised about variations in performance associated with socio-demographic and clinical characteristics (Salter et al., 2007).
Currently, there are no biological measures used in clinical practice for the screening of PSD.

The interaction between depression and stroke is very complex and the pathophysiological mechanisms have not as yet been fully elucidated. Alexopoulos et al. (1997a, 1997b) proposed the concept of vascular depression (VaD) to describe depression associated with cerebrovascular disease. VaD is thought to result from disruption of prefrONTAL systems and lesions damaging the striatopallido-thalamo-cortical pathways and other areas (Alexopoulos et al., 1997a, 1997b; Naismith et al., 2012). Neuroimaging techniques such as Magnetic Resonance Imaging (MRI) and functional Magnetic Resonance Imaging (fMRI) have revealed changes in white matter hyperintensities (WMH) and aberrant functional connectivity (De Groot et al., 2000; Sachdev et al., 2007; Wu et al., 2011) to support this hypothesis. Electroencephalogram (EEG) reflects the comprehensive electrophysiological activity of neuron populations and provides abundant physiological or psychological information. It has been widely used to investigate neurophysiological changes in depression, although not in depression following stroke (Li et al., 2008; Méndez et al., 2012; Stam, 2005; Lee et al., 2007).

Traditionally, EEG is analyzed by some linear approach, namely frequency-power analysis, like power spectrum, coherence, correlation. Several studies have reported abnormal EEG absolute power, hemispheric asymmetry or coherence in some specific frequency with depression patients (Knott et al., 2001; Lee et al., 2011; Lubar et al., 2003; Tas et al., 2015; Mathersul et al., 2008). However, these findings are inconsistent and sometimes even contradictory to each other (Carvalho et al., 2011; Flor-Henry et al., 2004; Reid et al., 1998; Stewart et al., 2011). It has been reported that most of linear parameters did not show a significant correlation with severity of clinical depression (Gold et al., 2013; Hinrikus et al., 2009; Lee et al., 2011; Motomura et al., 2002; Tas et al., 2015). In addition to factors of heterogeneity, age and gender, another important reason might be that the above linear analysis methods require high linearity, stability and signal to noise ratio for the processed signal, which EEG could not satisfied fully (Reid et al., 1998; Stam, 2005).

The human brain is a complex system, characterized by its dynamical neural communications in functionally specialized assemblies and long-range mutual interactions across these assemblies (Schnitzler and Gross, 2005; Sporns, 2011; Varela et al., 2011). The recent advent of nonlinear analytic methods, which have served for the quantitative description of the brain signal complexity, has provided new insights into aberrant physiological processes and neural connectivity in both healthy and pathological conditions (Garcia-Toro et al., 2001; Okazaki et al., 2013; Park et al., 2007; Takahashi et al., 2010; Yang et al., 2011). In contrast to conventional frequency-power analysis, nonlinear analytic methods focused on the time-varying characteristics of EEG and demanded lower stability to the processed signal (Stam, 2005). Lempel–Ziv complexity (LZC) is one of the nonlinear complexity measurements which characterize the disorder of a time series through testing the emergence rate of new model of the time series (Lempel and Ziv, 1976). It is based on counting the number of distinct substrings and their recurrence rate along the analyzed signal, assigns higher values to more complex data, and is well suited to the analysis of non-stationary biomedical signals of short length (Ferenets et al., 2006; Li et al., 2008; Wu and Xu, 1991). In recent years, it has been widely used in biomedical fields to estimate the complexity of discrete-time signals, which involves the analysis of EEG and MEG signals in mental disorders such as major depression (MDD), Alzheimer’s disease and schizophrenia disease (Ahásolo et al., 2006; Li et al., 2008; Méndez et al., 2011). Li et al. (2008) demonstrated higher LZC of EEG in patients with MDD compared to controls during the resting-state as well as mental arithmetic conditions. Méndez et al. (2012) reported that depressed patients showed higher LZC of MEG during pre-treatment than controls, and the higher complexity decreased after 6 months of effective pharmacological treatment along with the clinical symptom remission, suggesting that LZC was sensitive to the dynamic physiological changes observed in depression and may potentially offer an objective marker of depression and its remission after treatment.

Although certain aspects of mood disorders are recognized as disorders that might arise from aberrant neural complexity (Bahrami et al., 2005; Li et al., 2008; Méndez et al., 2011; Thomasson et al., 2000; Yang et al., 2011), there is a lack of investigation into the neural complexity in PSD patients. In this study, we aimed to study the relationship between neural complexity and PSD. Resting EEG of ischemic poststroke depression (PSD) patients, poststroke non-depression (PSND) patients and healthy controls (CONT) was analyzed using LZC measurement to explore the specific complexity characteristics of PSD patients. Statistical analysis was conducted to evaluate the difference among the three groups, to correlate EEG complexity with severity of depressive symptoms and discriminating ability of the LZC for PSD. The analysis is expected to identify aberrant nonlinear dynamical complexity of PSD patients in brain signals and hoped to be helpful for the objective screening of PSD disease.

2. Materials and methods

2.1. Participants

21 poststroke depression (PSD) patients, 22 poststroke non-depression (PSND) patients and 15 age-matched healthy controls (CONT) were included for this study. All of the participants were recruited from the Rehabilitation Medical Department of Tianjin Union Medical Center, and were informed of the aims and protocols of the experiments before the EEG recording. All of the participants were right handed and free of psychotropic drugs for at least one week before the study. For the PSD and PSND patients, inclusion criteria were: ① First onset ischemic stroke and damaged lesion was classified as involving the left hemisphere only or right hemisphere only confirmed by brain magnetic resonance imaging. ② Ability to complete the necessary investigations and questionnaires. ③ Chronic phase and less than 12 months post-onset of stroke. Exclusion criteria for all the participants were: ① Diagnosis of schizophrenia or other psychotic disorders, psychopathic personality disorder or alcohol/drug abuse of dependence; ② History of seizures, brain surgery, organic brain disease or organic affective disturbance; ③ Electroconvulsive therapy (ECT) history. PSD patients were diagnosed as having major or minor PSD according to the Diagnostic and Statistical Manual, Fourth Edition (DSM-IV) criteria (American Psychiatric Association, 1994b). The severity of depression was assessed by 24-item Hamilton Depression Rating Scale (HDRS) (Hamilton, 1960), which administrated by one trained psychiatric interviewer.

2.2. Experimental conditions and EEG acquisition

Participants were required to seat comfortably with eyes closed and consciousness during EEG recording. They were asked to avoid blinking and making movements. The EEG acquisition room kept quiet, dim light and away from electromagnetic interference. Five minutes of EEG data was recorded at 16 scalp electrodes (Fp1, Fp2, F3, F4, F7, F8, C3, C4, T3, T4, P3, P4, O1, O2, T5 and T6) in accordance to the international 10–20 electrode position system (American Electroencephalographic Society 1994a) using Nicole-tOne 32-channel digital video electroencephalograph. Linked
earlobes were chosen to be the reference electrodes. EEG data was recorded with Ag/AgCl electrodes and all electrode impedances were below 5 kΩ. The acquisition system parameter settings were as follows: 0.1–70 Hz frequency band, 250 Hz sampling rate, 12 bit analog-to-digital (A/D) converter. The EEG data was preprocessed by means of 0.6–46 Hz bandpass filter, independent component analysis (ICA) and significant artifacts manual rejecting. EEG data of 90 seconds after preprocessing was finally chosen for further processing.

2.3. Lempel–Ziv complexity (LZC)

LZC is a non-parametric measure for finite sequences related to the number of distinct substrings and the rate of their occurrence along the sequence, with larger values corresponding to greater complexity in the data (Lempel and Ziv, 1976). For this study, the EEG data was segmented into consecutive 5 s for LZC. The LZC of EEG data was calculated by the following formula (Lempel and Ziv, 1976):

$$\lim_{n \to \infty} \frac{c(n)}{n} = \frac{b(n)}{\log_2 n}$$

(1)

$c(n)$ was normalized by $b(n)$ so as to get a value which was independent of the sequence length $n$. So the LZC value was finally obtained as the following formula (Lempel and Ziv, 1976):

$$LZC = c(n)/b(n)$$

(2)

2.4. Statistical analyses

Between group comparisons (CONT and PSD, PSND and PSD separately) were made using the independent samples T-test. A two-way analysis of variance (ANOVA) was used to examine the main and interaction effects of the three groups and 16 electrodes. The LZC values were correlated with total score and 7 sub-score items of the HDRS using Pearson correlation coefficients to examine the neural complexity reflecting depression severity. Receiver operating characteristic (ROC) curves were used to estimate the discriminating ability of LZC for PSD through quantifying the balance between sensitivity/specificty. The mean area under curves (AUCs) of ROC near the upper left corner is close to 1, indicating better diagnostic capabilities. A classification model was established using binary logistic regression analysis to distinguish PSD patients from PSND patients. All the cases were used to evaluate the reliability of the classification model. Eighty-five percent of the stroke cases were randomly selected for classification modeling, and the rest 15% cases were used for model verification. The average results through 15 times were used to test the classification specificity, sensitivity and accuracy. All statistical procedures were performed using the IBM SPSS statistics 19.0 software.

3. Results

3.1. Demographic information and descriptive data

The demographic and clinical characteristics of the three groups are given in Table 1. There was no significant difference among the three groups in gender ($p = 0.602 > 0.05$) and age ($p = 0.383 > 0.05$). HDRS of the three group had a significant difference ($p = 0.000 < 0.05$). The mean HDRS score of PSD group was 21.10 (SD 8.24), and most of the PSD patients had mild or moderate depressive symptom. From the 7 items of sub-score (anxiety/somatization, weight, cognize, diurnal variation, retardation, sleep and despair), we can see the main symptoms of PSD patients were despair (6.33 ± 3.07), retardation (5.38 ± 2.01), anxiety/somatization (4.33 ± 2.90) and cognize (3.14 ± 2.17). There was no significant difference in the lesion side of PSD and PSND groups ($p = 0.463 > 0.05$), suggesting lesion lateralization may have no direct effect for depression. The duration of time since stroke in PSD group (5.45 ± 4.38 month) was more likely to be longer than PSND group (3.23 ± 2.80 month), but not significant ($p = 0.056 > 0.05$).

3.2. Between group comparisons of PSD and the other groups

**Table 1**

Demographic and clinical features of the three groups.

<table>
<thead>
<tr>
<th>Variables</th>
<th>PSD(n = 21)</th>
<th>PSND(n = 22)</th>
<th>CONT(n = 15)</th>
<th>F</th>
<th>df</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (Female/Male)</td>
<td>7/14</td>
<td>8/14</td>
<td>6/9</td>
<td>0.512</td>
<td>2/54</td>
<td>0.602</td>
</tr>
<tr>
<td>Age (mean ± SD)</td>
<td>62.05 ± 7.36</td>
<td>61.41 ± 8.42</td>
<td>58.57 ± 5.84</td>
<td>0.978</td>
<td>2/54</td>
<td>0.383</td>
</tr>
<tr>
<td>HDTRS (mean ± SD)</td>
<td>21.10 ± 8.24</td>
<td>6.14 ± 3.43</td>
<td>1.79 ± 2.46</td>
<td>80.485</td>
<td>2/54</td>
<td>0.000***</td>
</tr>
<tr>
<td>Anxiety/Somatization</td>
<td>4.33 ± 2.90</td>
<td>1.27 ± 1.64</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Weight</td>
<td>0.05 ± 0.22</td>
<td>0.14 ± 0.47</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Cognize</td>
<td>3.14 ± 2.17</td>
<td>0.77 ± 1.02</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Diurnal variation</td>
<td>1.29 ± 0.96</td>
<td>0.09 ± 0.20</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Retardation</td>
<td>5.38 ± 2.01</td>
<td>1.55 ± 1.60</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Sleep</td>
<td>2.29 ± 1.85</td>
<td>0.68 ± 1.13</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
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*** $p < 0.001$. 

**Table 1**

Demographic and clinical features of the three groups.
In order to research the relationship between EEG complexity and lesion side, we compared the LZC of left and right lesion side in PSD, PSND respectively. But no significant difference of any electrode \((p > 0.05)\) in both of the groups was found according to the independent samples T-test, which indicates lesion lateralization has little effects on the EEG complexity for stroke patients.

3.3. Main and interaction effect of different groups and different electrodes

As presented in Table 2, Two-way ANOVA was performed for the 3 groups × 16 scalp electrodes to evaluate whether there is a significant difference among groups and brain regions, as well as the interaction between groups and electrodes (Groups*Electrodes). A significant group effect was identified \(F(1, 2) = 243.09, p = 0.000 < 0.001\), indicating a significant difference of EEG complexity among the three groups. There is no significant effect of electrodes \(F(1, 15) = 1.429, p = 0.127 > 0.05\) and interaction effects of group and electrode \(F(1, 15) = 0.577, p = 0.967 > 0.05\), suggesting that effects of different groups for the complexity were global not some specific regions.

3.4. Correlation of EEG complexity with severity of Psychiatric symptomatology

The pearson correlation analysis didnot show significant correlation between LZC values and total score or 7 sub-score items of the HDRS in PSD patients \((p > 0.05)\). However, for the stroke patients (PSD and PSND patients) LZC values were negatively correlated \((p < 0.05)\) with HDRS significantly in the whole electrodes, especially FP1, F8, T3, T5 and T6 (Correlation Coefficient: \(r > 0.5, p \leq 0.001\)). The scatter diagram to the description of HDRS and LZC shows the high diagnostic ability of the LZC.

The discriminant model using binary logistic regression method to distinguish PSD from PSND patients was examined by statistical test. Table 3 showed the result of test. Statistical parameters \((Cox and Snell R^2 = 0.670, Nagelkerke R^2 = 0.894\) \(p = 0.999\) through Hosmer and Lemeshow test, which is much greater than 0.1) indicated that the model could fit the original data very well. Discrimination results of the 85% modeling cases were 94.2%, 93.3% and 93.9%, for the specificity, sensitivity and accuracy, respectively. The corresponding results of the 15% verification cases were 85.6%, 90.1%, and 86.4%, respectively, suggesting that the LZC was feasible as diagnostic indicators to the PSD disease.

3.6. Spectral analysis and correlations between LZC and spectral power

In order to compare the LZC with conventional linear analysis, we did spectral power analysis to investigate the difference of four frequency bands (delta (0.5–4 Hz), theta (4–8 Hz), alpha (8–13 Hz) and beta (13–30 Hz)) among the three groups with the same data set. For each record, the spectral power of the signal in the four frequency bands was extracted using Fast Fourier Transform (FFT) with Hamming window. Fig. 1 B, C and D showed spectral power density of delta, theta and alpha bands respectively. According to ANOVA, PSD patients showed increased spectral power \((p < 0.05)\) in the four frequency bands compared with PSND and healthy control subjects.

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in mainly frontal and central regions for delta bands, in the whole brain regions for theta bands. For alpha bands, spectral power of PSD patients significantly higher than CONT subjects only in inferior frontal and right temporal regions. There were no significant differences in spectral power of beta bands among different groups.

We also analyzed whether LZC was correlated with spectral power of each frequency bands. In this way, the pearson correlation coefficient was calculated between the LZC and HDRS of stroke patients. The results showed that the LZC was significantly correlated with HDRS in EEG recordings from 16 electrodes (Fig. 2). The ROC curves of LZC parameters of stroke patients in 16 electrodes are shown in Fig. 3.

### Table 3

Statistical magnitude for binary logistic regression.

<table>
<thead>
<tr>
<th>Source</th>
<th>Chi-Square</th>
<th>DF</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cox &amp; Snell R²</td>
<td>0.670</td>
<td>8</td>
<td>0.999</td>
</tr>
<tr>
<td>Nagelkerke R²</td>
<td>0.894</td>
<td>8</td>
<td>0.999</td>
</tr>
<tr>
<td>Hosmer and Lemeshow test</td>
<td>0.949</td>
<td>8</td>
<td>0.999</td>
</tr>
</tbody>
</table>

### Area under curves (AUC)

<table>
<thead>
<tr>
<th>Location</th>
<th>AUC</th>
</tr>
</thead>
<tbody>
<tr>
<td>FP1</td>
<td>0.923</td>
</tr>
<tr>
<td>FP2</td>
<td>0.857</td>
</tr>
<tr>
<td>F3</td>
<td>0.851</td>
</tr>
<tr>
<td>F4</td>
<td>0.820</td>
</tr>
<tr>
<td>C3</td>
<td>0.852</td>
</tr>
<tr>
<td>C4</td>
<td>0.873</td>
</tr>
<tr>
<td>P3</td>
<td>0.781</td>
</tr>
<tr>
<td>P4</td>
<td>0.938</td>
</tr>
<tr>
<td>O1</td>
<td>0.874</td>
</tr>
<tr>
<td>O2</td>
<td>0.837</td>
</tr>
<tr>
<td>F7</td>
<td>0.865</td>
</tr>
<tr>
<td>F8</td>
<td>0.818</td>
</tr>
<tr>
<td>T3</td>
<td>0.835</td>
</tr>
<tr>
<td>T4</td>
<td>0.877</td>
</tr>
<tr>
<td>T5</td>
<td>0.869</td>
</tr>
<tr>
<td>T6</td>
<td>0.933</td>
</tr>
</tbody>
</table>
correlation between LZA and spectral power was addressed and it was done for all the four bands. Table 4 showed the correlations results in all subjects. Delta and theta power in almost all of the brain regions, alpha power in left prefrontal and temporal regions and beta power in mainly frontal and occipital was correlated with LZA values, which illustrated that LZA performed information for all the rhythmic activity of EEG.

4. Discussion and conclusion

To investigate the relationship between neural complexity and PSD, this study analyzed resting EEG of three population groups (21 PSD patients, 22 PSND patients and 15 CONT subjects included) by means of LZC, a non-linear complexity measure about the rate of appearance of the new patterns in a time series. Larger LZC implies a greater chance of the occurrence of new sequence patterns and thus a more complex dynamical behavior (Lempel and Ziv, 1976; Takahashi, 2013).

We found that neural complexity, as measured using LZC of EEG signals, was abnormal in PSD patients. EEG complexity of the three groups (CONT, PSND and PSD) continuously declined in most of brain regions. LZC values decreased significantly in PSD patients compared with PSND patients and CONT subjects with the whole brain regions. Tononi and Edelman (1998) have found that EEG neural complexity is closely related to the integrity of inter-neuronal connectivity, and decrease with the declined capability of neural process. Subsequently, many studies assuming that aberrant neural connectivity in mental disorders might be reflected by abnormal complexity behavior in neurophysiologic signal (Benson et al., 2014; Sporns et al., 2000; Tadayonnejad et al., 2015; Taka- hashi, 2013). This may explain the decreased complexity of neural activity in PSD patients and PSND patients compared to healthy controls.

Using LZC or other complexity measurement methods, several studies got increased complexity of EEG/MEG in major depression patients (Li et al., 2008; Mendez et al., 2011; Fernandez et al., 2009). Li et al. (2008) found major depression and schizophrenia groups (middle-aged) had a significantly higher LZC in the resting EEG than healthy controls. In a more recent report, resting MEG in unmedicated patients with major depression, healthy controls, and patients with antidepressants treatment were investigated using LZC (Mendez et al., 2011). Depressed patients showed higher complexity during pre-treatment than controls. The higher complexity was attenuated after antidepressants treatment, and the reduction of complexity with treatment correlated with the degree of clinical symptom remission, significant results were found only in younger patients. In addition, Thomasson et al. (2000) demonstrated a clear correlation between the clinical improvement of depressive symptoms and a decrease of EEG complexity as measured by global entropy (another measure of complexity). The results we got from the current study appear contradictory with the above reports, suggesting specific neural complexity changes in PSD compared with other depression type. The inconsistency with other depression type may be due to following reasons.

(i) Stroke lesion. Focal and diffuse slow waves and theta-waves were found in stroke patients for the clinical EEG examination (Nagata et al., 1989), which may be a contribution of the complexity decline (Stam, 2005). (ii) Clinical characterization. Neural complexity might be reflected by clinical depressive symptoms. Instead of sadness in most young depression patients (Dafer, 2008), PSD patients in our study were more characteristically marked by despair, retardation and cognitive impairment, which is more similar to Alzheimer’s disease (AD) in clinical characterization. Increasingly numerous EEG and MEG studies using various complexity measures have revealed reduced complexity of AD
patients (Abásolo et al., 2006; Dauwels et al., 2010; Jeong, 2002; Stam, 2005), which was consistent with our results. (iii) Age differences. EEG complexity has been found to be associated with age (Fernandez et al., 2009; Mendez et al., 2011), and the MDD patients were more likely younger than PSD patients. Additionally, it seems that patient characteristics such as state of the mood, treatment or duration, may play a crucial role in the emergence of complexity behavior as well (Mendez et al., 2011; Pezard et al., 1996).

As the results indicated, there was no significant difference of EEG complexity among different brain regions, and no interactions between groups and electrodes, suggesting that the global difference in LZC observed among PSD patients and the other two groups between groups and electrodes, suggesting that the global difference of EEG complexity among different brain regions, and no interactions by stroke were usually diffuse though more pronounced around the injury lesion (Nagata et al., 1989), which may be another reason for the global aberrant neural complexity activity in PSD patients.

None of the LZC values significantly correlated with overall depressive severity or differentiated symptom severity of 7 items in PSD patients. But for stroke patients we found that EEG complexity was negatively related to the severity of psychiatric symptoms in the whole brain regions, especially in the frontal and temporal regions, indicating the neural complexity dropped down with high level of psychiatric symptoms in the whole brain regions, especially frontal and temporal. Temporal slow waves were found to be more common in mild cerebrovascular dysfunction patients with late-onset depression, suggesting vulnerability of temporal regions in late-onset depression (Motomura et al., 2002). Aberrant neuroanatomy in frontal and temporal regions was also founded using MRI examination (Poland-Ross et al., 2012; Kimura et al., 2002; Steffens et al., 2002; Taylor et al., 2003; Wang et al., 2012). We suggest that abnormal neural complexity (especially in frontal and temporal regions) may be associated with the clinical development of depression for stroke patients. Possible reason for the different results between PSD patients and stroke patients was that most of the PSD patients in our study had similar severity of depression (HDRS scores were between 15 and 20 in 71% of PSD patients, and 20% of PSD patients were between 20 and 30 HDRS scores).

Both the ROC curves and binary logistic regression of our study demonstrated high specificity, sensitivity and accuracy for PSD recognition, suggesting the LZC of EEG signals characterizing the neural complexity through non-linear dynamics may be feasible as diagnostic indicators to PSD and is worthy of further evaluation. Several studies also reported LZC values enabled classification of other mental disorders with high sensitivity and specificity (Abásolo et al., 2006; Fernandez et al., 2009).

Spectral power and correlation with LZC were performed in our study to investigate the relationship between conventional linear analysis and nonlinear complexity analysis. Increased slow wave rhythms especially for theta were found in PSD patients in the whole brain regions, which is contradictory with some previous study (Fachner et al., 2013; Iznak et al., 2013; Pollock and Schneider, 1990) for major depression. This is consistent to our complexity results in the extent that depression following stroke had its particular changes in EEG activity. Clearly correlation was confirmed between neuronal complexity and spectral power of EEG rhythms, which illustrated that neural complexity contains information of all the rhythmic activity of EEG (Abóþo et al., 2006), and was more sensitive and stationary than spectral power in PSD discrimination.

In conclusion, complexity analysis of neural activity using LZC is a sensitive measurement to detect abnormal brain activity in PSD patients and may offer a potential approach facilitating clinical discrimination of this disease. To the best of our knowledge this is the first study to evaluate neural complexity of PSD patients using LZC. Apparently, there are many limitations of our study and further studies are needed to confirm these observations. As infarction focus of the stroke patients distributed in various brain regions in our current study, future work should explore the neural complexity of PSD patients with specific lesion location. It would be necessary to evaluate the neural complexity using other nonlinear complexity analytic methods, such as multiscale entropy (MSE) (Costa et al., 2005), approximate entropy (ApEn) (Pincus, 1991), which are used in the studies of other mental disorders. In addition, future studies should focus on researching of the variation tendency of EEG complexity with the clinical symptomatology of PSD disease.

Conflict of interest

We have no professional, personal or financial affiliations that may be perceived to have biased the presentation.

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Contributors

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Changcheng Sun – He did the work of EEG data collection.
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Yongjun Wang – He worked for the depression diagnosis and severity assessment of poststroke patients.
Hongzi Qi – He did the figure collating of the article.
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Xin Zhao – He verified the results of the article.
Baikun Wan – He verified the results of the article.
Jingang Du – He recruited all the subjects of the study, and offered the electroencephalograph acquisition equipment.
Dong Ming – He designed the research plan.
All authors have approved the final article.

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