Design and Development of a Mobile Application to Explore Cognitive Skills in Parkinson's Disease Patients

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Abstract—**Parkinson's disease (PD) is one of the most common neurodegenerative diseases and its incidence is expected to growth in the next decades. Many efforts have been made in order to build a system for the remote monitoring and assessment of the motor symptoms in PD. Nevertheless, non-motor symptoms are usually not equally considered. This work is aimed at developing a mobile tool able to carry out a remote monitoring of different cognitive areas affected in the PD population and that could be integrated with the motor assessment of PD patients. This would allow not only a better monitoring of PD patients but also a better understanding of the disease progression.**

Keywords— **Parkinson's disease, cognitive monitoring, mHealth, mobile**

I. Introduction

Parkinson's disease (PD) is one of the most common neurodegenerative disorder, its prevalence in industrialized countries is generally estimated at 0.3% of the entire population and about 1% in people over 60 years of age (1).
Its prevalence increases with age for this reason, and due to the global ageing trends, PD is expected to impose an increasing social and economic burden on societies on the coming decades.

The major motor disturbances in PD are bradykinesia (i.e. slowness at movement), hypokinesia (decreased amplitude movements), resting tremor, rigidity, and postural instability (2). Moreover, PD patients are affected not only by motor complications but a wide range of non-motor signs and symptoms such as loss of sense of smell (anosmia), nerve pain, urination problems, constipation, depression and anxiety, sleeping problems (insomnia) leading in excessive sleepiness during the day, cognitive impairments, visual hallucinations (perception of something that does not exist) and delusions (believing things that are not true).

During the last decade the study of cognition in PD has gained always more and more attention. It has been shown how cognitive impairments could slightly appear since the first stages of the disease (3) depicting a condition called Mild Cognitive Impairment (MCI). PD-MCI is characterized by deficits in specific cognitive functions, nevertheless the functional autonomy is preserved (4).

Some of these deficits are strongly related to dopamine deregulation and might be accented or, on the contrary, ameliorated by L-dopa medication (5). They affect mainly the attentional/executive domain, interfering with dual task, attention shifting, working memory and planning processes. Other deficits are not susceptible to pharmacological therapy and may concern memory skills such as delayed recall, recognition, associative learning, or visuospatial and visuoperceptive abilities.

Moreover it is well known that PD patients have impairments in emotion recognition tasks and empathy (6,7). The recent scientific debate has drawn attention on PD-MCI prodromic condition for cognitive decline, showing how individuals with PD-MCI have a higher risk of developing dementia in the later stages of the disease (8). Therefore instruments for detecting and monitoring cognitive decline are needed and strongly recommended in order to better operate in patient management (9).

While the automatic detection and assessment of the motor symptoms is a topic that has been largely studied (10–13) and it used to be the focus when telehealth is considered for PD (14), the evaluation of the cognitive status in PD patients and the integrated study of cognitive and motor progression is not so well addressed. On this regards, the PD_manager project (www.parkinson-manager.eu) is aimed at building a novel mHealth platform for PD patients able to integrate motor and non-motor assessment including cognitive, speech, sleep monitoring and treatment adherence monitoring. It is also aimed at delivering different services for the patients, caregivers and professionals based on this holistic monitoring. This work presented here covers the design and development of the mobile application for the cognitive assessment that will be used within the preliminary PD_manager study with 20 patients with three main objectives: 1) to explore the feasibility of a mobile application for this kind of assessment in PD patients, 2) to get actual feedback from the patient in terms of usability and user experience in order to redesign the system for the second PD_manager study where 210 patients are expected to be involved and 3) to monitor changes in patient's cognitive state, according to his/her motor state .

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II. METHODS AND MATERIAL

A. Review of the state of the art

As an initial step a review of the state of the art was carried out to analyze and identify already scientifically validated tools for the cognitive assessment and to explore which of them could be more feasible to be incorporated in our mHealth solution, taking into account three considerations: 1) it should cover all the cognitive impairments presented in PD (above mentioned); 2) existence of scientific works validating its efficiency in the requested areas and 3) should be feasible to be implemented in a mobile platform. In total, 14 battery tests were identified and analyzed: Montreal Cognitive Assessment (MoCA), Tower of London (ToL), The Cambridge Neuropsychological Test Automated Battery (CANTAB), Mini-mental State Examination (MMSE), Modified Mini-Mental State Examination (3MSE), Wisconsin Card-Sorting Test (WCST), Automated Neuropsychological Assessment Metrics (ANAM), The Computer-Administered Neuropsychological Screen for Mild Cognitive Impairment (CANS-MCI), CNS Vital Signs, Computerized Neuropsychological Test Battery (CNTB), CogState, MCI Screen, MicroCog, Mindstreams (Neurotrax). Table 1 shows a summary of the analysis of these battery tests.

B. Development environment and guidelines

The development of the prototype was carried out in Android environment using Android Studio 1.4 and it was developed for Android 4.0 or higher. For the design of the applications the "*Issue Papers for the The Cognitive and Learning Disabilities Accessibility Task Force (COGA)*" and the "*Web Content Accessibility Guidelines (WCAG) 2.0*" from the World Wide Web Consortium (W3C) and available online (https://w3c.github.io/coga/issue-papers/ and http://www.w3.org/TR/WCAG20/) were taken into account. Also, previous research works where the usability of mobile applications for PD patients were studied (15,16) were also considered. Some of the guidelines followed to build this app are summarized in the next points:

Text size and color. Text size was higher enough to facilitate the reading of the screen for elderly people, also the color of the text and the background color were chosen taken into account the accessibility recommendations of the W3C. WCAG 2.0 level AA requires a contrast ratio of 4.5:1 for normal text and 3:1 for large text (14 point and bold or larger, or 18 point or larger). Level AAA requires a contrast ratio of 7:1 for normal text and 4.5:1 for large text.

Use of signifiers. The technological and computer skills of the target population are very limited, for that reason conventions are not necessarily well understood for this group of users (17). Consequently, all the potential actions allowed within the app are clearly signified with a self-contained text.

Minimalism. To avoid unexpected actions and confusions the app has been designed with a full screen layout eluding potential distractions and source of errors (e.g. the notifications bar).

Reinforcement and feedback. Text-to-speech has been used to literally read all the textual instructions that are given to the patients. This function is expected to reinforce the instructions given to the patients in order to properly carry out the different tests. Also, both visual and auditory feedback s provided in the different tests.

Table 1 Battery tests for cognitive assessment

Name	Notes
MoCA	Some tasks are language dependent. The test was conceived to be done on paper and with a test examiner.
ToL	It is a very specific test that do not cover the whole cognitive areas.
CANTAB	CANTAB test offers several benefits for its implementation on a mobile context: 1) it has specifically designed to be delivered in a touch screen (consequently it could be easily translated into a mobile phone context); 2) it covers a wide range of cognitive aspects and 3) it is widely accepted in the scientific community as gold standard to assess cognitive capabilities.
MMSE	MMSE is affected by demographic factors; age and education exert the greatest effect (18). The most frequently noted disadvantage of the MMSE relates to its lack of sensitivity to MCI and its nonlinearity or insensitivity to progressive changes (19,20). As the content of the MMSE is highly verbal, lacking sufficient items to adequately measure visuospatial and/or constructional praxis.
3MSE	Lack of scientific validation on elderly and PD patients.
WCST	Simple tests but does not cover many aspects of the cognitive impairments.
ANAM	It was not specifically designed for elderly populations. The test requires an examiner to be administered.
CANS-MCI	It requires a proprietary hardware. It is language dependent. It also requires an examiner.
CNS Vital Signs	Some tests are language dependent. But it is not a substitute for formal neuropsychological testing, it is not diagnostic, and it will have only a limited role in the medical setting, absent the active participation of consulting neuropsychologists (21).
CNTB	It's language dependent. It includes motor assessment which likely be impaired in PD. It is fully administered by a technician and thus is not a self-administered, automated test battery.
CogState	Limited data on validation (22).
MCI Screen	It's language dependent. It is required an examiner to administer the test.
MicroCog	It requires an restricted set of keyboard responses
Mindstreams	Too long. Language dependent.

III. RESULTS

A. Identification of the most appropriate tests

Computerized cognitive testing offers significant advantages respect to the traditional paper-based or oral testing standardization of administration and stimulus presentation, accurate measures of response latencies, automated comparison in real-time with an individual's prior performance as well as with age-related norms, and efficiencies of staffing and cost (22). In our particular case, the CANTAB battery test has shown to be most feasible system to be incorporated in the PD_manager platform:

Most of its tests are language independent, therefore it is possible to select a subset of tests covering all the cognitive impairments in PD that can be used across the different pilot sites included in the PD_manager project allowing a direct analysis of the patients' responses independently of the country where the study is carried out. This is crucial within PD_manager in order to be able to homogenously analyze all the generated data. Finally, for future development it makes easier the scalability of the system across Europe and worldwide.

It has been largely validated among elderly populations and with PD patients. CANTAB battery test is widely accepted in the scientific community as a valid tool to be used as a gold standard in terms of cognitive assessment. Moreover it does not require a test administer and it has been specifically designed for a digital context and to be implemented in a touch screen.

Nevertheless, some adaptations were made to make the CANTAB battery test (23) more appropriate for our target group and objectives. Some of the CANTAB tests were excluded in order to minimize language bias and/or the involvement of motor components in accomplishing the task. Tests that were too challenging for PD in advanced stage (high risk of floor effect) were also excluded. However the selected bias free tests were sufficient to explore the interplay between motor and cognitive symptoms associated with normal PD symptoms' fluctuations.

Each test monitored the patient performance, providing feedback about response accuracy and increasing the level of difficulty to avoid ceiling effect in automatic way. Patients enrolled to the study should complete a training period which will minimize bias due to the learning effect (cognitive amelioration).

The descriptions of the implemented tests is as follows:

a) Paired Associates Learning

In the first part of the test boxes are displayed on the screen and opened in a randomized order. One or more of them will contain a pattern. In the second part of the test, the patterns are displayed in the middle of the screen, one at a time, and the participant must touch the box where the pattern was originally located. The difficulty level increases through the test. The number of patterns to locate will increase along with the difficulty level (from one in the first level to eight in the last level). If the participant reaches the 6th level, the number of boxes will increase from 6 to 8. If the participant locates correctly the pattern, a positive feedback will be showed (a green tick mark and a positive auditory signal), otherwise a negative feedback will be showed (a red x mark and a negative auditory signal).

To skip to the next level, the patient must locate correctly all patterns. In case of error, the level is repeated and the patterns are represented to remind the participant of their locations. If participant locates wrongly all patterns in two consequent trials of the same level, the test will stop.

b) Pattern Recognition Memory

The participant is presented with a series visual patterns, one at a time, in the centre of the screen. These patterns are designed so that they cannot easily be given verbal labels.

After the presentation phase, there is a recognition, in which the participant is required to choose between a pattern he has already seen and a novel pattern. In each level, the test patterns can be presented in the reverse order to the original order of presentation (reverse mode) or in a totally random order (random mode).

If the participant selects the correct pattern, a positive feedback will be showed (a green tick mark and a positive auditory signal), otherwise a negative feedback will be showed (a red x mark and a negative auditory signal).

The difficulty level increases through the test, i.e., the number of patterns increases from two –first level - to six – last level -.

c) Spatial Working Memory

The test begins with eight white squares boxes being shown on the screen. The aim of this test is that, by touching the boxes and using a process of elimination, the participant should find one blue 'token' only in a few of the white boxes presented on the screen, and use them to fill up an empty column on the right hand side of the screen. The number of blue 'tokens' is gradually increased, up to eight boxes.

d) Spatial Span

Eight white squares are shown, some of which briefly change color in a variable sequence. The participant must then touch the squares which changed color in the same order that they were displayed by the device. In each level, there are three trials with the same spatial configuration of white squares and the same length of variable sequence. The sequence of colored boxes will get as long as the level difficulty increases (from two colored boxes in the first level to eight colored boxes in the last level). To skip to the next level, the

patient must make correctly at least two of three trials. However, with two or more incorrect trials the test stops.

e) Stop Signal Stop

This test consists of two parts. In the first part, the participant is introduced to the press pad, and told to press the left hand button when he sees a left-pointing arrow, and the right hand button when he sees a right-pointing arrow. In the second part, the participant is told to continuously press the buttons on the press pad when he sees the arrow, as before, but, if the arrow presentation is combined with an auditory signal (a beep), he should withhold his response and not press the button.

The number of trials of each part is 50 and the length of each trial is three seconds.

f) Attention Switching Task

The test displays an arrow which can appear on either side of the screen (right or left) and can point in either direction (to the right or to the left). Each trial displays a cue at the top of the screen that indicates to the participant whether he has to press the right or left button, according to the "direction in which the arrow was pointing" (first part) or the "side on which the arrow appeared" (second part). Some trials display congruent stimuli (e.g. arrow on the right side of the screen pointing to the right) whereas other trials display incongruent stimuli which require a higher cognitive demand (e.g. arrow on the right side of the screen pointing to the left). The total number of trials of each part is 13.

g) Visual Analogue Scales

The participant must respond to 8 questions, as they appear on the screen by touching the on-screen slider and moving it to the appropriate position on the scale.

B. Tests administration schedule

In order to optimize detection of PD symptoms' fluctuations, patients should be assessed three times a week, two sessions per day during their best (10-12 am) and worst ON state (13-15 pm). To do this, each test should be randomly administered in one of the two daily sessions.

Furthermore patients should provide a weekly self-report diary about their activities, keeping track of patient's mood, pain and self-efficacy (or self performance perception), according to motor and cognitive fluctuations.

Name	Description	Measures
Paired Associates Learning	Good and reliable tool for the spatial memory assessment: it involves visuo-perceptive abilities and episodic spatial memory. It allows also to monitor switching abilities	For each level: Number of errors, average time between taps (s), standard deviation of time between taps (s)and total time (s)
Pattern Recognition Memory	Good also for advanced patients, it provides visual cues.	For each level: Type of task (e.g. reverse or random mode), Number of stimuli, Number of errors, average time between taps (s), standard deviation of time between taps (s), total time (s)
Spatial Working Memory	It involves spatial exploration and visuo - spatial working memory. It might be a bit too demanding.	For each level: Number of blue tokens, number of empty boxes opened, number of empty boxes reopened, number of blue token boxes reopened, average time between two consecutive taps (s), standard deviation of time between two consecutive taps (s), average time between two blue tokens recollected (s), standard deviation of time between two blue, tokens recollected (s) and total time (s)
Spatial Spam	Spatial Span assesses vision-spatial short term memory capacity; it is an analogue of the Corsi Span test. The little motor component involved could affect the performance.	For each level: Number of moves, number of correct trials, maximum number of consecutive correct taps, average number of consecutive correct taps, average time between two consecutive correct taps of a sequence (s), standard deviation of time between two consecutive correct taps of a sequence (s), average trial time (s), standard deviation of trial time (s) and total time (s)
Stop Signal Task	Stop signal task assesses response inhibition (impulse control).	For each part: Type of test (e.g. GO for the first part and No-GO for the second part), number of stimuli, number of stimuli with audio, number of direction errors, number of tap errors, number of timeouts, average reaction time (s), standard deviation of reaction time (s) and total time (s)
Attention Switching Task	It gives a good measure of cognitive response to conflictual stimuli, and it is susceptible to dopamine levels and levodopa medication.	For each level: tap time (s), result of test (e.g. true or false) and type of test (e.g. congruent/incongruent – position/direction).
Visual Analogue Scale	Simple tool for measuring (by continuous data) anamnestic data, perceived medication effect, pain, mood and quality of life information	For each question: Question number, scale minimum value – scale maximum value answer (%) and time (s)

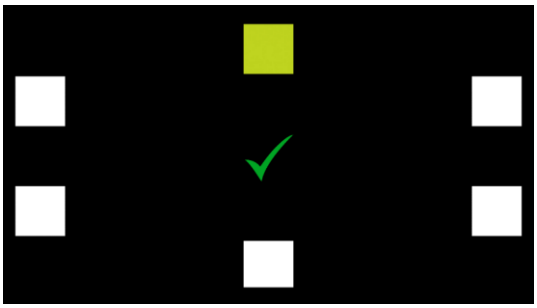

Fig. 1 Example of Paired Associates Learning implementation

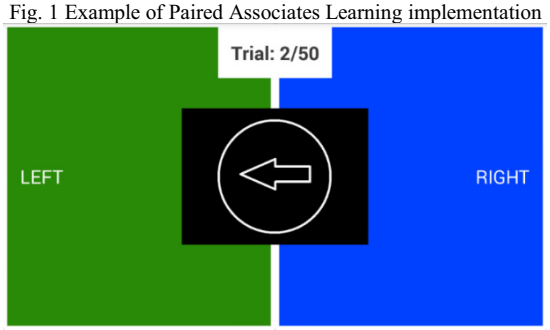

Fig. 2 Example of Attention Switching Task implementation

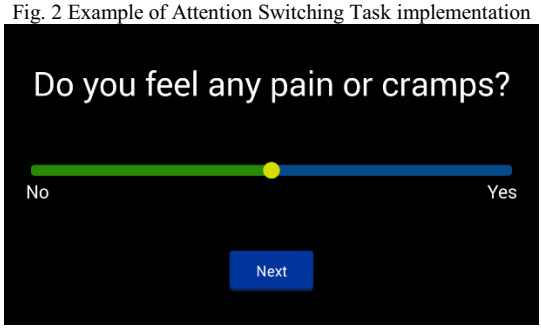

Fig. 3 Example of *Visual Analogue Scales implementation*

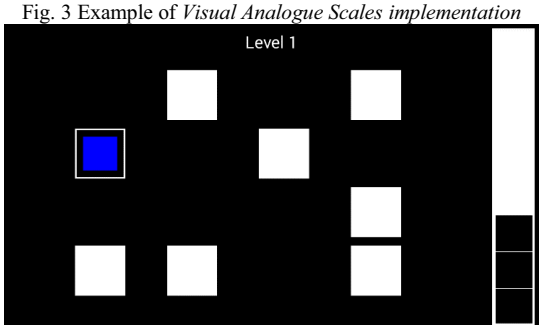

Fig. 4- Example of Spatial Working Memory implementation

IV. CONCLUSIONS

This app is the result of a multidisciplinary work where different test batteries for cognitive assessment have been analyzed and translated to a mobile application taking into account the particularities of the target group of study. Both the motor and cognitive limitations of PD patients, as well as the cognitive areas of decline of this group, were used as a key elements to select and customize a set of cognitive tests that were translated to a mobile platform taking into consideration the design insights from previous research. This application will be evaluated in the coming months with a reduced number of patients in order to explore its feasibility and usability with PD patients using a mobile application and it will be later redesigned and integrated into the PD_manager platform in order to carry out a holistic monitoring of the patients covering motor, cognitive and treatment adherence components.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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