Timed Up and Go test and wearable inertial sensor: a new combining tool to assess change in subject with Parkinson's disease after automated mechanical peripheral stimulation treatment

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Abstract— Parkinson's disease (PD) is characterized by degeneration of dopamine neurons in the substantia nigra pars compacta with consequent depletion of striatal dopamine leading to the core motor features of the disease. The mainstay of treatment is levodopa, the aminoacid precursor of dopamine. However, chronic oral levodopa therapy is associated with development of potentially disabling motor complications (motor fluctuations and dyskinesia) in most patients. Treatments based on peripheral stimulations of the sensory-motor system (bottom-up stimulation) have been inspiring new rehabilitation approaches in PD especially to reduce the levodopa wash-out. This study is focalized on the evaluation of a specific bottom up treatment, based on the stimulation of specific areas of both feet, also defined automated mechanical peripheral stimulation (AMPS). This study aims at evaluating a group of PD patients PRE and POST AMPS evaluated with the Timed Up and Go (TUG) test, a widely used clinical performance-based measure of fall risk, measured with an inertial sensors. Fifteen subjects with PD and 15 age-matched healthy subjects (CG) participated in this study. A dedicated medical device (GondolaTM, Ecker Technologies, Switzerland) was used to administer the AMPS. All PD patients were treated in OFF levodopa phase and were evaluated using the TUG test pre and post the intervention (acute phase). The Unified Parkinson's Disease Rating Scale (UPDRSIII) was used to clinically evaluate the outcomes of the treatment. After verifying that the parameters were normally distributed by means of Kolmogorov-Smirnov test, the ANOVA one-way for repeated measures (α<0.05) was performed to assess the differences between PRE and POST AMPS; also, the ANOVA one-way for independent measures (α<0.05) was performed to assess the differences between PD PRE and POST AMPS versus control group. The results showed that the use of the TUG test based on wearable inertial sensors allows a detailed kinematic evaluation of the single phases of the up and go movement. Besides this, PD patients post AMPS treatment performed faster TUG test, presented higher acceleration during the stand-up phase, performed the first and final rotation phases faster with higher mean velocity . These findings indicate that the AMPS improves the ability to perform the TUG test as well as the clinical status evaluated with UPDRS in patients with PD. The AMPS stimulation consequently appears as a promising treatment for patients with PD, even if more further studies are required.

Index Terms— Parkinson's Disease, Automated Mechanical Peripheral Stimulation, TUG, risk of falls, Gondola device.

I. INTRODUCTION

Several rating scales have been developed to measure the impact of Parkinson`s Disease (PD) on a patient and family. These scales are used to assess in clinical use the severity and disease progression and also in research to determine eligibility to participate in a research trial. Scales may also be used in clinical practice to identify and monitor problems or gauge clinical function and degree of progression. One of the most commonly used functional measurements in PD is the Timed Up & Go Test (TUG), which is a clinical measure of the balance and of the mobility of elderly people; the TUG includes a scoring based on an ordinal scale from 1 to 5 based on an observer's perception of the performer's risk of falling during the test.

It assesses the time that a person takes to rise from a chair, walk three meters, turn around, walk back to the chair, and sit down. The scores of ten seconds or less indicate normal mobility, 11 – 20 seconds are within normal limits for frail elderly and disabled patients, and greater than 20 seconds means the person needs assistance and requires further examination and intervention. A score of fourteen seconds or higher suggests that the person may be prone to falls [1, 2]. Usually the time to execute the TUG test is acquired using a chronometer, manually activated by the observer; sometime the start and the end of the movement is subjective and not easily detectable. Furthermore, the result of this test is summarized in a number which corresponds only to the total duration of the test, but does not measure the duration of the separate test phases (sit to stand, walking and sitting down). A quantitative approach to better measure the movement is proposed by using a wearable inertial sensor, which is a technology already validated for the evaluation of walking phases [3], in order to achieve an objective quantification of

the TUG test. This approach, thanks to technological advancements, is now possible, and the outcomes of the TUG test and of its separate phases are specifically suitable to detect outcomes of specific treatments.

Levodopa is the mainstay treatment for PD: it is the aminoacid precursor of dopamine [4, 5, 6]. Nearly all patients with PD have a beneficial response [6], however, chronic oral levodopa therapy is associated with development of potentially disabling motor complications (motor fluctuations and dyskinesia) in most patients. Motor fluctuations consist of an initial benefit after a dose of levodopa (ON-time) followed by a return of parkinsonian features (OFF-time) before onset of benefit from the subsequent dose [6].

Schaafsma et al. [7] studied the relationship between levodopa therapy and falls in individuals with PD and found that levodopa significantly reduces stride time variability, which has been found to increase the fall incidence in this population. From this study and others, it is clear that pharmacotherapy has a positive effect, however, the effects of these medications can wear-off over time and have negative side-effects such as night time or early morning deteriorations, and medication induced dyskinesias [8, 9]. Thus, it is important to investigate additional possible strategies as possible treatments of this disease.

A significant avenue to explore is the role of the sensory system in individuals with Parksinon's disease; reduced peripheral sensitivity has been implicated as a reason for postural instability and motor impairments [10]. It is necessary to determine if any intervention using the sensorial system information could be employed to counteract the effects of the dysfunctional basal ganglia in PD patients. To reduce the motor fluctuations, new treatments based on peripheral stimulation of the sensory-motor system (bottom-up stimulation) have been inspiring new rehabilitation approaches in PD [11,12].

More recently, a medical device has been developed (GondolaTM, Ecker Technologies, Switzerland) to allow the application of the MPS in a repeatable automated way (automated mechanical peripheral stimulation, AMPS). Stocchi et al [13] evaluated the change in gait and the clinical status of 18 PD patients after 6 sessions of a treatment based on automated mechanical peripheral stimulation (AMPS). The study results indicate that the AMPS treatment has a positive effect on bradykinesia and allows improving walking velocity; furthermore, AMPS has a positive effect on the step and stride length, and on walking stability, measured as the increase in stride length and the reduction of double support time during walk. These results are consistent with improvements measured via clinical scales.

This study aims at evaluating the improvement in functional ability induced by the AMPS treatment, measured with TUG test parameters based on inertial wearable sensors.

II. METHODS

Participants The Parkinson group (PD) consisted of 15 patients affected by Parkinson's disease (5 females and 10 males). The average characteristics of the PD group were the following: age = 67.22 ± 6.70 years; body mass = 76.5 ± 18.83 kg; height = 161.59 ± 11.01 m; and, H&Y = $2.76\pm0,788$. PD was diagnosed based on clinical criteria [14, 15], dopamine transporter (DaT) scans and/or magnetic resonance imaging. The patients were similar in terms of disease duration and were also free of peripheral sensory neuropathy and other disorders based on their reported histories, symptoms, physical examinations and clinical tests. Patients with liver, kidney, lung, or heart disease, diabetes or other causes of autonomic dysfunction were not included in the study.

The control group (CG) consisted of 15 healthy adults (5 females and 10 males) with the following average characteristics: age = 66.27 ± 6 years; body mass = 73.22 ± 11.45 kg; and height = 164.81 ± 10.10 m.

The study was approved by the Ethics Research Committee of the IRCCS San Raffaele Institute and written informed consent was obtained by the patients. The trial was registered online at ClinicalTrials.gov (number Identifier: NCT0181528). All procedures were explained and carried out with an adequate understanding and written informed consent of the subjects.

Data Collection

During all tests PD patients were in OFF phase. Trained professionals performed the motor section of the Unified Parkinson's Disease Rating Scale (UPDRS III) [16], pre- and post- the AMPS treatment.

Treatment

A dedicated medical device (Gondola™, Ecker Technologies, and Switzerland) delivered the AMPS. The system consists of feet supports (left and right) with electrical motors that activate two metallic stimulators with a diameter of 2 mm (Figure 1b); the motor-activated stimulators apply a mechanical pressure in two specific areas for each foot: on the head of the hallux, left and right, and on the 1st metatarsal joint, left and right.

The pressure was applied in a range of 0.3-0.9 N/mm2 at each point (Figure 1a). The pressure of stimulation, always in the indicated range, was set for each subject upon appearance of the monosynaptic reflex in the Tibialis Anterior muscle by the detection of a liminaris contraction while applying pressure in the contact areas. Once the pressure value had been set using this procedure, the value was recorded to administer the AMPS. Specifically, the treatment consisted of 4 cycles; one cycle included a stimulation of the 4 target areas for 24 sec, whereas the overall treatment included four cycles lasting a total of 96 seconds. The patients lay down during the treatment (Figure 1c).

During the current study, every patient underwent one AMPS session, and the TUG test and clinical evaluations were preformed before and immediately after the treatment (10 minutes after the stimulation).
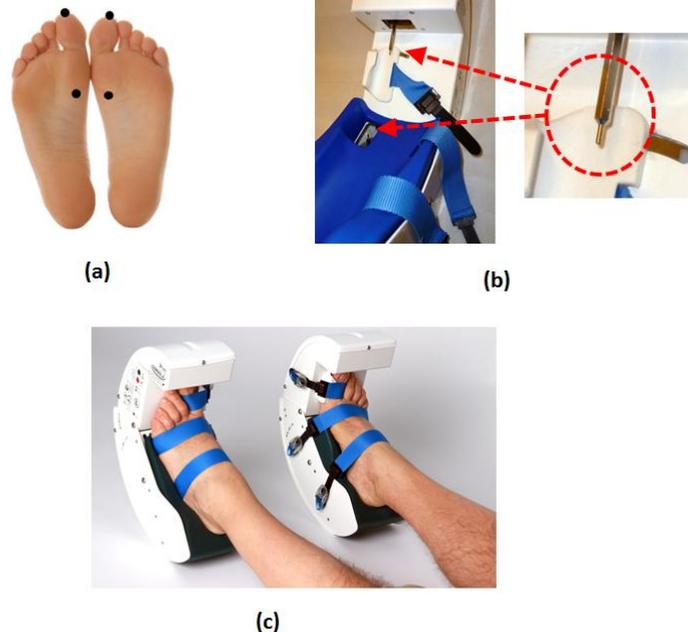
Fig 1. The device used for the AMPS treatment (a) the sites of feet stimulation; (b) the two moving steels; (c) patient positioning.

Experimental Procedures for motion analysis
The inertial sensor

The single inertial sensor is a wireless inertial sensing device (GSensor, BTS Bioengineering S.p.A., Italy) which provides accelerations along three orthogonal axes: antero-posterior, mediolateral and super inferior. Acceleration data were transmitted via Bluetooth to a PC and processed using dedicated software (BTS G-STUDIO, version: 2.6.12.0).

The portable Gsensor consists of a wireless network of inertial sensors for human movement analysis. The sensors are controlled by a data logger unit (up to 16 elements) by a ZigBee radio type communication. Each sensor is sized 62 mm $\times$ 36 mm $\times$ 16 mm, has a weight of 60 g, and is composed of a 3-axis accelerometer (max range $\pm$ 6 g), a 3-axis gyroscope (full scale $\pm$ 300∘/s) and a 3-axis magnetometer (full scale $\pm$ 6 gauss). This sensing device is calibrated with the gravitational acceleration immediately after manufacturing. For this work only one sensor was used. It was attached to the subject's waist with a semi-elastic belt, covering the L4–L5 inter-vertebral space, in a way acceleration is collected about the three orthogonal anatomical axes, i.e. the anterior–posterior, medio-lateral and vertical axes.

The reference coordinate frame had the z-axis oriented to the front, x-axis oriented vertically upward and y-axis orthogonal to the other two, towards the right. This motion analysis was performed with a sensitivity for the F4A accelerometer of 3G and a sampling frequency of 50 Hz. Acceleration data were transmitted via Bluetooth to a PC and processed using dedicated software (BTS G-STUDIO, version: 2.6.12.0) which automatically provides the parameters following described.

The subjects were asked to stand up and remain in the up-right posture for a few seconds before performing the TUG test, pre- and post- AMPS. To perform the TUG, participants started sitting in a chair with a back. From this position, they were instructed to start on the word "Go" message, to stand up, walk a distance of 3 meters in front of the chair were a cone was used as reference point, turn around, walk back to the chair and sit down as quickly as they could, safely and without running, as illustrated in Figure 2. Usually, the performance is rated in seconds and the overall measurement begins at the moment the rater sais "Go" and ends when the subject is back sitting correctly on the chair with the back resting on the back of the chair. In this study, instead, a more detailed kinematics evaluation was done as in addition to the usual measurement we studied the acceleration signals and the times needed to perform the single phases of the TUG test, as described here following:

-TUG time: the time to perform the test in seconds.

- Phase 1 (Figure 2a): the stand-up phase.
  (a) Stand-up Phase: the time to stand-up, in seconds.
  (b) Stand-up vertical acceleration: the maximum Vertical Acceleration (VA) during the stand-up phase, in m/sec^2.

-Phase 2 (Figure 2b):
  (a) 3 meters going: the time to perform the first 3 meters of the TUG test in seconds.

-Phase 3 (Figure 2c): first rotation 180°.
  (a) First rotation phase: the time to perform the first rotation, in seconds.
  (b) First rotation means velocity: the velocity to perform the first rotation, in degrees per second.

-Phase 4 (Figure 2d):
  (a) 3 meters back: the time to perform the last 3 meters of the TUG test in seconds.

-Phase 5 (Figure 2e): final rotation 180°.
  (a) Final rotation phase: the time to perform the final rotation, in seconds.
  (b) Final rotation mean velocity: the velocity to perform the final rotation, in degrees per second.

-Phase 6 (Figure 2f): sit down.
  (a) Sit down Phase: the time to stand-up, in seconds.
  (b) Sit down vertical acceleration: the Maximum Vertical acceleration during the sit down phase, in m/sec^2.
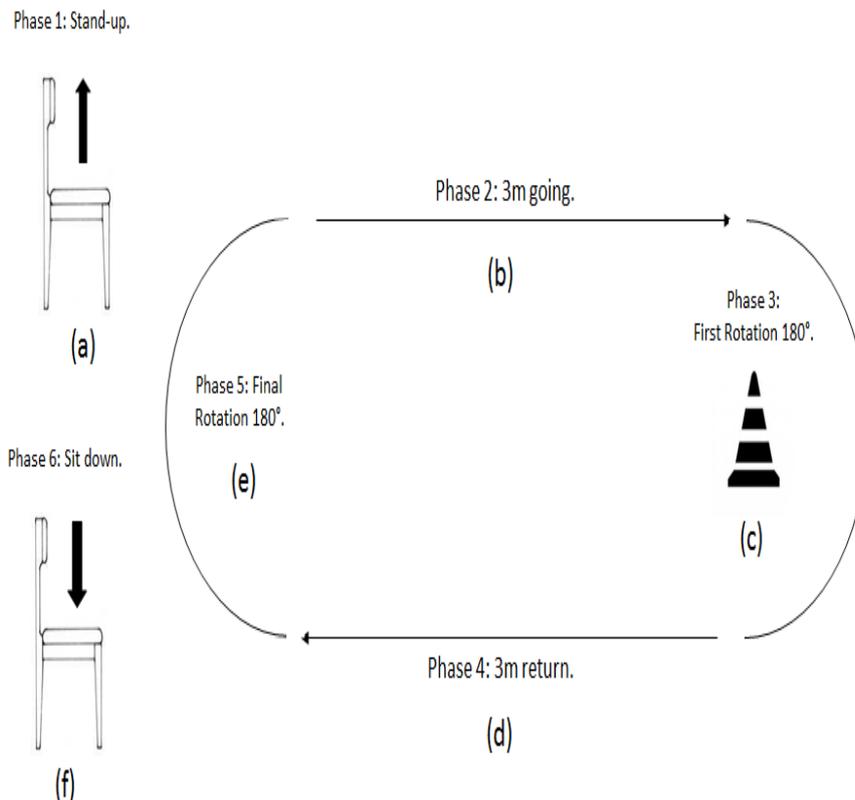
Fig 2. The TUG test phases: (a) the stand stand-up phase; (b) the 3 meters going phase; (c) the first rotation phase;; (d) the 3 meters return phase; (e) the final rotation phase; and, (f) the sit down phase.

Statistical Analyses

For the statistical analyses, the data were first tested for normality with the Kolmogorov-Smirnov test. Because all of the behavioral data exhibited normal distributions, parametric statistics were applied. The one-way ANOVAs ($\alpha<0.05$) were applied to compare the anthropometric data (i.e., age, body mass and height) between the PD group and the CG. Furthermore, this test was applied to compare the differences between the right and left lower limbs of the PD group and the CG. Because no significant differences were found between the right and left limbs, the left limb was selected to represent the CG and PD bodies for all curve comparisons.

Then, all previously defined parameters were computed for each participant and for each trial, then mean values and standard deviations of all indexes were calculated for each group. After verifying that the parameters were normally distributed by means of Kolmogorov-Smirnov test, the ANOVA one-way for repeated measures ($\alpha<0.05$) was performed to assess the differences between PRE and POST AMPS; also, the ANOVA one-way for independent measures ($\alpha<0.05$) was performed to assess the differences between PD PRE and POST AMPS and control group.

III. RESULTS

A one-way ANOVA revealed no significant differences between the subjects with Parkinson's and the control group in terms of age (p=0.883), body mass (p=0.291) or height (p=0.853).

The Figures 3 and 4 illustrates the TUG test results pre- and post- AMPS. The patients with PD post- AMPS treatment performed faster TUG test, presented higher acceleration during the stand-up phase; also, they performed the 3 meters going, 3 meters return and the first and the final rotation phases faster, with increased mean velocity compared to the TUG test performed pre-AMPS. However, the control group showed better performance during the same phases.
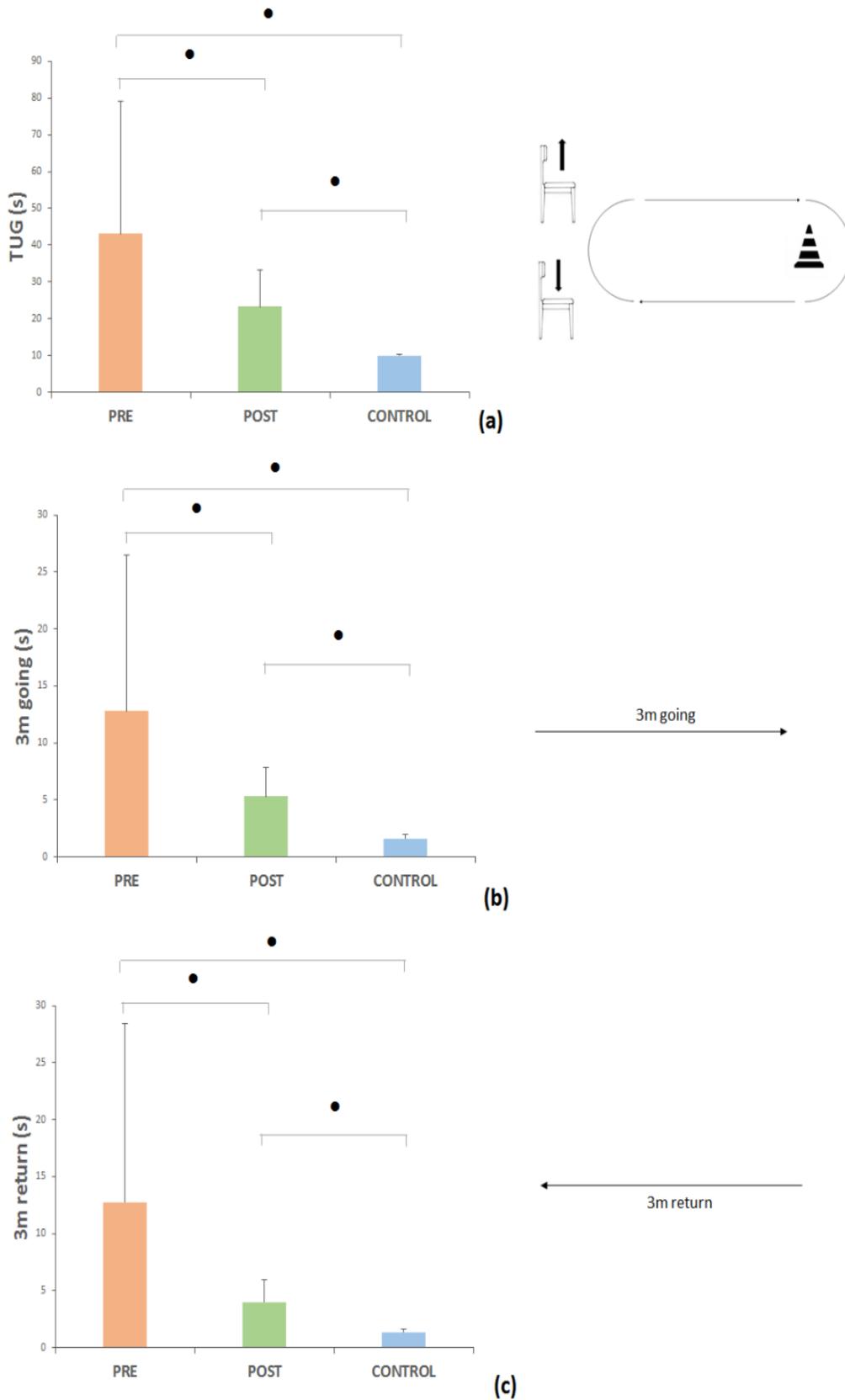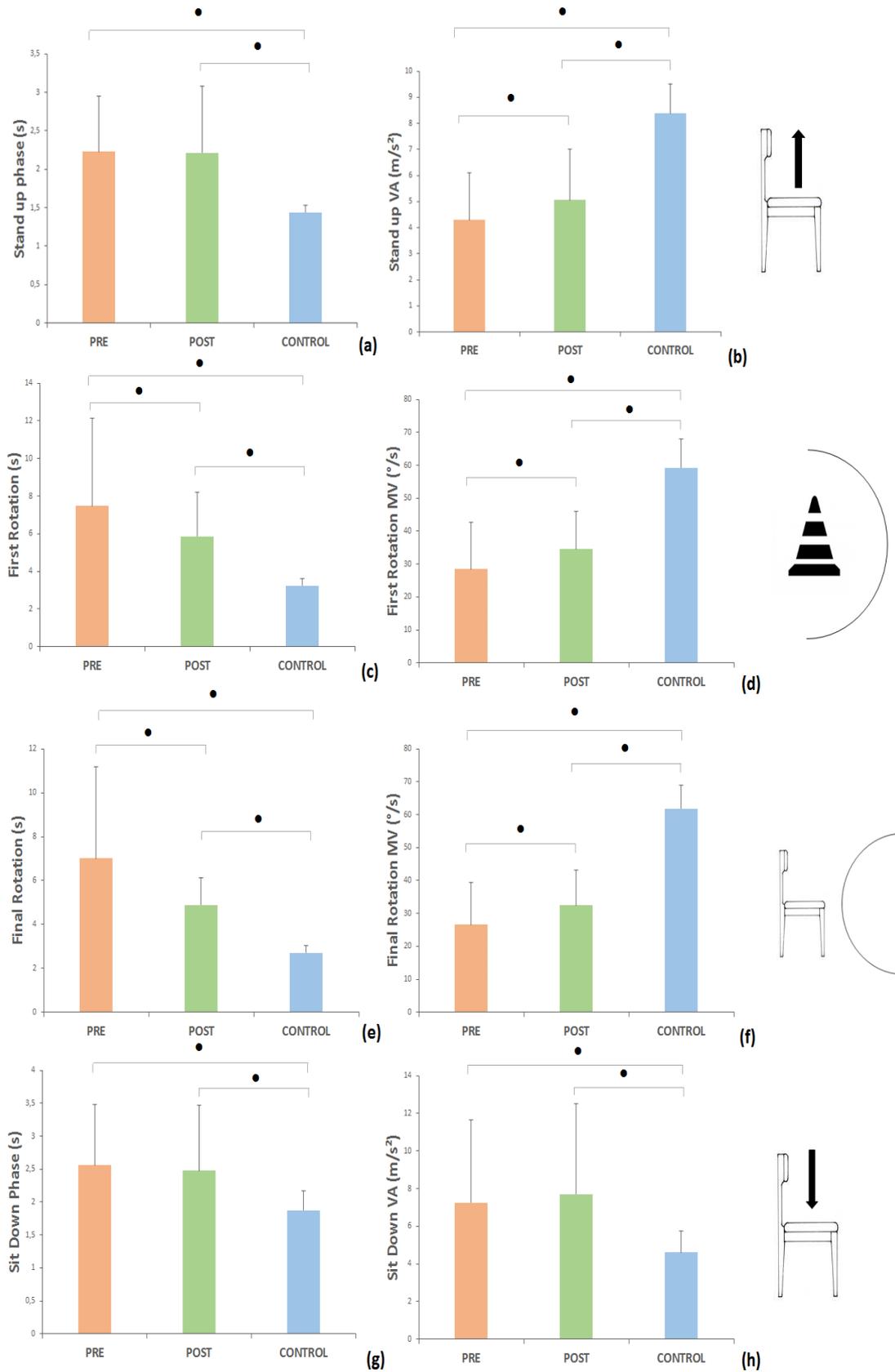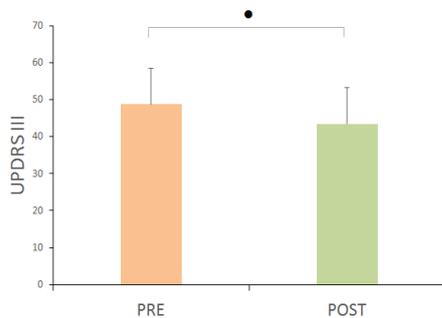
Fig 3. Mean and standard deviation of TUG test variables pre- and post- AMPS: (a) TUG time; (b) 3m going time; and, (c) 3m return time. Legend: ● = p≤ 0.05.

Fig 4. Mean and standard deviation of TUG test variables pre- and post- AMPS: (a) Stand-up phase; (b) Stand-up vertical acceleration; (c) First rotation phase; (d) First rotation mean velocity; (e) Final rotation phase; (f) First rotation mean velocity; (g) Sit down phase; (h) Sit down vertical acceleration. Legend: ● = $p \leq 0.05$.

Figure 5 shows the UPDRS III results pre- and post- AMPS. PD patients had motor improvement post AMPS treatment.

Fig 5. Mean and standard deviation of UPDRS III pre- and post-AMPS.

IV. DISCUSSION

The aim of this study was to evaluate the effect of AMPS treatment in PD subjects using TUG test measured with quantitative parameters of the single phases which compose the test.

Notwithstanding remaining in the "OFF medication" state, after AMPS the PD group performed the TUG test faster. The time needed to complete the test is strongly correlated to the level of functional mobility of the patient, and it helps in measuring the risk of falls. Elderly subjects and PD patients who are able to complete the TUG test in less than 20 seconds show to be independent in performing tasks and activities of daily living, and walk at gait speeds that are considered to be sufficient for community mobility (0.5 m/s) [17]. In contrast, older adults and PD patients requiring 20 seconds or longer to complete the test tend to require assistance and assistive devices during daily activities.

Interestingly, the AMPS treatment also induced increased acceleration during the stand-up phase, and mean velocity in the first and final rotation phases. PD subjects, especially during the OFF medication state, are usually characterized by: delayed reaction time, hypometric preparatory adjustments, bradykinesia and hypokinesia during movements [18, 19]. Also, postural instability in PD is the cause of deficits in the ability to control the center of mass within the base of support during mobility, both during walk and during stand-up / sit-down movements. Such deficits often manifest themselves in near falls or falling episodes that - at best - result inself-imposed mobility restrictions, or - at worst - fractures and mortality [20, 21]. Moreover, difficulties during turns is a common problem of people with PD [22]; a previous study noted that more than 50% of patients with PD have difficulties in turning that can lead to falls [22]. Mak and Pang [23] noted that the TUG test can be used to distinguish fallers from non-fallers; a longer TUG time (16 seconds) is independently associated with an increased risk of falls in PD patients.

So, the results of this study shows that the AMPS helps in reducing the risk of falls in patients with PD.

The motor subsection of the Unified Parkinson Disease Rating Scale (UPDRS III) is used by clinicians to assess the motor signs and symptoms of PD [16]; after the AMPS treatment PD patients presented lower UPDRS III scores, which means that motor impairment and symptoms were reduced by AMPS.

The results of this study give a new insight of the AMPS being an effective therapy for the well-being of PD patients and for improving their balance. One novelty of this study was the use of an inertial wearable sensor to collect the TUG test data. This device proved to be fast and easy to use, not impeding subject movements; furthermore, the TUG test performed using this wearable accelerometer provides automatically additional, relevant information to better evaluate the performance of the patients. The inertial sensor is a portable tool to evaluate the gait of patients and to perform other functional tests in clinical settings, allowing physicians and health professionals to have a fast diagnosis of the patient and an instantaneous, reliable, non-subjective feedback about the efficacy of treatments.

This study has some limitations. The small number of participants of the groups resulted in limited strength of the statistical findings. However, it documents the use of two novel technologies, the first one the innovative AMPS treatment applied via a dedicated portable device for the rehabilitation of PD patients; the second one the use of an inertial wearable sensors to document and quantify gait skills of PD patients during the TUG test.

V. CONCLUSION

The present findings indicate that the AMPS treatment improves the walking stability and seems to reduce the risk of falls in patients with PD. After the AMPS patients performed the TUG test faster and improved some kinematic parameters as the velocity to stand-up from a chair and to sit down. This study contributes to a growing body of evidence that shows that AMPS may be an effective treatment to reduce gait impairment and risk of falls of PD patients. Moreover, accurate characterization of the walking performance of PD subjects during clinical encounters is a well-known challenge for clinicians. The use of inertial wearable sensors to measure and document walking skills of PD patients can allow clinicians to better identify the patients at risk of falls, and to prescribe preventative or rehabilitation approaches to reduce the risk of falls and the potentially severe consequent injuries.

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