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Multi-view classification of psychiatric conditions based on saccades

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ABSTRACT

Early diagnosis of psychiatric conditions can be enhanced by taking into account eye movement behavior. However, the implementation of prediction algorithms which are able to assist physicians in the diagnostic is a difficult task. In this paper we propose, for the first time, an automatic approach for classification of multiple psychiatric conditions based on saccades. In particular, the goal is to classify 6 medical conditions: Alcoholism, Alzheimer's disease, opioid dependence (two groups of subjects with measurements respectively taken prior to and after administering synthetic opioid), Parkinson's disease, and Schizophrenia. Our approach integrates different feature spaces corresponding to complementary characterizations of the saccadic behavior. We define a multi-view model of saccades in which the feature representations capture characteristic temporal and amplitude patterns of saccades. Four of the current most advanced classification methods are used to discriminate among the psychiatric conditions and leave-one-out cross-validation is used to evaluate the classifiers. Classification accuracies well above the chance levels are obtained for the different classification tasks investigated. The confusion matrices reveal that it is possible to separate conditions into different groups. We conclude that using relatively simple descriptors of the saccadic behavior it is possible to simultaneously classify among 6 different types of psychiatric conditions. Conceptually, our multi-view classification method excels other approaches that focus on statistical differences in the saccadic behavior of cases and controls because it can be used for predicting unseen cases. Classification integrating different characterizations of the saccades can actually help to predict the conditions of new patients, opening the possibility to integrate automatic analysis of saccades as a practical procedure for differential diagnosis in Psychiatry.

1. Introduction

Differential diagnosis is commonly used by physicians to diagnose a specific disease in a patient or at least to discard potential candidate conditions. Differential diagnosis may be complicated in the early stages of some diseases, and further complicated if the symptoms are common to different medical conditions. The use of automatic procedures that analyze patient data can contribute to improve early diagnosis. However, the implementation of these procedures is not straightforward in many cases due to the characteristics of the available biological data, its complexity, and the wide variability between patients.

It has been recognized that eye movement recordings may serve as an early differential diagnostic tool for many psychiatric conditions [1–5]. Fixation and saccades are two primary eye movements whose association to psychiatric conditions has been extensively investigated. Oculomotor fixation is defined as the ability to suppress ocular drifts while maintaining a steady retinal image of a single target of interest. A saccade is a rapid intermittent eye movement, such as that which occurs when the eyes fix on one point after another in the visual field.

In this paper we focus on the use of saccadic recordings for the classification of psychiatric conditions. While several researchers confirm that the saccadic behavior contains relevant information, a more challenging task is to actually use this information to predict the psychiatric condition of a given subject. From the machine learning point of view, the prediction task is considerably difficult due to the intrinsic nature of the saccade information (e.g. short time series with a different number of samples) and the potentially wide inter-trial and inter-subject variability. There are also a number of alternative ways to track eye movement that influence the choice of the classification technique. Usually, the electric signal that can be derived using two pairs of contact electrodes placed on the skin around one eye, i.e., electrooculogram (EOG), is used. Another possibility is the use of a portable saccadometer that consists of a transducer, which is worn on the head and measures the subject's eye movement using infra-red reflection.

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We used data from the 2012 International Joint Conference on Neural Networks (IJCNN 2012) Competition: "Classification of Psychiatric Problems Based on Saccades". The IJCNN 2012 Competition comprised different classification tasks that involved 165 subjects with 6 medical conditions: Alcoholism, Alzheimer's disease, opioid dependence (two groups of subjects with measurements respectively taken prior to and after administering synthetic opioid), Parkinson's disease, and Schizophrenia. Three different types of saccade measurements were available, although not every type of measurement was available for each subject. The general classification task was to maximize the accuracy of the classifiers using the leave-one-out cross-validation paradigm.

Our approach is based on the use of multiple and complementary views of the data. We design features that capture characteristic temporal and amplitude patterns of the saccades. Features are extracted from the direct measurements of the saccades and from interpolations derived from these measurements. We use four possible representations of the data and combine them in different ways in order to identify relevant feature combinations. We show that this multi-view representation of the same data can help to increase the amount of information available for the classification process. Finally, the application of appropriate classifiers, which are able to benefit from this multiple representation is proposed. We evaluate four different classifiers: affinity propagation [6], k-nearest neighbor classifier (KNN) [7], support vector machines (SVM) [8], and random forests [9].

2. Related work

A number of papers have reported the association between saccadic behavior and different psychiatric conditions. Saccadic eye movement dysfunction has been identified in Alzheimer's disease [2,3]. Impairment in the complex saccade performance in patients with Parkinson's disease dementia and dementia with Lewy bodies was reported in [4]. Saccadic eye movements were also associated with a family history of alcoholism at baseline and after exposure to alcohol [1]. In [5], evidence is presented that eye velocity preceding saccades is significantly lower among schizophrenic patients. Grace et al. [10] used saccadic eye movements to measure psychomotor impairment in two groups of opioid-tolerant and opioid-naive subjects. The study revealed greater saccadic movements in participants in the first group. A recent study [11] has successfully applied machine learning techniques to the analysis of reflexive saccade latencies, together with other information from the subjects, for the prediction of symptom development in Parkinsons patients.

Classification of saccadic data has been previously conducted in other contexts. In [12], classification algorithms for identification of oculomotor fixation and saccadic behavior are presented. These algorithms intend to identify particular types of oculomotor behavior and not to associate this behavior to a given psychiatric condition. The question of labeling oculomotor behavior as fixations or saccades is fundamentally different to the problem of identifying saccadic patterns that can be useful for differential diagnosis. Furthermore, the methods proposed in [12] for classification heavily depend on a given threshold that helps to distinguish a fixation from a saccade. Since we work with saccades that have already been identified, there is no need for a threshold for the application of the classification algorithms.

Other authors investigate potential relationships between the saccade system function and different psychiatric or neurological conditions. In [13], the relationship between demential severity and saccade system function for Alzheimer disease (AD) is analyzed on a set of 45 healthy volunteers and 35 patients with AD. The relationship is investigated in terms of the statistical differences in the saccadic behavior of cases and controls. No attempt is made to predict the "class" of the subject based on the saccadic data. Similarly, in [14] the correlation between saccadic measures with underlying gray matter loss is investigated for Huntington disease progression. A Spearman nonparametric correlation is used to test for an association between saccadic impairment and brain atrophy in saccade-related regions. The application of statistical tests to detect significant changes in saccadic behaviors due to mental or neurological disorders is the way of using saccadic data most commonly found in the literature [4,15–17]. We emphasize that classification of disease conditions based on saccades goes beyond testing for, and eventually identifying, associations between saccades and different disease conditions. Being able to predict, even if with a moderate accuracy, the type of disease of a patient, can help the physician to make decisions in everyday practice.

Finally, the application of classification algorithms to multiple domains of biomedical analysis and bioinformatics has gained pace in the last years [18–22] due to the important contribution that these methods can make to a more efficient use of available information for accurate prediction. Every domain of application requires a particular approach that takes advantage of the information known a priori about the problem domain. In multi-view classification [23,24], different representations of the data, that correspond to different views or characterizations of the problem are simultaneously applied to model the problem. This is a natural approach to analyze complex phenomena that can be approached using diverse modeling strategies, and each one admits the definition of a specific feature space. We show in this paper that information extracted from temporal and amplitude patterns of saccades are complementary and can be very useful to discriminate between different psychiatric conditions.

3. Materials and methods

This section presents a description of the data, classification tasks, and evaluation methodology used in the paper.

3.1. Data description

In a visually guided saccade experiment, after an initial fixation period, a visual stimulus appears in the visual field of the subject. Then the subject has to look in the direction of the stimulus. The saccadometer records the amplitudes of the eyes after stimulus presentation and from this information saccades are detected. Two different experimental paradigms are usually applied. In the first (VG), the initial fixation point remains visible until the end of the trial. In the second, it disappears shortly after presentation. This second experimental paradigm is called GAP trial [25]. Similarly, in a variation of the experiment the subject can be required to make an eye movement away from the visual stimulus to its mirror position and this type of trials is used to measure antisaccades (AT). Fig. 1 shows a typical saccade curve obtained in a visual guided experiment. In this figure, time points are represented on the x axis, and amplitude measurements at each time point recorded from one eye are represented on the y axis.

Data have been collected for each patient under controlled experimental conditions. In the data presented, the saccades amplitudes are the averaged values (with measurements sampling rate 1000 Hz) recorded from both eyes and consist of three types of measurements:

1. Measurements of visually guided saccades (denoted VG)
2. Measurements of visually guided saccades with a time gap of around 200 ms after presentations of the visual stimulus (denoted GAP)