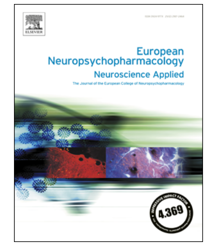
European Neuropsychopharmacology (2016) 26, 246–254



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Multivariate pattern analysis of obsessive-compulsive disorder using structural neuroanatomy

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Received 9 October 2014; received in revised form 15 November 2015; accepted 1 December 2015

KEYWORDS
Obsessive-compulsive disorder;
Structural magnetic resonance imaging;
Multivariate pattern analysis;
Support vector machine;
Gaussian process classifier

Abstract
Magnetic resonance imaging (MRI) studies have revealed brain structural abnormalities in obsessive-compulsive disorder (OCD) patients, involving both gray matter (GM) and white matter (WM). However, the results of previous publications were based on average differences between groups, which limited their usages in clinical practice. Therefore, the aim of this study was to examine whether the application of multivariate pattern analysis (MVPA) to high-dimensional structural images would allow accurate discrimination between OCD patients and healthy control subjects (HCS). High-resolution T1-weighted images were acquired from 33 OCD patients and 33 demographically matched HCS in a 3.0 T scanner. Differences in GM and WM volume between OCD and HCS were examined using two types of well-established MVPA techniques: support vector machine (SVM) and Gaussian process classifier (GPC). We also drew a receiver operating characteristic (ROC) curve to evaluate the performance of each classifier. The classification accuracies for both classifiers using GM and WM anatomy were all above 75%. The highest classification accuracy (81.82%, $P<0.001$) was achieved with the SVM classifier using WM information. Regional brain anomalies with high discriminative power were based on three distributed networks including the fronto-striatal circuit, the temporo-parieto-occipital junction and the cerebellum. Our study illustrated that both GM and WM anatomical features may be useful in differentiating OCD patients from HCS. WM volume using the SVM approach showed the highest accuracy in our population for revealing group differences, which suggested its potential diagnostic role in detecting highly enriched OCD patients at the level of the individual.

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http://dx.doi.org/10.1016/j.euroneuro.2015.12.014
0924-977X/

1. Introduction

Obsessive-compulsive disorder (OCD) is a common psychiatric disorder characterized by the presence of obsessions in the form of intrusive and distressing thoughts, ideas or images as well as the urge to perform repetitive or ritualistic behaviors known as compulsions. OCD has a lifetime prevalence rate of approximately 2.3% in the general population, thus making it a major burden to society (Ruscio et al., 2010). Currently, OCD is diagnosed solely on the basis of a subjective clinical interview and rating measures rather than objective laboratory tests, which often leads to diagnostic variability among different clinicians, cultures and districts (Phillips et al., 2009). It is thus highly desirable to develop additional valid and objective biomarkers to distinguish patients with OCD from healthy control subjects (HCS).

In recent years, neuroimaging has attracted considerable attention in defining the neural correlates of OCD and has raised hopes that it may one day aid the clinical assessment of individuals with this disorder (Linden and Fallgatter, 2009; Savitz et al., 2013). Preliminary results obtained from volumetric studies have revealed differences in both cerebral gray matter (GM) and white matter (WM), as well as specific regional abnormalities in the basal ganglia and cerebellum (de Wit et al., 2014; Hoexter et al., 2012; Szeszko et al., 2008; van den Heuvel et al., 2009). Meanwhile, a growing number of neuroimaging studies have reported evidence of functional neural abnormalities in OCD relative to HCS, pointing to the involvement of a cortico-striatal circuit in the behavioral control functions of OCD (Anticevic et al., 2014; Marsh et al., 2014; Milad et al., 2013). Because functional neuroimaging studies are methodologically demanding and can vary dramatically in paradigms and analytic methodologies, structural neuroimaging is more often performed in clinical practice. Thus, structural neuroimaging is potentially more suitable for providing measures for clinical diagnostic applications. However, the majority of available studies that provide evidence for cerebral structural abnormalities between OCD patients and HCS are based on average estimates at a group level, which limit their usages in clinical practice where doctors need to make decisions about individuals.

In an effort to increase the translational applicability of neuroimaging results, there has been a recent shift toward the use of multivariate pattern analyses (MVPA) techniques (Dosenbach et al., 2010), which have emerged as a powerful tool owing to their ability to extract spatial and/or temporal patterns from neuroimaging data and use this information to categorize individuals into different categories (Lao et al., 2004). This approach has been applied to differentiate OCD subjects from HCS based on functional magnetic resonance imaging (fMRI) (Weygandt et al., 2012) and diffusion tensor imaging (DTI) data (Li et al., 2014). Compared with traditional standard mass-univariate analytical methods, the MVPA approach has two main advantages. First, MVPA allows inferences at the level of the individual and can thus provide results with higher translational applicability in everyday clinical practice. Second, MVPA takes interregional correlations into account and therefore may be more sensitive to subtle and spatially distributed differences (Pereira et al., 2009).

To our knowledge, no study has directly compared structural neuroimaging measures between individuals with OCD and HCS with MVPA, though there have been numerous studies on alterations of GM and WM in OCD with pooled results from meta-analyses (Piras et al., 2013; Radua and Mataix-Cols, 2009; Rotge et al., 2010). Nearly all previous neuroimaging classifications were performed using a specific MVPA approach known as support vector machine (SVM) (Orru et al., 2012), whereas probabilistic classification models such as Gaussian process classifier (GPC) were largely ignored. The SVM is an algorithm designed for binary classification that maximizes the margin between classes in a high dimensional space. Mathematically, the discriminant function is defined by a weight vector orthogonal to the decision boundary, which can be uniquely specified by the samples that lie closest to the decision boundary, referred to as support vectors. The decision boundary represents the rule for classification of new examples. The GPC is a probabilistic model and is a Bayesian extension of logistic regression classifier. In contrast to SVM, the predicted class is augmented by an estimate of the certainty of the prediction. GPCs are best described as a distribution over functions. Based on Bayes' rule the posterior distribution of functions which represent the training data is found in an optimal way. This posterior distribution is used to classify new examples according to the rules of probability (Wolfers et al., 2015). Therefore, we aimed to apply both SVM and GPC classification approaches to discriminate patients with OCD from controls based on whole-brain structural GM and WM images. We hypothesized that (1) GM and WM may contribute differently to the classification of OCD and (2) SVM and GPC may show differences in discriminating OCD from HCS.

2. Experimental procedures

2.1. Subjects

The study was approved by the Ethics Committee of the West China Hospital, Sichuan University, and written informed consent was obtained from each participant. A total of 33 OCD patients and 33 sex-, age- and years-of-education-matched HCS participated in the present investigation (Table 1). All participants were right-handed and native Chinese speakers. OCD patients were recruited from the Mental Health Center, West China Hospital, Sichuan University, and diagnoses were confirmed using the Structured Clinical Interview for DSM-IV Axis I disorders (SCID) by two experienced psychiatrists (B. Li and W. Tang). Exclusion criteria included (1) participants younger than 18 years or older than 60 years; (2) psychiatric comorbidity assessed using the SCID; (3) any history of major physical illness, cardiovascular disease or psychiatric or neurological disorder; (4) substance abuse or dependence and (5) pregnancy. The Yale-Brown Obsessive Compulsive Scale (Y-BOCS) was used to rate the severity of OCD symptoms, whereas the 14-item Hamilton Anxiety Scale (HAMA) and 17-item Hamilton Depression Scale (HAMD) were used to rate anxiety and depressive symptoms, respectively. HCS were recruited from the local area using poster advertisements and were screened using the SCID (non-patient edition) by the same psychiatrists to confirm the current absence of psychiatric and neurological illness as well as no history of psychiatric illness among first-degree relatives.