Feature extraction and classification for pupillary images of rats

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Abstract: The investigation of the pupillary light reflex (PLR) is a well-known method to provide information about the functionality of the autonomic nervous system. Pupillometry, a non-invasive technique, was applied in our lab to study the schizophrenia-related PLR alterations in a new selectively bred rat substrain, named WISKET. The pupil responses to light impulses were recorded with an infrared camera; the videos were automatically processed and features were extracted. Besides the classical statistical analysis (ANOVA), feature selection and classification were applied to reveal the significant differences in the PLR parameters between the control and WISKET animals.

Keywords: schizophrenia, pupillometry, classification, curve properties

Introduction

Patients with schizophrenia, besides the well-known behavioral symptoms, also show autonomic dysregulation, including impaired pupillary function, which is a sensitive and reliable source of information about the function of the nervous system [1].

Pupillometry is a simple, non-invasive technique for the assessment of the autonomic nervous system function by testing the pupillary light reflex (PLR), meaning the contraction of the pupil in response to light. During the test, the changes of the pupil diameter are recorded and the size of the pupil is measured offline in each video frame.

Our study investigates the PLR to reveal the schizophrenia-related autonomic alterations in WISKET rats. Related works are summarized in Section 2. The novelties of the measurement and feature extraction methods are described in Section 3 and in Section 4, respectively. Section 5 shows the steps of data analysis. In Section 6 the results of the analysis are presented. Possible directions of future work are mentioned in Section 7 and Section 8 includes a short summary.

Related works

Developing reliable and predictive animal models for any complex psychiatric disorders, such as schizophrenia, is essential to improve our understanding of the neurobiological basis of the disorder. Recently, a new rat model of schizophrenia has been developed, named WISKET [5, 6, 8, 11].

Clinical studies in schizophrenic patients using pupillometry revealed impaired autonomic regulation [1, 2, 4, 9, 12]. PLR was also investigated in rodents [10]; however, no data are available from animal models of neuropsychiatric disorders, including schizophrenia.

Measurement process

Two series of experiments were performed in sedated (n=54) or anesthetized (n=20) male control Wistar, and WISKET rats. After a 10-minute dark adaptation period, the recording lasted for 15s in sedated, and for 60s in anesthetized animals. The animals were positioned in front of a camera, and exposed to an intensive light stimulus (approx. $300cd/m^2$ for $600ms$) into the left eye. The digital camera recorded pupillary responses at a speed of 24 frames-per-second under infrared illumination.

During the PLR measurements, the rats show several minor movements, which can affect the quality of the recorded videos. Furthermore, these albino rats lack pigments in their body including their eyes, reducing the contrast between the iris and the pupil. Specifically designed pupil detection and measurement algorithms were used to handle these quality drawbacks [7]. The input of the algorithm is a video recording and the output is a curve based on the measured pupil diameters in each frame.

Feature extraction

To compare the responses of the animals, we extracted well-describing features from the PLR curves, which are relevant from the pathophysiological point of view and are suitable to emphasize the differences between the groups regarding the autonomic nervous system activities.

An automated feature extraction method was designed, which produces 40 features. Many of them are basic, traditional parameters like initial diameter, which is the size of the pupil before the light impulse; minimum diameter; reaction time; maximum redilated diameter; etc. We also implemented new features to obtain information about the dynamics of the response, thus 11 velocity related descriptors were introduced. For example, the average and the maximal contraction velocities were determined and the time required to reach the latter was measured. The velocities at different points of the redilation phase were also calculated.

We introduced novel, smoothness related descriptors, as well. A polynomial curve with a given order was fitted on the redilation part of the response. The area between the original and fitted curves serves as a measure of non-smoothness. We chose 5^{th} order polynomials, which were flexible enough to follow the slow perturbations of the original curve and indicated only the short, abnormal swings. In Figure 1, a representative response curve and a marked subset of the extracted features is presented.

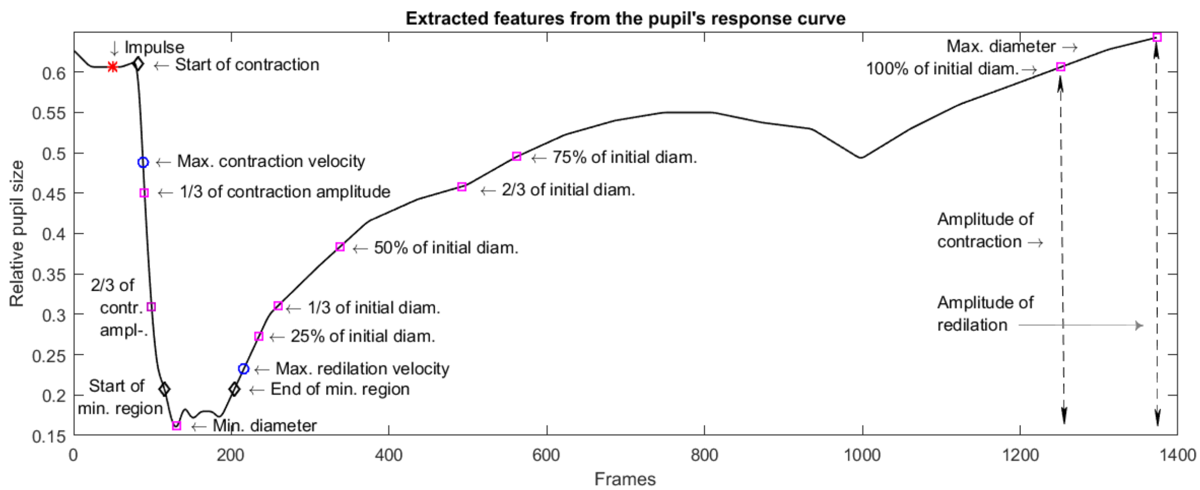

Figure 1: Pupillary light response curve and a marked subset of the 40 features.

Analysis

The sedated and the anesthetized animals were analyzed separately.

One-way ANOVA was used for the analysis of the extracted features. The relationships between pupil parameters were assessed by linear regression analysis and calculation of the Pearson correlation coefficient. Only probabilities lower than 0.05 were considered significant.

Besides the investigation of the differences in PLR parameters, the other goal is to use pupillometry as a quick examination to help classify the animals during the breeding process. Therefore, we trained a binary decision tree to investigate the possibility of classification and evaluated the model by using cross validation.

Results

The detailed discussion of the results of statistical analysis can be found in our recent study [3]. The trained decision tree selected almost the same features as predictor variables as the results of statistical analysis suggested.

In the sedated group, which has the bigger cardinality, the control and test animals show differences in many features. The initial and minimum pupil diameters are larger and the degree of the constriction was lower in the WISKET rats. The flatness of the curve (length of the minimum region) and the contraction time were shorter in the control group. These results are in accordance with previous studies mentioned in Section 2. The decision tree achieved 71% accuracy measured by cross-validation. The algorithm selected the following predictors: minimum diameter; initial diameter; contraction time; average redilation speed.

The analysis showed that the group of anesthetized animals cannot be divided into two classes. We assume that while anesthesia can prevent the stress and allows a convenient investigation of pupillary reactions for a longer period, it also diminishes the autonomic responses. The classifier achieved only 60% accuracy; the selected predictors were: amplitude of contraction; average redilation speed; time required to reach the maximal redilation speed.

Future work

As the number of animals is limited and the cost of one sample is high, we are reconsidering the measurement process, extending the recording time and stimulating the rats with different light sequences. Thus, with this method more features could be extracted and new correlations between PLR parameters might be explored. Our further purpose is to develop a more robust recording process. We have already designed a pilot setup, in which an IR LED ring is applied to illuminate the eye and to induce a ”bright pupil effect” resulted by the reflection of light from the retina.

Summary

We applied pupillometry to study how the schizophrenia-like alterations affect the PLR in the WISKET rats. We assigned a 40-dimensional feature vector to each recorded video and analyzed the dataset with statistical methods, and also trained a decision tree based classifier. The results demonstrate that pupillary control shows significant alterations in WISKET rats, and classification based on pupillometry might be applied as an additional examination during the breeding process.

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