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Digital Biomarker Identification for Parkinson's Disease Using a Game-Based Approach

Ilman Shazhaev[1], Dimitry Mihaylov[2,3], Abdulla Shafeeg[3]

[1]Management Department, Farcana, United Arab Emirates
[2]China Branch of BRICS Institute of Future Networks, Shenzhen, China
[3]Science Department, Farcana, United Arab Emirates
Email: abdulla.shafeeg@farcana.com

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Abstract

Despite the fact that their neurobiological processes and clinical criteria are well-established, early identification remains a significant hurdle to effective, disease-modifying therapy and prolonged life quality. Gaming on computers, gaming consoles, and mobile devices has become a popular pastime and provides valuable data from several sources. High-resolution data generated when users play commercial digital games includes information on play frequency as well as performance data that reflects low-level cognitive and motor processes. In this paper, we review some methods present in the literature that is used for identification of digital biomarkers for Parkinson's disease. We also present a machine learning method for early identification of problematic digital biomarkers for Parkinson's disease based on tapping activity from Farcana-Mini players. However, more data is required to reach a complete evaluation of this method. This data is being collected, with their consent, from players who play Farcana-Mini. Data analysis and a full assessment of this method will be presented in future work.

Keywords

Machine Learning, Biomarker, Parkinson's Disease

1. Introduction

Slowness of movement, or Bradykinesia, is a primary clinical symptom of Parkinson's disease (PD). Upper extremity bradykinesia may be evaluated using finger tapping tests, which are often used in neurophysiological exams. The gold standard in finger tapping assessment is the Movement Disorder Society Unified

Parkinson's Disease Rating Scale (MDS-UPDRS), which uses a 5-point rating scale to evaluate the condition. The MDS-UPDRS III's integer scale inhibits the identification of minor motor changes. Despite this, it is a complete evaluation. Inter-rater agreement is at best modest, with a score of 5. Because of this, there is an obvious need for techniques of evaluating motor dysfunction that are objective and consistent. An early and correct diagnosis is essential for patients to have access to the variety of available treatments and therapies. Early intervention may enhance life quality. The validation may aid experts in reducing differential diagnostic uncertainty, thereby eliminating the requirement for DaTSCAN and saving time and money. Priority may be given in triage to timely access to optimal therapy over wasteful recommendations of the worried-well.

It is possible to create unique games based on known behavioral correlates that are designed to put a player in a certain circumstance and track their actions. Custom assessment games have been designed to measure several elements of physical [1] and mental [2] well-being. The activity traces that are left behind by natural interactions with digital games may be employed as a digital biomarker of health and health deterioration.

As a result, in this paper, we hypothesize that changes in the patterns of finger movement while playing the Farcana-Mini game might be utilized to differentiate and categorize people with Parkinson's disease from those without the condition in the early stages of the disease. The difficulties in identifying PD stem from the lack of a conclusive test; at present, the condition must be diagnosed based only on clinical and observational criteria. Numerous symptoms of PD are unclear and are shared with other neurodegenerative and non-neurodegenerative disorders. The Unified Parkinson's Disease Rating Scale (UPDRS) is a tool for evaluating Parkinson's disease that is based on a score determined from a physician's neurological assessment; hence, it is a subjective measure that lacks objectivity, reproducibility, and sensitivity [3].

The majority of games need motor input to play. Touch input (*i.e.*, in mobile games); mouse and keyboard input (desktop games); and controller input, which comprises of buttons to push and thumbsticks or small joysticks to manipulate, are the most common types of input devices used in games (*i.e.*, in console games). Occasionally, gaming consoles have cameras that record the user's motions (e.g., Microsoft Kinect and Sony PlayStation Camera). Varying degrees of motor coordination are required to play different games: Many games demand complicated sequences of input (e.g., Street Fighter), whilst others require a relatively basic motor action, but require it to be performed rapidly and often (e.g., Cookie Clicker) or in conjunction with cognitive decisions (e.g., Farcana-Mini) [3].

2. Literature Review

Decho Surangsrirat *et al.* [4] have used the mPower dataset to examine how finger tapping activities on a mobile phone correlated with the MDS-UPDRS I-II and PDQ-8. mPower is mobile application-based research used for the study of

the progression and diagnosis of Parkinson's disease. Today, it is the biggest open-access, mobile Parkinson's Disease study. Any public researcher was given access to data from seven modules with 8320 individuals who gave data for at least one task. Demographics, MDS-UPDRS I-II, PDQ-8, memory, tapping, voice, and walking are all included in this package. It is one of the activities that is straightforward to complete and has been evaluated quantitatively for PD measurement. They have only included individuals who completed both the tapping activity and the MDS-UPDRS I-II rating scale. According to the results of the statistical analysis, subjects were divided into three severity groups using the tapping characteristics. Based on the MDS-UPDRS I-II and PDQ-8 scores, each group indicated a distinct degree of Parkinson's disease (PD) severity.

Using 75,048 tapping accelerometer and position data, Kaiwan Deng *et al.* [5] built deep learning algorithms that generated an AUC (Area under the Receiver Operator Characteristic Curve) of 0.933 when detecting PD patients among 6418 individuals. The performance of tapping was superior to that of gait/rest and voice-based models derived from the same population used as a benchmark. When the three models were combined, the AUC increased to 0.944. Notably, the models not only corresponded significantly with patient-reported symptom levels, but also outperformed them in identifying PD. This work illustrates the complementary predictive potential of tapping, gait/rest, and speech data, and creates models based on integrative deep learning for detecting PD.

Noreen Akram *et al.* [6] developed a novel distal upper-limb exam called Distal Finger Tapping (DFT). Kinetic metrics include kinesia score (key taps over 20 s), akinesia time (mean dwell-time on each key), and incoordination score (IS20, variance of travelling time between key taps). To design and analyze a keyboard-tapping test for PD distal motor function. 55 PD patients and 65 controls took DFT and BRAIN. The MDS-UPDRS-III finger tapping sub-scores were correlated with test results. Nine more PD patients were recruited for motor monitoring. KS20 performed best, with 79 percent sensitivity and 85 percent specificity; AUC = 0.90. DFT and BRAIN enhanced discrimination (AUC = 0.95) KS20 correlated moderately with the MDS-UPDRS finger-tapping sub-score (Pearson's r = 0.40, p = 0.002). DFT They observed minor variations in motor fluctuation states that were not reflected in MDS-UPDRS-III finger tapping sub-scores. The DFT test assesses distal movements in PD and may be used to evaluate motor problems longitudinally. Lopez-de-Ipina Karmele *et al.* [7] developed a unique technique based on the integration of handwriting and neuroimaging data for the early clinical identification and monitoring of ET. A computerized Archimedes' spiral exercise measures fine motor abilities and correlates with ET MRI biomarkers. With their novel modeling technique, they offered a supplementary and promising tool for the clinical diagnosis of ET as well as tremors from a wide variety of sources.

3. Proposed Method

Farcana-Mini as shown in **Figure 1**, is a 2D game. As the character in the game

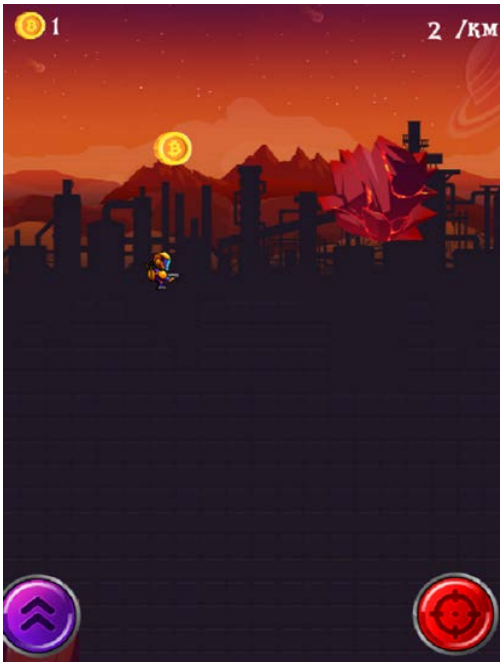

Figure 1. Farcana-mini.

moves forward player is required to continuously keep tapping the purple button at the lower left of display to avoid obstacles along the way as shown in Figure 1. The red button on the lower right of display can be used by player to shoot bitcoins at enemies or obstacles. If the character gets in contact with an obstacle or enemy the game restarts.

3.1. Data Collection

The Farcana-Mini is currently being played by thousands of players around the world and their finger tapping activity is being recorded and stored in a cloud server. With the consent of the players, we use this data for research. The assumption is that Parkinson's disease (PD) patients would have worse coordination and slower movements during gameplay compared to healthy individuals. This will result in erroneous and/or shifting tapping contact point locations.

In today's web2 ecosystem, service providers have complete control over the obtained user data. While the initial intended use of such data is largely for smart IoT systems and device control, the data is frequently utilized for additional uses that the users have not explicitly approved to. To preserve the integrity of data acquired by Farcana-mini players, we deploy Nevermined's innovative data exchange and storage structure (nevermined.io). It promises to provide users with complete data privacy control by seamlessly combining smart contracts, Data in Situ Computation, Federated Learning, and Provenance-based data integrity testing and verification in cloud settings for the usage of Service Execution Agreements (SEAs) between parties. The data owner not only controls who can have what access to his/her data, but also be ensured that the data is used only for the intended purposes.

3.2. Prediction Model

Neighborhood Components Analysis (NCA) is a distance metric learning algorithm that aims to improve nearest neighbor classification accuracy over standard Euclidean distance. The algorithm directly maximizes the one-to-one elimination (KNN) stochastic k-nearest neighbor estimator on the training sample. It can also learn a low-dimensional linear projection of the data, which can be used for data visualization and quick classification.

We focus on stochastic KNN classification. The thickness of the connection between a sample and another point is proportional to their distance and can be thought of as the relative weight (or probability) that a stochastic nearest neighbor prediction rule would assign to that point. In the original space, the sample has many stochastic neighbors from different classes, so the correct class is unlikely. However, in the predictive space learned by NCA, the only stochastic neighbors with a non-negligible weight are in the same class as the sample, which guarantees that the latter will be well classified.

NCA can be used for controlled dimensionality reduction. The input data is projected onto a linear subspace consisting of directions that minimize the NCA goal. The desired dimension can be set using the *n*_components parameter. For example, the following figure shows a comparison of dimensionality reduction using Principal Component Analysis (PCA), Linear Discriminant Analysis (Linear Discriminant Analysis), and Neighborhood Components Analysis on a Digits dataset, a dataset with size where the dataset is split into training and test sets of equal size and then standardized. For evaluation, the classification accuracy of 3 nearest neighbors is computed from the 2-dimensional predictive points found by each method. Each data sample belongs to one of 10 classes.

The goal of NCA is to learn the optimal linear transformation matrix of size, which maximizes the sum over all samples (*n*_components, *n*_features) *i* of the probability p_i that *i* is correctly classified, that is:

$$\operatorname{argmax}_L \sum_{i=0}^{N-1} p_i \tag{1}$$

involving $N = n$_samples and pi, the probability of sample *i* being correctly classified according to the stochastic nearest neighbor rule in the learned nested space:

$$p_i = \sum_{j \in C_i} p_{ij} \tag{2}$$

where C_i—is a set of points of the same class as sample *i*, and p_{ij} is softmax at Euclidean distances in the nested space:

$$p_{ij} = \frac{\exp\left(-\left\|Lx_i - Lx_j\right\|^2\right)}{\sum_{k \neq i} \exp\left(-\left\|Lx_i - Lx_j\right\|^2\right)} \tag{3}$$

3.3. Machine Learning Feature Selection

During data processing, distinguishing features between individuals who have

signs of PD and individuals with no signs of PD are selected. These features include: Signal peak; Power spectral density average; Deviation standard of the power spectrum. In order to verify our work, we will use 10-fold cross validation to assess the predictive models' accuracy. In 10-fold cross validation method there are 10 iterations of cross validation in which a total of 90% of the entire training set is chosen at random, and 10% is utilized as a holdout group for testing and validation. In this study, there are two data groups: the training group and the test group. In the training group, the determinant attributes (processed data) and the class corresponding to each individual was provided; in the test group, only the attributes were provided, and the classification algorithm determined which group each individual belonged to. We will use the K-NN Classifier algorithm [8].

4. Conclusion and Future Work

In this paper, we have reviewed some of the methods found in the literature that were developed to identify problematic digital biomarkers. Most of the methods have performed quite well, but to the best of our knowledge, this is the first research to identify problematic digital biomarkers from data gathered while playing commercially available games that are meant for entertainment. We proposed a machine learning approach for early identification of hand tremor which is considered a sign of Parkinson's disease. We require more data to reach a complete evaluation. This data is being collected, with their consent, from players who play Farcana-Mini. Data analysis and a full assessment of this method will be presented in future work.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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