Journal of Affective Disorders 188 (2015) 310–318

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Research report

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

Ying Zhang [a,1], Chunfang Wang [a,b,1], Changcheng Sun [a], Xi Zhang [b], Yongjun Wang [a], Hongzhi Qi [b], Feng He [b], Xin Zhao [b], Baikun Wan [b], Jingang Du [a], Dong Ming [b,*]

[a] *Rehabilitation Medical Department, Tianjin Union Medicine Centre, Rehabilitation Medical Research Center of Tianjin, Tianjin, China*
[b] *Lab of Neural Engineering & Rehabilitation, Department of Biomedical Engineering, Tianjin University, Tianjin, China*

ARTICLE INFO

Article history:
Received 13 March 2015
Received in revised form
5 September 2015
Accepted 9 September 2015
Available online 11 September 2015

Keywords:
Poststroke depression (PSD)
Neural complexity
EEG
Lempel–Ziv Complexity (LZC)

ABSTRACT

Background: Poststroke depression (PSD) is one of the most common emotional disorders affecting post-stroke 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.
Limitations: Lesion location of stroke patients in the study distributed in different brain regions, and most of the PSD patients were mild or moderate in depressive severity.
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.

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 impedes 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).

* Correspondence to: Department of Biomedical Engineering, College of Precision Instruments and Optoelectronics Engineering, Tianjin University, Tianjin 300072, China. Fax: +86 22 27406726.
E-mail address: richardming@tju.edu.cn (D. Ming).
URL: http://tunerl.tju.edu.cn/ (D. Ming).
[1] Equally contributed to this work.

http://dx.doi.org/10.1016/j.jad.2015.09.017
0165-0327/

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 striato-pallido-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 stoke (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, cordance. 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 (Abásolo et al., 2006; Li et al., 2008; Mendez 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; Mendez 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 NicoletOne 32-channel digital video electroencephalograph. Linked