Assessment of upper limb motor function in patients with Multiple Sclerosis using the Virtual Peg Insertion Test: a pilot study

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***Abstract*—Quantifying and tracking upper limb impairment is of key importance to the understanding of disease progress, establishing patient-tailored therapy protocols and for optimal care provision. This paper presents the results of a pilot study on the assessment of upper limb motor function in patients with multiple sclerosis (MS) with the Virtual Peg Insertion Test (VPIT). The test consists in a goal-directed reaching task using a commercial haptic display combined with an instrumented handle and virtual environment, and allows for the extraction of objective kinematic and dynamic parameters. Ten MS patients and eight age-matched healthy subjects performed five repetitions of the VPIT with their dominant and non-dominant hand. Upper limb movements were found to be significantly slower, less smooth and less straight compared to healthy controls, and the time to complete the VPIT was well correlated with the conventional Nine Hole Peg Test (r=0.658, p<0.01). Tremor in the range of 3-5 Hz could be detected and quantified using a frequency analysis in patients featuring intention tremor. These preliminary results illustrate the feasibility of using the VPIT with MS patients, and underline the potential of this test to evaluate upper limb motor function and discriminate characteristic MS related impairments.**

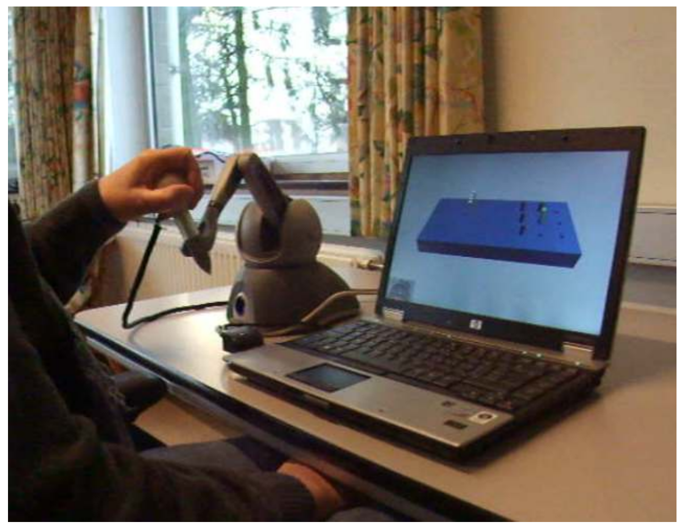

Fig. 1. MS patient performing the Virtual Peg Insertion Test. The setup is composed of a haptic device, an instrumented handle and a virtual reality environment. A computer placed in front of the user displays a virtual pegboard, a cursor representing the instrumented handle, and 9 virtual pegs.

I. Introduction

Multiple sclerosis (MS) is a demyelinating autoimmune and neurodegenerative disorder associated with sensorimotor disintegration, motor and sensory impairment and reduced coordination [1]. Arm and hand dysfunction increasingly occur at a more advanced disease stage, with impairments often seen on both sides, strongly limiting the ability of MS patients to perform activities of daily living [2], [3]. Typical upper limb impairments may include deterioration of the ability to precisely control grip force [1], muscle weakness [4], decreased movement speed [5] and sensory deficits [6]. Furthermore, about one quarter of MS patients suffer from intention tremor in the frequency range of 3-5 Hz [7], [8].

Understanding and quantifying the extent of upper limb impairment is of key importance to establish patient-tailored therapy protocols and for care provision. Arm and hand function in MS patients are usually evaluated using clinical assessments for neurologically impaired patients such as JAMAR hand-held dynamometer, the Fugl-Meyer assessment (FMA), the Nine Hole Peg Test (NHPT), the Action Research Arm Test (ARAT), and the upper extremity performance test for the elderly (TEMPA) [9]–[11]. More specific tests have been developed to investigate tremor, such as the Fahn Tremor Rating Scale (FTRS) [12], including assessments based on video recordings, handwriting analysis or spirography, which showed good correlations with clinical scales [7], [8]. Nevertheless, existing clinical tests focus on maximal capacity with a result outcome, but do not consider objective kinematic evaluation nor grasping force control, a crucial element for object manipulation [1].

In this paper, we evaluate upper limb function in MS patients using the Virtual Peg Insertion Test (VPIT), an assessment tool combining haptic feedback and virtual reality which was previously evaluated with stroke patients [13]. Ten MS patients with various levels of upper limb impairment participated in a pilot study aiming at (i) demonstrating the feasibility of using the VPIT to assess upper limb function in this patient population, and (ii) identifying kinematic and dynamic parameters representative of characteristic MS related sensorimotor impairments. We hypothesized that a goal-directed task requiring accuracy, force and speed such as the VPIT would provide meaningful information on upper limb deficits observed in MS patients.

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TABLE I. MS (M1-M10) AND HEALTHY (H1-H8) SUBJECT DEMOGRAPHICS.

Subject	age	gender	handedness	EDSS	NHPT (D) [s]	NHPT (ND) [s]	FTRS (D)	FTRS (ND)	Nb. completed VPIT repetitions (D/ND)
M1	36	M	R	7.5	22.02	32.95	1	1	5/5
M2	40	F	R	7.5	53.70	50.66	1	1	4/0
M3	35	F	R	4.5	22.75	23.15	0	0	5/5
M4	63	F	R	8	146.25	78.33	3	3	0/0
M5	52	M	R	5.5	29.52	33.18	0	0	5/5
M6	65	M	L	7.5	44.86	46.81	0	0	2/5
M7	53	F	R	2.5	30.38	48.83	0	0	5/0
M8	36	F	R	4	29.55	33.05	n.a.*	n.a.*	5/5
M9	59	F	R	4	44.53	38.36	0	0	5/5
M10	35	M	R	7.5	60.86	58.02	3	2	1/5
mean (SE) MS	47.40 (3.89)	4M/6F	1L/9R	-	48.44 (11.63)	44.34 (5.03)	-	-	-
H1	59	F	R						5/5
H2	44	M	R						5/5
H3	64	M	R						5/5
H4	48	F	R						5/5
H5	44	M	R						5/5
H6	65	F	R						5/5
H7	32	M	R						5/5
H8	33	F	R						5/5
mean (SE) healthy	48.63 (4.58)	4M/4F	0L/10R						-

*Results of FTRS for patient M8 were not available (n.a.).
EDSS: Expanded Disability Status Scale, NHPT: Nine Hole Peg Test, FTRS: Fahn Tremor Rating Scale, D: dominant hand, ND: non-dominant hand.

II. MATERIALS AND METHODS

A. Subjects

Ten MS patients (M1-M10, 47.40 ± 3.89 years old, 4 males and 6 females) were recruited among patients attending the Rehabilitation and MS Center Overpelt, Belgium. Patients with a diagnosis of MS (McDonald criteria) [14] and able to touch their chin with their hand were included. The exclusion criteria were severe orthopaedic or rheumatoid impairments interfering with upper limb function, other neurological conditions, cognitive or visual dysfunction hampering the execution of tests, and a relapse or relapse-related treatment in the last month prior to the study. The Expanded Disability Status Scale (EDSS) [15], was conducted by a neurologist to rate the neurological impairment (0 = normal to 10 = death due to MS) for descriptive purposes. Hand dominance was determined with the help of the Edinburgh Handedness inventory [16]. All MS patients gave informed consent; the study was approved by the Ethics Committee of Hasselt University and the local committee of the Rehabilitation and MS Center Overpelt.

Eight healthy subjects (H1-H8, 48.63 ± 4.58 years old, 4 males and 4 females) participated in this study to collect baseline performance data for the comparison with MS patients performance. Healthy subjects were recruited through local advertisements around ETH Zurich. All healthy subjects gave informed consent, and the experimental protocol was approved by the ETHZ Ethics Committee (EK 2010-N-40). Table I summarizes the subject demographics.

B. Apparatus

The Virtual Peg Insertion Test (VPIT) is a test developed for the assessment of upper limb sensorimotor function during which subjects are asked to perform a goal-directed reaching task consisting of the insertion of nine virtual pegs into nine virtual holes displayed on a monitor (Figure 1). The VPIT setup combines a commercial haptic device (Phantom Omni, SensAble Technologies, USA) and a custom-made instrumented spherical handle, which is mounted on the end-effector of the haptic device, and is used to grasp and release the virtual pegs. The haptic device provides feedback of the interaction force with the virtual environment (i.e. the board and the holes), while precisely measuring movement trajectories. Grasping force is simultaneously recorded using three force sensors located inside the handle. The VPIT setup is described in more details in previous work [13], [17].

C. Experimental Protocol with the VPIT

Subjects were seated in front of a computer displaying the virtual environment of the VPIT. The haptic device was placed on the side of the tested limb, and its position was adjusted to ensure 45° shoulder abduction and 90° elbow flexion when placing the hand on the handle in its resting position. Prior to the execution of the test, subjects were instructed about the task to perform, i.e., to grasp the nine virtual pegs and insert them one by one into the nine virtual holes in a minimum amount of time. In order to grasp/insert a peg, a cursor representing the position and orientation of the handle had to be aligned with a peg/hole within a defined alignment threshold. To grasp a peg, a grasping force had to be applied to the handle above a defined force threshold after properly aligning the cursor with a peg, and maintained during the transport of the peg. To successfully insert the peg, grasping force had to be released below the force threshold while being aligned with a hole. In the present study, the alignment threshold was set to 7 mm and the force threshold to 2 N. A test trial was first performed during which subjects were encouraged to explore the virtual environment and experience the force feedback provided by the haptic device. This test trial was excluded from the data analysis. Subjects were then asked to perform five repetitions of the test and were allowed to rest between each repetition. After completion of the five repetitions, the haptic device was moved to the other side and the same procedure (including the test trial) was repeated with the non-dominant hand. The entire experiment lasted about 20 minutes for healthy subjects and 45 minutes for MS patients.

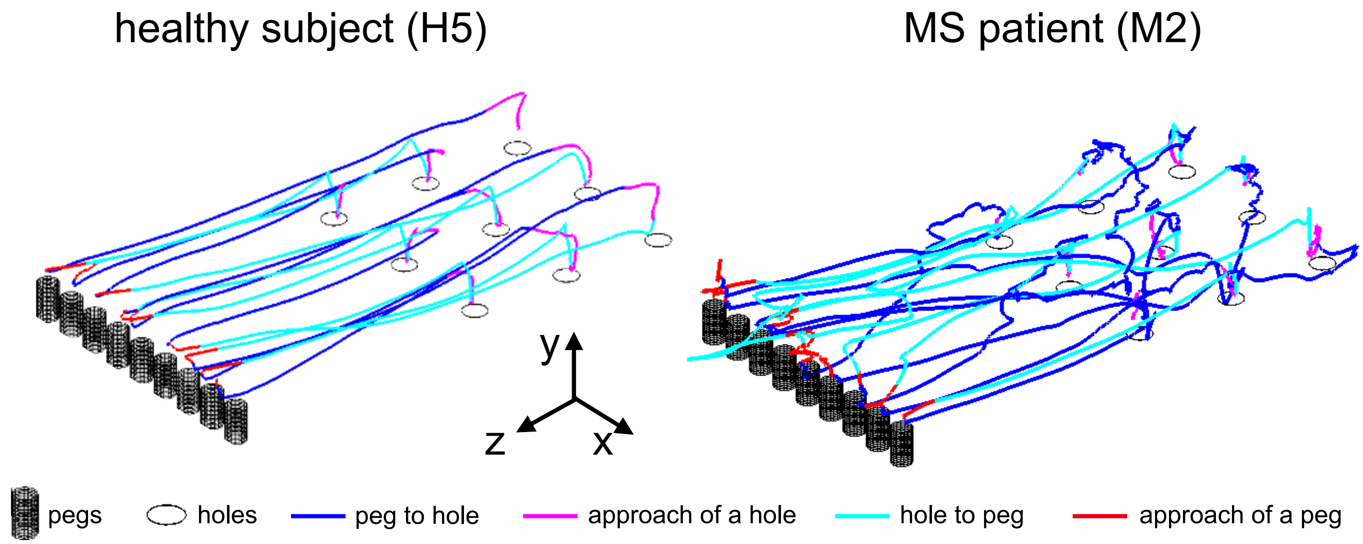

Fig. 2. Trajectories of representative repetitions of the VPIT for a healthy subject (H5, left) and a MS patient (M2, EDSS=7.5, right). The trajectories are divided into different movement components representing the gross transfer (peg to hole in blue, and hole to peg in cyan) and fine adjustments (approach of a hole in pink, and approach of a peg in red).

D. Outcome Measures

Position in x, y, z, handle orientations, and grasping force applied to the handle were recorded with a sampling frequency of 1 kHz. Data were processed using Matlab (The MathWorks, USA) to derive velocity and acceleration from position signals. Velocity was filtered using a 2^{nd} order Butterworth low-pass filter with a cut-off frequency of 10 Hz. Each repetition of the test was divided into nine trajectories corresponding to the handling of each peg. Each trajectory was then further divided into four different components, i.e., the approach of a peg, the gross movement from the peg to a hole, the approach of the hole and the gross movement from the hole to the next peg. The end of a gross movement to a peg/hole was defined as the moment the movement velocity decreases below a velocity threshold representing 10% of the maximal movement velocity before entering a 1 mm sphere around a peg/hole. The end of the fine approach movement to a peg/hole was defined as the moment a peg is successfully grasped/inserted.

In this pilot study, several kinematic and dynamic parameters were extracted in order to quantify upper limb impairment in MS patients. In addition to the total execution time T_{ex} to complete a repetition of the VPIT, the time required to achieve each movement component was calculated for each peg (T_{ph}: peg to hole, T_{ah}: approach of a hole, T_{hp}: hole to peg, T_{ap}: approach of a peg). During the gross movement, movement smoothness was evaluated by computing the number of zero-crossings of the acceleration N_{zc}, normalized over the movement duration. This parameter is used as an estimate of the number of submovements a movement is composed of [18]. The trajectory error E_{traj} is calculated as the distance between the trajectory and a straight line between the hole and the peg in the horizontal plane, normalized by the length of the displacement. The mean grasping force F_g applied during the transport of a peg to a hole was also computed. To evaluate intention tremor in MS patients, the position traces of an entire repetition were first filtered using a 2^{nd} order Butterworth low-pass filter with a cut-off frequency of 10 Hz, then a Fast Fourier Transform (FFT) was applied to extract the frequency content of the signal.

For all MS patients, commonly used clinical tests to evaluate fine manual dexterity and tremor in the upper limbs were performed on a separate day. All clinical tests were performed separately for each upper limb. The NHPT was conducted to assess fine manual dexterity [19], [20]. The time required to place and remove the nine pegs with one hand was recorded. The time limit for each repetition of the test was 300 seconds. The average of two repetitions for each upper limb was calculated. Intention tremor in the upper limbs was evaluated during the finger-nose test [21]. Tremor severity was rated using the FTRS, which is a five-point ordinal scale ranging from 0-4 (0 = none and 4 = severe amplitude). The FTRS has been shown to have good psychometric properties [12].

E. Data Analysis

Statistical analysis was done using PASW SPSS v18 (IBM Corp., USA). Repeated measures ANOVAs were performed for each parameter to test for statistically significant differences between the two groups of subjects. Pearsons correlation was used to test for correlations between extracted parameters and clinical measures. The significance level was set to 0.05.

III. Results

Five MS patients completed all trials of the VPIT with both hands, four failed to complete some trials with one of their hands, and only one patient (M4) was not able to complete any repetition of the test due to severe upper limb weakness in combination with tremor. Typical trajectories of one complete repetition of the test for one representative healthy subject (H5) and one MS patient (M2) are presented in Figure 2. Healthy subjects followed straight trajectories from peg to hole, with only few fine position adjustments around pegs and hole. MS patients were slower in performing the tasks and movement

TABLE II. MEAN ± SE OF THE PARAMETERS EXTRACTED FROM THE RAW DATA OF THE VPIT

Parameters	healthy (D) (n=8)	healthy (ND) (n=8)	MS (D) (n=5)	MS (ND) (n=5)	p-value
T_{ex} [s]	34.94 ± 4.22	38.97 ± 5.32	83.31 ± 18.92	76.63 ± 6.37	**0.002**
T_{ph} [s]	1.18 ± 0.13	1.15 ± 0.13	3.43 ± 0.90	2.35 ± 0.26	**0.001**
T_{ah} [s]	0.76 ± 0.20	0.65 ± 0.09	1.80 ± 0.38	1.64 ± 0.26	**0.001**
T_{hp} [s]	1.04 ± 0.13	1.33 ± 0.18	2.07 ± 0.58	2.98 ± 0.55	**0.013**
T_{ap} [s]	0.91 ± 0.16	1.26 ± 0.26	2.19 ± 0.74	1.55 ± 0.18	0.091
N_{zc} [1/s]	8.67 ± 0.47	8.50 ± 0.35	12.18 ± 0.65	10.36 ± 0.15	**0.001**
E_{traj} [mm/mm]	0.36 ± 0.05	0.52 ± 0.05	0.59 ± 0.12	0.74 ± 0.05	**0.028**
F_g [N]	13.04 ± 1.59	10.73 ± 1.34	10.00 ± 2.88	7.65 ± 1.22	0.214

Only the five MS patients who completed all five repetitions of the test with their dominant and non-dominant hand are considered in this analysis. Bold values represent significant differences between the two groups of subjects.

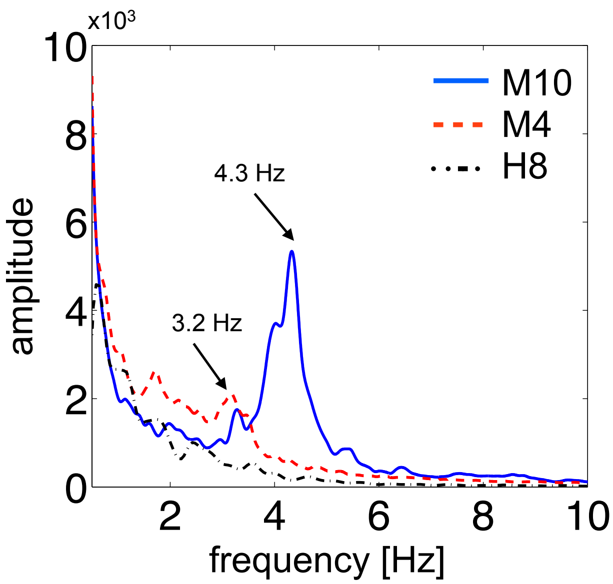

Fig. 3. Frequency spectrum (1-10 Hz) of the position traces during a repetition (9 movements) of the VPIT performed with the dominant hand for the 2 MS patients featuring tremor on the Fahn Tremor Rating Scale (MS10=3, MS4=3) and a representative healthy subject (H8).

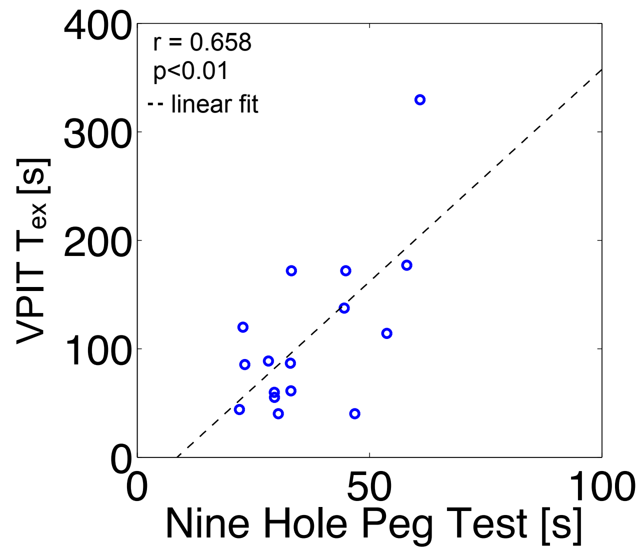

Fig. 4. Correlation between the mean total execution time T_{ex} of the VPIT and clinical scores of the NHPT for all patients that completed at least one repetition with the tested hand.

trajectories were jerkier, especially when moving further away from the body.

The means of the kinematic and dynamic parameters extracted from the raw data collected during the repetitions of the VPIT for the five MS patients that completed all repetitions of the test as well as for the eight healthy subjects are presented in Table II. MS patients required significantly more time to execute repetitions of the VPIT ($F(1,11)=17.55$, $p<0.01$), with each phase of the test being significantly longer than for healthy subjects, with the exception of the peg approach. These observations were valid for both dominant and non-dominant hands. Calculated parameters confirmed visual observations that gross movements to transport a peg to a hole were significantly less smooth and less straight in MS patients, as shown by increased N_{zc} ($F(1,11)=23.00$, $p<0.01$) and E_{traj} ($F(1,11)=6.40$, $p<0.05$).

Examples of the frequency spectra of the position traces for one repetition of the test are presented in Figure 3 for two representative MS patients showing tremor (M4 and M10, see Table I) and one healthy subject. Note that for patient M4 data from the initial test trial were used, as this patient was not able to complete any further repetition due to impairment severity. Abnormal peaks in the 3-5 Hz frequency range can be seen for both MS patients. Figure 4 further compares clinical results of the NHPT with the T_{ex} of the VPIT, as measures of overall upper limb function of MS patients. T_{ex} of all MS patients who completed at least one repetition of the test are plotted in Figure 4. A significant high correlation (r=0.658, $p<0.01$) was found between the execution time of the NHPT and T_{ex} of the VPIT.

IV. DISCUSSION

This paper presented results of a pilot study with 10 multiple sclerosis patients performing repetitions of the Virtual Peg Insertion Test, an assessment device with low output impedance to evaluate motor function and consisting of a goal-directed reaching task in a virtual environment rendered through a haptic device. Other studies have used similar commercial haptic devices linked to virtual environments for assessment or rehabilitation of object manipulation in neurological patients [4], [5], [22], [23]. Compared to other studies, a unique feature of the VPIT is its instrumented handle, allowing for the implementation of a goal-directed task requiring coordination of fine hand positioning and grasp force control, which are key elements of fine manipulation tasks. The grasping and manipulation of the spherical VPIT handle was feasible for all MS patients who participated to this study.

Despite various levels of impairment, nine out of the ten MS patients were able to perform at least one repetition of the VPIT, illustrating the feasibility of using this setup with this patient population, and the potential of this tool to monitor disease progression.

Six of the eight parameters extracted from the VPIT data were significantly different in MS patients compared to healthy controls. As reported in other studies, movements of MS patients were found to be slower and less smooth [4], [5], [23]. Interestingly, patients were especially slower in the gross movement phases of the test (i.e. from peg to hole and from hole to peg). This might be linked to arm weakness, causing difficulties in extending the arm to reach a target, and resulting in less straight trajectories during execution of the VPIT, with patients keeping their arm close to their body. Arm weakness is indeed a limiting factor for the use of the VPIT, as subjects have to lift the arm against gravity in order to manipulate the haptic device. Patients with higher disability level (EDSS>7) were typically not able to perform all repetitions of the VPIT.

Two MS patients featured intention tremor. Despite poor performance of these patients in the VPIT, a frequency analysis of position traces allowed for detection and quantification of tremor frequency peaks, which were found within the 3-5 Hz frequency range characteristic of intention tremor [7], [24]. This underlines the potential of this tool to evaluate intention tremor in the context of a visually guided task requiring precision and force coordination, thanks to the low output impedance (i.e. high transparency) of the device. The time to complete a repetition of the VPIT correlated well with the NHPT scores. Nevertheless, it should be noted that the two tests are fundamentally different, as the VPIT aims at evaluating overall upper limb function and captures kinematic and dynamic parameters characteristic of upper limb deficits, while the NHPT evaluates fine dexterity, using a different type of grip (requiring a real grasp and release of the pegs) and possible arm support.

Future work will focus on extending these pilot results with a larger population of MS patients, and examining variations in extracted parameters within subgroups of patients with specific upper limb impairments (e.g. muscle weakness, tremor, sensory deficits). Differences in impairment levels of both upper limbs will also be investigated, in an attempt to better understand and quantify the MS pathology and its progression. For use in clinical trials, reliability in different patient groups with different impairments will be investigated.

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