Instrumental Assessment of Bradykinesia: A Comparison Between Motor Tasks

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***Abstract*—Bradykinesia, a common symptom in psychiatry, is characterized by reduced movement speed and amplitude. Monitoring for bradykinesia is important, as it has been associated with reductions in quality of life and medication compliance. Subtle forms of bradykinesia have been associated with treatment response in antipsychotic-naïve first episode patients. Therefore, accurate and reliable assessment is of clinical importance. Several mechanical and electronic instruments have been developed for this purpose. However, their content validity is limited. This study investigated which tasks, or combinations thereof, are most suitable for assessing bradykinesia instrumentally. Eleven motor tasks were assessed using inertial sensors. Their capability of distinguishing bradykinetic patients with schizophrenia ($n = 6$) from healthy controls ($n = 5$) was investigated. Seven tasks significantly discriminated patients from controls. The combination of tasks considered most feasible for the instrumental assessment of bradykinesia was the gait, pronation/supination, leg agility and flexion/extension of elbow tasks (effect size = 2.9).**

***Index Terms*—Antipsychotic-induced, bradykinesia, instrumental assessment, motor task, schizophrenia & psychotic states.**

I. Introduction

ANTIPSYCHOTIC-INDUCED bradykinesia is associated with physical disability, social stigmatization, lower quality of life, and reduced medication compliance [1]–[4]. Bradykinesia expresses itself as a reduction in speed and amplitude of voluntary movement [5]. Bradykinesia occurs as a symptom of Parkinson's Disease, drug-induced parkinsonism, depression, negative symptoms of schizophrenia, and others. The pathophysiological basis of bradykinesia lies in a dysregulation of the basal ganglia, specifically the pathways involved with the scaling of the amplitude and velocity of movement [5]. Dysregulation of these pathways can be a result of psychotic disorders and/or antipsychotic treatment [6].

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In first-episode antipsychotic naïve patients with schizophrenia, bradykinesia is a predictor of reduced treatment response [7]. Bradykinesia can also debut as a prodrome for psychosis in antipsychotic-naïve ultra-high risk (UHR) groups [8]. Therefore, accurate assessment of bradykinesia is of clinical and scientific importance. Bradykinesia is typically assessed using observer rated scales, for example, the Unified Parkinson's Disease Rating Scale (UPDRS) and the St. Hans Rating Scale For Extrapyramidal Side-Effects (SHRS). However, the assessment of movement disorders using observer rated scales is subjective, has a moderate reliability, and shows a low sensitivity to subtle forms of movement disorders [9], [10]. Consequently, rating scales are less suitable for both the monitoring of bradykinesia and the detection of subtle prodromal bradykinesia. A logical alternative would be instrumental assessment.

Several objective and reliable instrumental methods of assessing bradykinesia have been developed [8], [11]–[18]. However, they are rarely applied in research and clinical practice, likely due to their cost and ease of use in comparison to rating scales. Nowadays, more affordable and user-friendly motion capture technologies are available [13], [15]–[17]. To assess the severity of bradykinesia instrumental assessments mechanically or electronically capture performances on motor tasks [8], [11]–[18]. These instruments focus on measuring a specific motor task, for example, handwriting or spiral drawing. As a result, the scope of these instruments does not cover the entire construct of bradykinesia.

Content validity of instrumental assessments can be improved by assessing a broader selection of motor tasks. As a proof of principle discriminability between patients with bradykinesia and healthy controls was investigated for a wide range of motor tasks. We hypothesized that a suitable selection of tasks should be able to discriminate between these two groups.

II. Methods

A. Subjects

Power calculations indicated that in order to significantly discriminate between groups, $n = 5$, an effect size of at least 2.0 is required to ensure a p-value of 0.05 with a power of 0.8. Therefore, we opted to investigate two very distinct populations in order to be able to achieve meaningful results with a small subject population. We recruited six DSM-IV schizophrenic inpatients with antipsychotic-induced bradykinesia from Zon

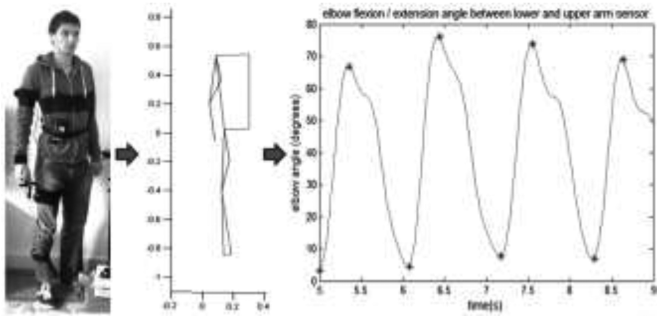

Fig. 1. Overview of the instrumental setup and data analysis. Left: Placement of the inertial sensors attached to the index and middle fingers, upper, and lower arm and leg, and sternum. Sensors connected to a Bluetooth receiver worn around the waist. Middle: 3-D-Model constructed from sensor data. Right: Elbow angle (degrees) plotted against time (seconds) during the flexion/extension task. Asterisks indicate when the elbow is fully extended and flexed, and were used to determine the mean duration, amplitude and velocity of a flexion/extension cycle.

& Schild, a psychiatric hospital in the Netherlands. Criteria for bradykinesia were at least one moderate or two mild scores on the UPDRS bradykinesia items [19]. Five healthy controls were recruited from the staff and local community. Criteria for inclusion were age between 40 and 60 and male gender, as age and gender affect bradykinesia [20]. Considering the scale of this study, we opted to investigate a homogeneous population to reduce the risk of a type II error. Exclusion criteria were use of other medication that can induce movement disorders, severe cognitive impairment or mental retardation and injuries or neurological diseases affecting movement.

All subjects provided informed written consent, and the study was approved by the local ethics committee.

B. Instruments

Subjects' movements were registered using six inertial sensors (MTx, XSENS, Enschede, the Netherlands). In contrast to inertial sensors used in previous studies [12]–[14], these sensors use a proprietary Kalman filter that combines data from the accelerometer, gyroscope, and magnetometer to reduce sensor drift and improve the accuracy of movement registration [21]. Sensors were attached to the subjects' dominant upper and lower arm and leg, ring and middle finger, and to their sternum using Velcro straps. The sensor secured to the ring and middle finger was only attached during the hand movements task. Exact placement of the sensors is illustrated in Fig. 1. Each sensor connected to an XBUS receiver (XSENS, Enschede), worn around the waist, that registered data and sent it via Bluetooth to a computer running MT software 1.8.1 (XSENS, Enschede, the Netherlands).

C. Tasks

Repetitive movements are one of the primary clinical measures of bradykinesia. Velocity and amplitude are impaired when performing repetitive motor tasks at high movement rates with large amplitudes [22]. Therefore, the selection of tasks primarily existed of repetitive motor tasks. Tasks were derived from existing observer rated scales and instrumental assessments. The following tasks were selected: 1) hand movements, 2) pronation/supination movements of hand, 3) leg agility, 4) arising from chair, and 5) gait tasks from the UPDRS following previous studies [13], [14]–[15]. Tasks selected from other instruments were the 6) Flexion/extension of elbow [19] and small and large 7) tapping and 8) tracing tasks [17]. On the tapping and tracing tasks subjects were instructed to repeatedly tap on two lines, 30 and 55 cm apart, and trace circles, 17 and 32 cm in diameter. Patel *et al.* proposed that the instrumental assessment of bradykinesia could be extended to motor tasks derived from activities of daily living [12]. Therefore, the following three tasks were also included: 9) pouring water from a plastic jug into four plastic glasses, 10) repeatedly flipping over a plastic glass and setting it down on the table, and 11) twisting a peppermill (similar to the pronation/supination movements of hand task of the UPDRS). Subjects were instructed to perform tasks with a large amplitude as fast as possible for 30 s. Except for the gait, arising from chair and pouring tasks. In these tasks subjects were instructed to walk in their own pace for 20 m between two markers on the floor spaced 5 m apart, arise from their chair and sit back down twice, and pour a marked volume of water into four glasses. Subjects were given 30 s to practice each task and 2 min rest between tasks.

D. Task Outcomes

For each task mean cycle duration, amplitude and velocity were determined. An exception was made for the arising from chair and pouring glass tasks, because they were only performed a couple of times. A linked segment model was built using the sensor output, the sensors absolute orientation as a rotation matrix, in MATLAB 2012a (Mathworks), Fig. 1. Segment lengths were corrected for body height [23].

Analysis of hand movements, flexion/extension of elbow, pronation/supination movements of hand, leg agility, flipping glass, and peppermill tasks was based on joint angles. These angles were defined as the angle between the sensors proximal and distal to the joint, determined using Euler decomposition and filtered using a low pass bidirectional Butterworth filter. The cutoff frequency was determined by adding 2 Hz to the frequency with the highest power in the joint angle signal, calculated using Direct Fourier Transformation. Each tasks' average cycle duration, amplitude, and velocity were calculated from the joint angle using a peak detection algorithm, where peaks in joint angle were defined as subsequent minima an maxima that are at least one standard deviation apart, see Fig. 1.

To analyze gait, arising from chair and the small and large tapping and tracing tasks, the positions of either the ankle, torso or wrist were investigated, respectively. The linked segment model was used to determine the position of the ankle/wrist relative to the hip/shoulder joint in the transversal plane, the plane parallel to the ground. To analyze arising from the chair the sternum's position was used relative to the ankle in the longitudinal plane, perpendicular to the transversal plane. The gait task also required regular walking to be differentiated from turning, which was defined as a rotation over 160° of the sensor attached to the sternum. Mean cycle/stride durations, amplitudes, and velocities on these tasks were obtained by analyzing the positions of the ankle, wrist, and sternum filtered and analyzed using the same method and algorithm as mentioned above. For the arising from chair task the average durations of standing up and sitting down were determined as well as their average velocities.

Differences in the execution of the pouring glass task resulted in data not suitable for automated analysis. Therefore, the average pouring time per glass was determined by visually inspecting the data.

E. Statistical Analysis

Statistical analysis was performed using SPSS 17.0 for Windows (IBM). Group means of task outcomes were determined for patients and controls. To investigate the discriminability of the combined task outcomes (durations, amplitudes, and velocities) of selections of tasks, the outcomes were normalized and summed. Differences between group were investigated with two tailed t-tests assuming unequal variances. To achieve sufficient statistical power to significantly differentiate patients from controls an effect size above 2.0 was required. Therefore, effect sizes, Cohen's D, were determined using the pooled standard deviations of the groups.

III. Results

A. Subjects

Age and height of patients and controls were 52.2 ± 6.8 and 52.0 ± 3.9 years, and 1.87 ± 0.10 and 1.80 ± 0.07 m. One patient used a walking aid, therefore, his scores on gait, leg agility and arising from chair tasks were excluded from the analysis.

B. Tasks

Gait, leg agility, elbow flexion/extension, arising from chair, small and large tracing, small and large tapping, and flipping glass tasks significantly discriminated patients from controls, Table I. Differences between patients and controls were largest on the flipping glass task. This was also the only task to significantly discriminate on its duration, amplitude and velocity, with respective effect sizes of 2.3, 2.8, and 2.8. Thereafter the flexion/extension of the elbow task was most discriminative, effect sizes for duration and velocity were 2.1 and 2.7, as seen in Fig. 2. An interesting finding is that in contrast to standing up, patients sat down significantly slower than controls.

C. Task Combinations

Combining tasks increased effect sizes by as much as 50%, illustrated in Fig. 2. Table I lists the differentiability of the combinations of tasks derived from the UPDRS (hand movements, pronation-supination movement of hands, leg agility, and gait tasks), tracing/tapping tasks (small and large tapping and tracing tasks), the combination of all tasks, except for the arising from chair and pouring glass tasks. These tasks could not be combined with the other task due to their outcomes being different.

Also included in Table I is the recommended selection of tasks (flexion/extension of elbow, gait, leg agility, and pronation/supination movements of hand tasks).

Criteria for the selection of these tasks are described in the discussion. The highest effect size, 4.2, was reported for the combined durations of all tasks.

D. Task Outcomes

Mean cycle/stride duration, amplitude, and velocity significantly discriminated between patients and controls in four, one, and seven tasks, respectively. Velocity discriminated most in five of the seven tasks. Duration was most discriminative in the other two tasks.

When task outcomes were combined, only duration and velocity achieved significance, and most discrimination was reported for the combined durations.

IV. Discussion

The majority of the tasks are suitable for assessing bradykinesia instrumentally, as seven of the 11 tasks significantly discriminated patients with bradykinesia from controls. As expected, combining outcomes of different tasks markedly improved discriminative potential.

Other studies reported that gait, arising from chair, leg agility, flexion/extension of the elbow and pro/supination movements of hand tasks are capable of measuring bradykinesia instrumentally [8], [11]–[18]. This is confirmed by our findings and indicates that these tasks are suitable for measuring bradykinesia in long term psychiatric patients, with the exception of the pro/supination task. Granted that the instrument in the study of Patel *et al.* measured bradykinesia less accurately than tremor and dyskinesia [12].

In the selection process of tasks for the instrumental assessment of bradykinesia, practical aspects should also be considered, see Table II. The flexion/extension and gait tasks are most feasible, being similar to tasks on validated observer rated scales. Other tasks are less feasible, because 1) they are less practical due to the requirement of additional standardized materials (leg agility, arising from chair, tapping, tracing, pouring, flipping, and peppermill). 2) The tasks could not discriminate patients from controls (hand movements, pronation/supination, pouring and peppermill). 3) Performance on the tasks depended on more than the underlying construct of bradykinesia. For example, muscle weakness, rigidity, tremor, and required accuracy of movements also affect movement speed [24], [25]. Therefore, confounding could have been an issue in the tapping, tracing, pouring, and flipping glass tasks.

Variance in expression of bradykinesia between patients is considerable, partly since severity can differ per region (head/neck/arms/trunk/legs). Observer rated scales rely on the analysis of a broad selection of tasks to achieve adequate content validity. Our results also show that assessing a combination of tasks improves discriminability. Although combining all tasks achieved best discriminability, this is an impractical solution as an assessment would cost too much time, approximately 30 min. Therefore, to improve the content validity of the instrumental

TABLE I
TASK OUTCOMES AND COMBINATIONS THEREOF SIGNIFICANTLY DISCRIMINATING PATIENTS FROM CONTROLS

Task	Duration (s)			Amplitude (deg)■			Velocity (deg/s)■		
	Patient Mean (SD)	Control Mean (SD)	p-value (effect size)	Patient Mean (SD)	Control Mean (SD)	p-value (effect size)	Patient Mean (SD)	Control Mean (SD)	p-value (effect size)
Arising from chair▲	0.7 (0.1)*	0.6 (0.1)	0.23 (0.8)	< 0.1 (< 0.1)*	< 0.1 (< 0.1)	0.32 (0.7)	**0.4 (0.1)***	**0.6 (0.1)**	**0.01 (2.2)**
Gait	1.3 (0.1)*	1.2 (< 0.1)	0.05 (1.7)	1.3 (0.1)*	1.5 (< 0.1)	0.03 (1.9)	**1.0 (0.2)***	**1.3 (<0.1)**	**0.03 (2.1)**
Flexion / Extension of elbow	**1.2 (0.4)**	**0.6 (0.1)**	**<0.01 (2.1)**	76.8 (22.9)	81.4 (23.9)	0.75 (0.2)	**138.9 (43.0)**	**290.0 (68.2)**	**<0.01 (2.7)**
Tapping small	1.1 (0.2)	0.6 (0.2)	0.01 (1.9)	0.1 (< 0.1)	0.2 (< 0.1)	0.38 (0.5)	**0.3 (0.1)**	**0.6 (0.2)**	**0.02 (2.1)**
Tapping large	**2.0 (0.7)**	**0.8 (0.3)**	**<0.01 (2.3)**	0.3 (0.1)	0.3 (0.1)	0.28 (0.7)	**0.3 (0.1)**	**0.9 (0.4)**	**0.02 (2.3)**
Tracing large	**3.9 (1.2)**	**1.2 (0.6)**	**<0.01 (2.7)**	0.2 (< 0.1)	0.3 (< 0.1)	0.05 (1.4)	**0.2 (0.1)**	**0.9 (0.4)**	**0.02 (2.5)**
Flipping	**2.8 (0.9)**	**1.2 (0.4)**	**<0.01 (2.3)**	**32.8 (14.4)**	**88.1 (24.8)**	**<0.01 (2.8)**	**24.6 (18.1)**	**164.3 (71.5)**	**0.01 (2.8)**
Combined scores of UPDRS● tasks	**1.7 (2.5)**	**-2.0 (0.5)**	**0.01 (2.0)**	-0.7 (2.0)	0.8 (1.2)	0.16 (0.9)	-1.4 (2.4)	1.7 (1.4)	0.02 (1.5)
Combined scores of tapping and tracing tasks	**2.5 (1.6)**	**-3.1 (1.9)**	**<0.01 (3.2)**	-1.1 (1.6)	1.3 (0.9)	0.02 (1.7)	**-2.5 (0.7)**	**3.0 (3.2)**	**0.02 (2.5)**
Combined scores of recommended tasks	**2.1 (2.2)**	**-2.5 (0.8)**	**<0.01 (2.7)**	-0.8 (2.0)	0.9 (2.4)	0.25 (0.8)	**-1.9 (1.5)**	**2.3 (1.4)**	**<0.01 (2.9)**
Combined scores of all tasks	**-7.1 (1.6)**	**5.9 (4.0)**	**<0.01 (4.2)**	-2.5 (3.0)	3.0 (2.9)	0.01 (1.9)	**-5.6 (3.2)**	**6.7 (4.9)**	**< 0.01 (3.0)**

List of all the outcomes of the tasks and combinations thereof significantly discriminating patients with bradykinesia (n = 6) from controls (n = 5). The combined scores consisted of UPDRS● tasks (hand movements, pronation-supination movement of hands, leg agility and gait tasks), of the tapping and drawing tasks (small and large tapping and tracing tasks), the recommended selection of tasks detailed in the discussion (flexion/extension of elbow, gait, leg agility and pronation-supination movement of hands tasks) and all tasks (Excluding tasks producing different outcomes, arising from chair and pouring glass task). Significant differences, Cohen's D > 2.0, are in bold.* n = 5. ■ For the gait, arising from chair, tapping and tracing tasks amplitude and velocity are expressed in meters and meters per second. ▲ The average vertical velocity, in meters per second, while standing up and sitting down are reported in the amplitude and velocity columns. ● Unified Parkinson's Disease Rating Scale.

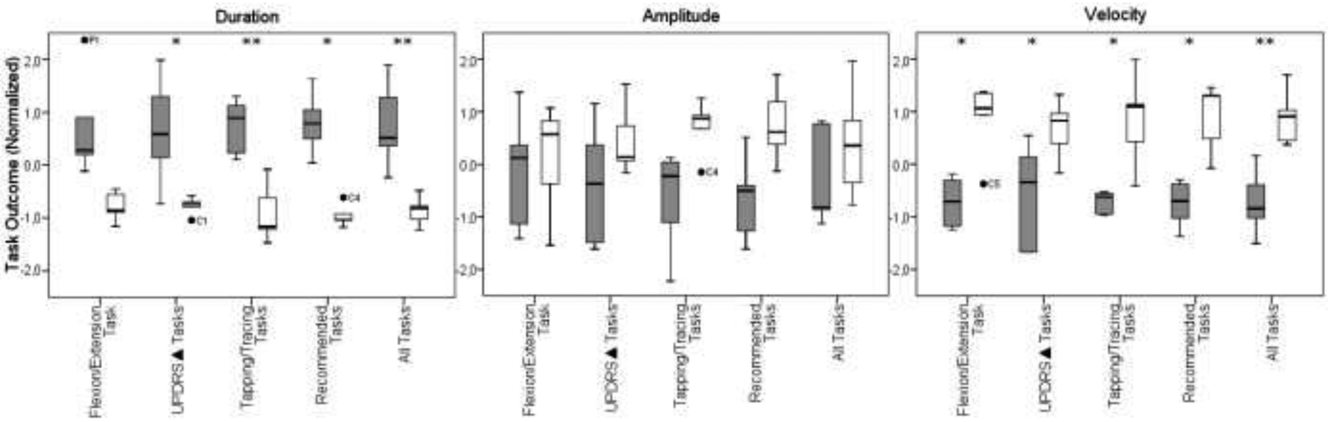

Fig. 2. Three sets of boxplots detail differentiability of the outcomes for duration, amplitude and velocity. Data of patients with bradykinesia are grey and data of controls are white. To aid the visual comparability scores were normalized (including the normalized sum scores of the combinations of task outcomes). Scores were reported for the flexion/extension of elbow task and the combined scores of the tasks derived from the UPDRS▲ (hand movements, pronation-supination movement of hands, leg agility, flexion/extension of elbow and gait tasks), of the tapping and drawing tasks (small and large tapping and tracing tasks), the recommended selection, see discussion, of tasks (flexion/extension of elbow, gait, leg agility and pronation-supination movement of hands tasks) and of all tasks (Excluding tasks producing different outcomes, arising from chair and pouring glass task). This figures illustrates that most differentiability is achieved by combining tasks • Outliers labelled to indicate which group the subject was in and their respective number in the study. ▲ UPDRS.∗ Indicates an effect size greater than a Cohen's D of 2.0. ∗∗ Indicates an effect size greater than a Cohen's D of 3.0.

TABLE II
TASKS FEASIBILITY FOR ASSESSING BRADYKINESIA

Task	Materials	Content Validity	Discriminability
Hand Movement	++	++	−
Gait	++	++	+
Pronation/Supination Movements of hand	++	++	−/+
Leg Agility	−/+	++	+
Flexion/extension of elbow	++	+	++
Arising from chair	−/+	++	++
Pouring water in glass	−−	−	−−
Tracing (small and large)	−−	−	++
Tapping (small and large)	−−	−	++
Flipping glass	−	−	++
Peppermill	−	+	−

Overview of practical aspects tasks must meet to be feasible for use in an instrumental assessment. Tasks are scored on the extra materials required to perform the tasks, favoring tasks that do not require any. Content validity indicates to what degree a task measures the underlying construct of bradykinesia. Scores for discriminability were based on the effect sizes found in this study. Scores range from −−, −, −/+, + to ++.

assessment of bradykinesia a combination of tasks investigating different body parts is required and the selection of tasks should be limited to tasks with a high content validity, adequate discriminability and that are easy to perform and require few additional materials. Thus, the recommended selection of tasks for the design of an instrumental assessment for bradykinesia is the combination of the average cycle/stride velocities on the gait, pronation/supination, leg agility, and flexion/extension of elbow tasks. This selection can be performed in less than ten min. and discriminates very well between patients with bradykinesia and controls, Cohen's D = 2.9.

The external validity of this study could be limited. As this study was limited to male subjects, aged 40 to 60. Although age and gender affect the severity of bradykinesia, they do not affect in which parts of the body bradykinesia is most prominent. In addition, the large effect sizes and the fact that performances on the tasks were based on repeated movements, contribute to a high statistical power. Therefore, this study's findings can likely be generalized to other populations. Investigators were not blinded to the status of the participants, patient or control, or the aim of the study. As patients were compared to healthy controls it was clear which group they were part of. However, data were collected electronically reducing the possibility of estimator bias. Nevertheless, it remains possible that minor variations in instructions between groups resulted in a slight bias.

Instrumental assessment of bradykinesia is ideal for research and monitoring patients, because in contrast to rating scales it is easy to achieve sensitive, reliable, and objective measurements without extensive training. An interesting application is instrumentally assessing the UHR group for psychosis. There is evidence that in UHR individuals, subtle forms of movement disorders, such as bradykinesia, predict conversion to psychosis [9]. If so, instrumental screening of bradykinesia may be of high clinical value as a biomarker to predict conversion to psychosis in UHR populations.

V. CONCLUSION

We confirm that instrumental assessment of bradykinesia is feasible and that content validity can be improved. The selection of tasks considered most feasible for an instrumental assessment was the flexion/extension of elbow, gait, leg agility, and pronation/supination tasks. Larger studies are warranted to investigate the validity and reliability of instruments based on these tasks.

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