Journal of Neuroscience Methods xxx (2015) xxx–xxx

Contents lists available at ScienceDirect

Journal of Neuroscience Methods

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

Computational Neuroscience

Evaluation of different classification methods for the diagnosis of schizophrenia based on functional near-infrared spectroscopy

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HIGHLIGHTS

- We applied the multichannel NIRS system to measure brain activations during the verbal fluency task in a large sample of schizophrenia and healthy subjects.
- Q2 The classification performance of four classification methods was evaluated on the NIRS-aided schizophrenia diagnosis.
- A maximum accuracy of 85.83% and an overall mean accuracy of 83.37% were achieved using a PCA-based feature selection on oxygenated hemoglobin signals and support vector machine classifier.

ARTICLE INFO

Article history:
Received 21 September 2014
Received in revised form
25 November 2014
Accepted 24 December 2014
Available online xxx

Keywords:
Schizophrenia
Near-infrared spectroscopy (NIRS)
Verbal fluency task (VFT)
Principal component analysis (PCA)
Support vector machine (SVM)
Classification algorithm evaluation

ABSTRACT

Background: Based on near-infrared spectroscopy (NIRS), recent converging evidence has been observed that patients with schizophrenia exhibit abnormal functional activities in the prefrontal cortex during a verbal fluency task (VFT). Therefore, some studies have attempted to employ NIRS measurements to differentiate schizophrenia patients from healthy controls with different classification methods. However, no systematic evaluation was conducted to compare their respective classification performances on the same study population.
New method: In this study, we evaluated the classification performance of four classification methods (including linear discriminant analysis, k-nearest neighbors, Gaussian process classifier, and support vector machines) on an NIRS-aided schizophrenia diagnosis. We recruited a large sample of 120 schizophrenia patients and 120 healthy controls and measured the hemoglobin response in the prefrontal cortex during the VFT using a multichannel NIRS system. Features for classification were extracted from three types of NIRS data in each channel. We subsequently performed a principal component analysis (PCA) for feature selection prior to comparison of the different classification methods.
Results: We achieved a maximum accuracy of 85.83% and an overall mean accuracy of 83.37% using a PCA-based feature selection on oxygenated hemoglobin signals and support vector machine classifier.
Comparison with existing methods: This is the first comprehensive evaluation of different classification methods for the diagnosis of schizophrenia based on different types of NIRS signals.
Conclusions: Our results suggested that, using the appropriate classification method, NIRS has the potential capacity to be an effective objective biomarker for the diagnosis of schizophrenia.

1. Introduction

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Schizophrenia is a common mental disorder, but its cause has not been fully elucidated. Patients with schizophrenia are often associated with abnormalities in multiple aspects of cognitive behavior (Kuperberg and Heckers, 2000). Currently, clinical diagnostic criteria are predominately based on the behavioral

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http://dx.doi.org/10.1016/j.jneumeth.2014.12.020
0165-0270/© 2015 Published by Elsevier B.V.

symptoms and neuropsychological assessments from standard classification systems, such as the DSM-IV (American Psychiatric Association, 1994) or the ICD-10 (World Health Organization, 1992). This requires the psychiatrist to have professional knowledge and is relatively subjective. Therefore, more objective methods are highly desired. In recent years, neuroimaging techniques (such as structural and functional magnetic resonance imaging (MRI)) have been widely used to investigate the brain changes in patients with schizophrenia. Compared with healthy controls, various studies have indicated that schizophrenia patients had significant structural abnormalities, such as brain volume atrophy (Steen et al., 2006) or cortical thickness thinning (Narr et al., 2005), as well as significant functional alternations in brain activation (Callicott et al., 2003) or the pattern of functional connectivity (Lynall et al., 2010). These findings provide the potential to discover neuroimaging-based clinical biomarkers. Some studies have utilized these neuroimaging features and pattern recognition methods to develop diagnostic systems for distinguishing individuals with schizophrenia from healthy controls (Arbabshirani et al., 2013; Kawasaki et al., 2007; Shen et al., 2010; Yoon et al., 2007). The results have confirmed the potential benefits of these diagnostic tools.

Near-infrared spectroscopy (NIRS) is a painless and noninvasive optical imaging technology that is based on the absorption and scattering properties of near-infrared lights in different brain tissues (Ferrari and Quaresima, 2012). It can be employed to detect the local concentration changes of oxygenated hemoglobin ([oxy-Hb]) and deoxygenated hemoglobin ([deoxy-Hb]). These NIRS signals have been considered an indirect measure of neural activity (Ferrari and Quaresima, 2012). Compared with other neuroimaging tools, NIRS exhibits several advantages, such as a lower cost and greater portability, which make it very suitable for psychiatric research and indicate it may be a candidate instrument for clinical use (Ehlis et al., 2014). During the past several years, many studies have applied the NIRS technique to investigate the brain activation patterns in patients with schizophrenia. Converging evidence suggests schizophrenia patients are often associated with reduced activities and inappropriate activity timing around the bilateral prefrontal cortex during a verbal fluency task (VFT) or other cognitive tasks (Ehlis et al., 2007, 2014; Koike et al., 2013; Suto et al., 2004; Takizawa et al., 2008).

Based on these findings, some studies have attempted to apply the NIRS signal as a diagnostic tool with different pattern recognition methods (Azechi et al., 2010; Chuang et al., 2014; Hahn et al., 2013; Koike et al., 2013; Takizawa et al., 2014). Azechi et al. measured the changes of the [oxy-Hb] signal during multiple cognitive tasks from two NIRS channels located in the bilateral prefrontal areas and then applied stepwise linear discriminant analysis to distinguish patients with schizophrenia from healthy subjects (Azechi et al., 2010). They separated the total sample into two groups, and each group consisted of 60 subjects (including 30 patients with schizophrenia and 30 age- and gender-matched healthy controls). The experimental results demonstrated that there was an accuracy rate of 88.3% for classification in the first group, and the discrimination function derived from the first group correctly differentiated 75% of the subjects in the second group (Azechi et al., 2010). To integrate spatial and temporal information in multichannel NIRS, Hahn et al. employed a novel probabilistic pattern recognition method called Gaussian process classifier (GPC) for the diagnostic classification of schizophrenia (Hahn et al., 2013). Using the temporal patterns of NIRS data measured during a working memory task, an overall accuracy of 76% was achieved in a group of 80 samples (Hahn et al., 2013). One recent study applied a 52 channel NIRS system to identify the significantly different regions in the prefrontal cortex during a VFT and then utilized a *k*-means clustering method for discriminant analysis between schizophrenia patients and healthy subjects (Chuang et al., 2014). The results indicated 68.69% and 71.72% of the participants were correctly classified as schizophrenic or healthy subjects with all 52 channels and six significantly different channels, respectively (Chuang et al., 2014). Recently, a multi-site study was conducted in a larger group to facilitate individual diagnoses for major psychiatric disorders, including schizophrenia, with a conservative receiver operating characteristic analysis; the results confirmed that NIRS data represent a promising biomarker in real clinical settings (Takizawa et al., 2014). Although these studies have achieved reasonable classification results, it is difficult to compare the classification performances among different methods because they were performed based on the NIRS activation from different cognitive tasks. To date, no systematic evaluation has been conducted for different classification algorithms on the same data in terms of their classification capabilities.

In this study, we aimed to compare different methods for the classification of patients with schizophrenia based on NIRS activation. To accomplish this goal, we measured the hemoglobin response in the prefrontal cortex during a VFT with a multichannel NIRS system. We selected the mean values of [oxy-Hb], [deoxy-Hb] and their sum [total-Hb] as the classification features, and employed a principal component analysis (PCA) to reduce the dimension of feature space. Four classification methods were evaluated in this experiment, including linear discriminant analysis (LDA), *k*-nearest neighbors (KNN), GPC, and support vector machines (SVM). We investigated which classification methods represent the most powerful diagnostic tools for patients with schizophrenia and whether dimensionality reduction with PCA affects the overall outcome.

2. Materials and methods

2.1. Subjects

The dataset used in this study was collected from Peking University Sixth Hospital. It included 120 patients with schizophrenia (mean age: 31.5 ± 11.5 years, female/male: 57/63) and 120 age- and sex-matched healthy controls (mean age: 32.8 ± 10.7 years, female/male: 53/67). All subjects were right-handed and native Chinese speakers. The diagnosis for schizophrenia was based on the Structured Clinical Interview for the DSM-IV (American Psychiatric Association, 1994). The healthy controls were enrolled through the local community and then assessed to confirm no history of psychiatric or neurologic disorders. This study was conducted in accordance with the Declaration of Helsinki and was approved by the ethics committee of Peking University Sixth Hospital. All subjects provided written informed consent after the experimental procedure had been fully explained.

2.2. Task description and NIRS measurement

The experiment was performed in a quiet environment. All subjects were required to maintain emotionally stability prior to the experiment and to avoid moving the head as much as possible during the measurement. We designed a Chinese version of phonological VFT. The task comprised a 30-s pre-task baseline period, a 60-s task period, and a 30-s post-task baseline period (Fig. 1). During the pre- and post-task baseline periods, the subjects were instructed to constantly repeat counting from one to five. During the task period, they were instructed to produce as many phrases or four-character idioms as possible beginning with the designated Chinese characters ('白', '天', and '大', which indicate white, sky, and big, respectively). The three initial characters were changed every 20 s during the 60-s task period.