Towards Longitudinal Data Analytics in Parkinson's Disease

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Abstract. The CloudUPDRS app has been developed as a Class I medical device to assess the severity of motor symptoms for Parkinson's Disease using a fully automated data capture and signal analysis process based on the standard Unified Parkinson's Disease Rating Scale. In this paper we report on the design and development of the signal processing and longitudinal data analytics microservices developed to carry out these assessments and to forecast the long-term development of the disease. We also report on early findings from the application of these techniques in the wild with a cohort of early adopters.

1 Introduction

The CloudUPDRS app and its associated information management and analytics platform, have been designed and developed to meets the standards set for medical devices. CloudUPDRS achieves the accurate, precise, and repeatable assessment of motor symptoms for people with Parkinson's (PwP), which clinicians can use with confidence. The app itself is employed as a data capture device relaying captured information to a service back-end developed following the microservices pattern [4] incorporating a so-called signal processing service that converts raw observations to motor performance metrics and a data analytics service that carries out longitudinal analyses revealing the pattern of development of the disease over time.

CloudUPDRS capitalises on the observation that it is possible to employ certain aspects of movement that are disrupted in Parkinson's as surrogate biomarkers of dopamine levels, a fact that forms the basis for Part III of the MDS-UPDRS. Previously, we investigated the possibility to precisely quantify and implement the MDS-UPDRS methodology as a smartphone app to enable the assessment of motor performance through tremor, gait and bradykinesia measurements obtained from standard sensors embedded in smartphones within a clinical setting [1]. Extending this approach, we currently focus on capturing in-depth medical intelligence supporting the discovery of longitudinal trends, promoting deeper understanding of the patterns of normal daily symptom variations, and predicting the onset of dyskinesias thus facilitating high-precision personalised targeting

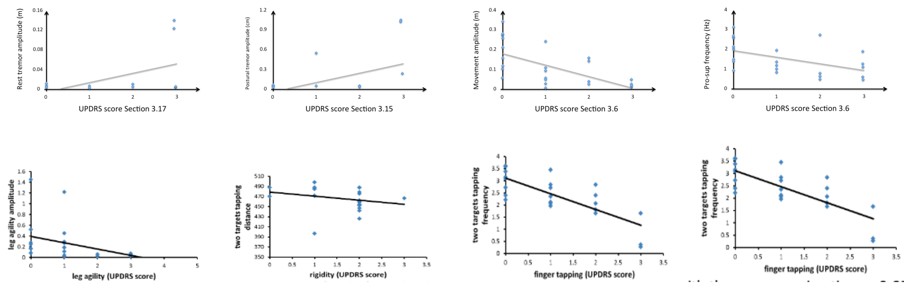

Fig. 1. Correlation between CloudUPDRS metrics and the corresponding sections of MDS-UPDRS.

of treatment. A key ingredient of this work is that we have successfully transferred the process that until recently was available only in the clinical setting so that PwP and their carers can administer the tests unsupervised at home we anticipate a significant reduction of the number of emergency hospital visits while considerably increasing data availability through high-frequency assessment of a large population of PwP.

2 The CloudUPDRS app and Service Platfrom

Overall, the CloudUPDRS system consists of the following elements:

1. PD patient smartphone apps for Android and iOS that carry out motor performance measurements and wellness self-assessment; conduct session management; securely transfer captured data to the CloudUPDRS service; and, present an interface providing guidance and feedback.
2. Cloud-based scalable dats collection engine that safely and securely collects data from patients' smartphones; ensures secure data management; and applies the MDS-UPDRS signal processing pipeline.
3. A data analytics toolkit for medical intelligence incorporating quantitative and semi-structured data, and longitudinal analyses, clustering and classification; and a clinical user interface incorporating visualisation.

The CloudUPDRS service platform enables the secure capture, management and analysis of data collected by the app and provides effective communication of insights generated to clinicians enabling them to explore alternative treatment scenarios. To cater for the diverse needs of the PwP population in the UK, the platform has been engineered to facilitate scalable performance by adopting the microservices architecture [6]. The microservices architectural style is set in contrast to traditional monolithic web applications and aims to maximise opportunities for vertical decomposition and scaling-out, which are critical for high performance and service resilience in data intensive situations.

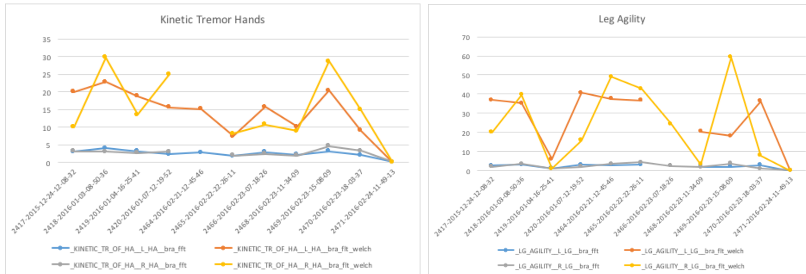

Fig. 2. Individual patient longitudinal analysis of kinetic tremor of the left hand and left leg agility showing significant daily variations.

3 Signal Processing Toolkit

Standard practice in conducting assessments of the severity of PD symptoms involves visit to a clinic and the use of clinical rating scales such as the MDS-UPDRS [**?**], using patient diaries or other self-completed scales. Nevertheless, it is possible to perform more precise objective assessment of tremor, bradykinesia and gait using laboratory equipment and closely tracing Part III of the MDS-UPDRS protocol. Indeed, this is common practice when detailed and accurate information is required for example when researching the effectiveness of new treatments. Such laboratory equipment typically includes specialised biomedical data acquisition systems incorporating transducers such as high-frequency/high-accuracy accelerometers and gyroscopes, signal amplifiers and filters and high-performance analog-to-digital converters as well as advanced single processing software. These systems are obtained by specialist commercial providers such as Cambridge Electronic Design Ltd in the UK, currently the market leader, with the total cost of a complete system rising to tents of thousands.

3.1 Tremor

Tremor measurements are recorded for both hands at rest, at posture and in action. For rest tremor measurements, users are asked to relax their hands on their lap in a supine position while the phone is lying in their palm. For the postural tremor measurements patients are guided to keep their arm outstretched directly at their front while holding the smartphone. Finally, for action tremor measurements they are required to hold the phone and move it between the chest and the fully outstretched position at their front. In all cases, acceleration is recorded along three axes in m/s^2 at the maximum supported sampling rate and timestamped at maximum resolution (typically microseconds).

Tremor is calculated as the cumulative magnitude of the scalar sum acceleration across three axes for all frequencies between 2 Hz to 10 Hz. To obtain this power spectrum the the signal is first filtered with a Butterworth high-pass second order filter at 2 Hz and the Fast Fourier Transform (FFT) subsequently applied to the filtered waveform data.

3.2 Bradykinesia

Mds-updrs assess bradykinesia, or else the slowness of movement, through three different factors: (i) pronation-supination movements, (ii) leg agility, and (iii) finger tapping. In the first test patients are asked to hold the phone and perform alternating pronation-supination movements, that is rotating the palm of the hand toward the inside so that it is facing downward and then toward the outside so that the palm is facing upward, as fast and as fully as possible. Leg agility measurements require the phone to be placed on the thigh of the patient while seated, holding the phone lightly with the ipsilateral hand, while raising and stomping the foot on the ground as high and as fast as possible. During both tests the phone is recording acceleration data in a manner similar to the tremor tests.

The assessment of the pronation-supination movements and leg agility tests requires the estimation of the frequency and power of movement. To obtain these, the toolkit first removes DC and applies a Butterworth low-pass second order filter at 4 Hz in order to exclude most of the tremor. Subsequently, the power of the movement is calculated as the total amplitude between 0 Hz and 4 Hz and the frequency derived from the power spectrum.

Finger tapping performance is assessed in two tests using single and dual targets presented on the screen of the phone at set locations with patients attempting to tap them as fast and as accurately as possible (alternating between targets in the dual-target case). When tapping accidentally occurs outside the screen area the test is repeated. The touch-sensitive screen of the smartphone is used to collect the information used for performance calculations, specifically the timing of each touch event, its duration, the direction of movement (upwards or downwards), the coordinates on the phone screen, and the amount of pressure applied are recorded. For the two-target variant it is necessary that the distance between targets be at a specific distance irrespective of the size of the screen or of the device.

To estimate finger tapping performance the analytical functions first identify all touch events and employ the associated timestamps to estimate tap frequency (expressed as number of taps per second), the mean hand movement time between taps (in milliseconds), and the actual movement distance between alternative tapings in the dual-target case (in centimetres). The calculation of distance requires scaling of measurements expressed in screen pixels to account for the pixel density characteristics of to particular smartphone models. Similar to tremor, bradykinesia functionalities in the CloudUPDRS analytics toolkit are implemented in python incorporating features from NumPy and SciPy.

3.3 Gait

Mds-updrs assesses gait by considering multiple behaviours including stride amplitude and speed, height of foot lift and heel strike, and turning and arm swing. The CloudUPDRS variant of this test requires the patient to walk along a straight line for five meters, turn around and return to the point of departure,

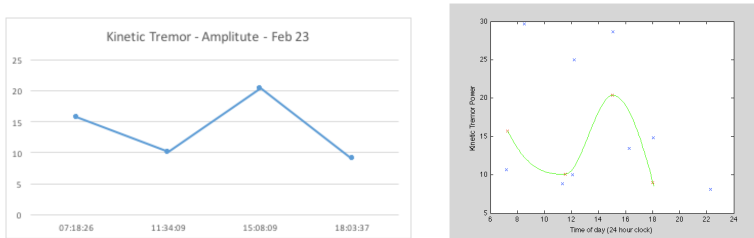

Fig. 3. Patterns of daily variation during a typical day of bradykinesia symptoms. The graph on the right displays a smoothed curve representing fine grain progression and offers a measure of variation between days.

while the smartphone is positioned either in their belt or trousers pocket. Since it is only possible to measure acceleration data from a single point at the waistline it is realistic to attempt the estimation of only stride frequency and length, velocity and turning time. The estimation of these measurements in CloudUPDRS follows the techniques suggested in [2] and [3] using PyWavelets for their implementation in python.

4 Testing

The performance of the CloudUPDRS signal processing toolkit was validated on a bespoke data set comprising of 20 complete sets of measurements. Results obtained from its application were compared against the same calculations implemented using Spike2 and matlab and compared against the UPDRS score provided for each test and patient by an experienced clinician after carrying out their standard assessment during a hospital consultation. This study [1] confirmed the consistent performance of CloudUPDRS against the golden standard i.e. clinical result and indeed indicated consistent accuracy exceeding 10^{-3} relative error suffices for MDS-UPDRS assessment.

5 Longitudinal Data Analytics

Having established the capability to conduct motor performance assessments at home and in the community using the CloudUPDRS app we have now developed a community of early adopters to develop and test a data analytics framework to study the longer-term development of the disease. Of particular interest is the investigation of ways to cluster patients in smaller groups that have similar progression patterns and are responsive to similar treatment. Indeed, symptoms vary greatly independent of treatment and PD progresses at different rates in different individuals, it requires regular clinical monitoring and medication adjustment. Our specific aim to develop novel opportunities to precisely quantify PD progression and the effectiveness of patient stratification [5]: the wider availability of data concerning individual variability and actual symptom trends provided by CloudUPDRS is expected to identify opportunities to adapt care to the needs of a particular individual at a specific time.

The first stage of this work is the identification of daily, weekly and longer patterns of variation in symptoms which would provide the baseline for adaptation. Figure 2 shows how upper and lower body performance varies during a period of weeks – clearly the day-to-day variation is significant and more importantly this variation is not typically captured by UPDRS scores that smooth out differences. Further, Figure 3 shows an aggregate pattern of performance variation for bradykinesia thus providing an early result towards the development of characteristic patterns of disease variation for the individual.

6 Work in Progress

The longitudinal analysis presented in the previous Section has been based on data collected during a period of four months and while further improvements were implemented in both analytics and app. In particular, we are now able to identify a subset of tests that are specifically selected for each patient matching their particular symptoms. This allows a considerable reduction in the time required to carry out the test thus allowing even more more frequent assessments. We anticipate that in the coming six month period we will have collected adequate information to be able to create progression profiles and in particular conduct reliable trend analysis on individual performance. This will further enable experimentation with clustering and classification techniques towards our objective of patient stratification.

Acknowledgments

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