Upper Limb Motor Skills Evaluation in Patients with Early Multiple Sclerosis Using the IDEA System

IDEA: Input Device Evaluation Application

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***Abstract*— Upper limb functionality is an integral part of everyday interaction with the environment right from the very first minutes of human life. This paper investigates the experimental application of the IDEA (Input Device Evaluation Application) system on patients with multiple sclerosis at an early stage and without clinically overt motor deficits, in order to assess their upper limbs' motor skills. The objective of the current study is to test the sensitivity and reliability of the IDEA system regarding the evaluation of multiple kinetic parameters of upper limbs. 29 patients who were hospitalized in the Demyelinating Diseases Section of Eginition Hospital's Neurological Clinic and 25 healthy participated in the experiments. Data derived from the experiment are complemented with demographics. The acquired results analysis reveals that the IDEA system sensitivity is high enough to predict the presence of early upper limb multiple sclerosis with a 69.1% success rate.**

I. Introduction

People with motor disabilities are now a large proportion of the world's population [1]. Motor capabilities of a person include dexterity, reaching, and stretching, as well as locomotion. Their mobility problems can be caused by accidents, illness or even at birth. Paraplegia, multiple sclerosis, myopathy and cerebral palsy are usual causes of mobility problems that also affect patents' hands. One of the main functions of hands is the containment and handling of several objects and external supports. This function is needed in everyday life and therefore a flawed function of the upper limbs (e.g., associated with a neurological disease or an injury) could be a major obstacle. The number of persons with motor disabilities on upper limps is not inconsiderable. For example, studies in Europe show that 0.3% of the general population cannot use fingers, 0.1% cannot use the arm, 2.8% have reduced hand strength and 1.4% have reduced hand coordination [2]. The total estimated prevalence rate of multiple sclerosis for the past three decades is 83 per 100 000 with higher rates in northern countries and a female:male ratio around 2.0 [3].

The aim of this research is the collection and statistical analysis of data from experiments and measurements of the upper limbs' movement skills, performed on patients diagnosed with multiple sclerosis at an early stage and without clinically apparent mobility deficits. The objective of the current study is to test the sensitivity and reliability of the IDEA (Input Device Evaluation Application) system regarding the evaluation of multiple kinetic parameters of upper limbs. The importance of this research lies on the fact that we concentrated on the correlations among the kinetic parameters and among the demographics of patients as well, using a novel, computer based system for cases where traditional tests, like the 9 Hole Peg Test [4-8], could not statistically detect a disability or deficit. In addition, for optimum reliability in statistical data analysis, we also acquired a control data set conducting the experiments on healthy volunteers.

The results lead to conclusions that can help better understand how early stages of multiple sclerosis affects the upper extremities of the human body, and to review the kinetic parameters that give evidence of the derived motor impairment. New and more effective treatments of the disease or more efficient medication could rely on the assessment of repetitive experiments' results.

II. Methodology

For the preparation of this work, we followed a systematic approach and methodology, which involves the conduction of kinetic/skill experiments and the use of psychometric scales and questionnaires.

A. The IDEA system

The main experiment was conducted using the IDEA system developed at the Laboratory of Speech & Accessibility of the Department of Informatics and Telecommunications of the University of Athens [9-12]. The system offers detailed movement analysis based on specific parameters, which are well accepted in the literature and will be described later in this section. The IDEA system can also measure the effectiveness of an input device that requires movement of the upper limb, such as a mouse, a trackball, a joystick, and alternative control

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methods such as a Brain Computer Interface, or a 3D force feedback mouse.

The experiment consists of one-dimensional (1D) pointing and clicking tasks (Fig.1). The user sits on a chair in front of a desk with an ergonomically defined position, with his/her hands on the desk, in order to use a standard mouse located on a mousepad on the desk for computer input, and look at a standard monitor on the desk for computer output. Two targets are graphically displayed on the computer screen and the user is required to move the cursor from the blue target (start) to the red target (end) and click on it pressing the left mouse button. Once a successful selection is made, the previously start and end targets are interchanged, as well as their colors, so the user will make repetitive pointing and clicking tasks on the horizontal axis, first time to the left, second to the right, then again to the left, and so on. The successful selection of a target is not the only challenge, as the user must aim and click as close to the center of the target as possible.

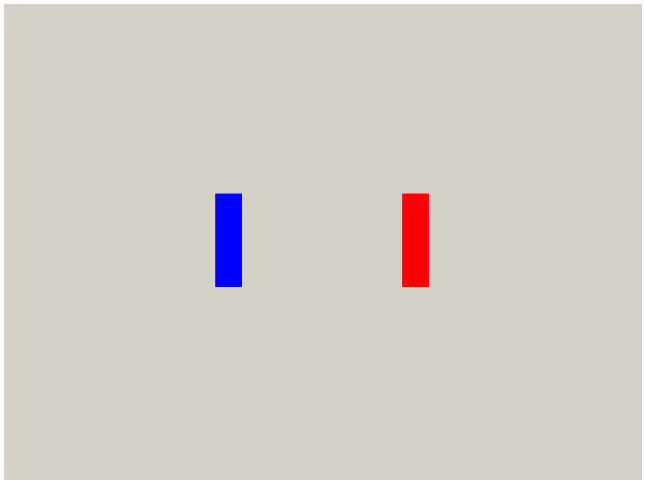

Fig. 1. The IDEA 1D test screen.

The experiment comprises of 3 sessions, each one with a different Index of Difficulty (*ID*), specified by 3 different target sizes. Each session includes 20 repetitions of moves (trials). The first move or trial starts from the left target, and requires the selection of the right target in order to be finished. The second move starts from the right target and ends with the selection of the left one. Consequently, trials are forth-and-back moves, and we have 20 trials per session, giving us 60 trials per experiment. We used 3 Indexes of Difficulty for the 3 corresponding sessions, namely ID_1=2.3, ID_2=3.2, and ID_3=4.1. These *IDs* correspond to 3 different target widths, namely 19, 37, and 76 pixels. The target height is fixed to 150 pixels, and their distance is also fixed to 300 pixels. A detailed explanation of the Index of Difficulty as well as all other metrics we used will follow.

The IDEA system relies on the ISO 9241.09 standard [13-14]. The International Standards Organization has published since 2000 the "ISO 9241.09 Ergonomic Requirements for Office Work with Visual Display Terminals – Part 9: Requirements for Non-Keyboard Input Devices", which provides guidelines and recommendations for the design of computer input devices (except the keyboard). In addition, it offers guidelines for the ergonomic design of devices such as mice, trackballs, touch screens and light pens. It also specifies methods through which someone can evaluate such a device. Finally, it gives instructions and layouts to design experiments that will assess the speed, convenience, accuracy and comfort with which the user performs actions such as pointing and clicking.

B. Accuracy and performance measures

Fitts [15-18] proposed a model for the tradeoff between accuracy and speed in human motor movements, to quantify a movement task's difficulty using information theory by the metric of "bits". According to Fitts, the **Movement Time (*MT*)** needed to hit a target must be linearly related to the **Index of Difficulty (*ID*)** of the task:

$$MT = a + (b \times ID), \tag{1}$$

where a and b are constants determined through linear regression, and

$$ID = \log2\,(D/W + 1), \tag{2}$$

where D and W are the target's Distance and Width respectively.

Fitts proposed to quantify the human rate of information processing in aimed movements using "bits per second" as units. He named the measure "Index of Performance"; today it is more commonly known as **Throughput (*TP*)**, in bits/s. Although different methods of calculating Throughput exist in literature, the preferred method is the one proposed by Fitts in 1954 [16]. The calculation involves a direct division of means: dividing *ID* (bits) by the mean *MT* (seconds), computed over a block of trials (session):

$$TP = ID_e/MT \tag{3}$$

The subscript e in ID_e reflects a small but important adjustment, which Fitts endorsed in a follow-up paper [19]: The "adjustment for accuracy" involves first computing the **Effective Target Width (W_e)** as:

$$W_e = 4{,}133 \times SD_x \tag{4}$$

where SD_x is the observed standard deviation in a participant's selection coordinates over repeated trials with a particular *D-W* condition. Computed in this manner, W_e includes the spatial variability, or accuracy, in responses. In essence, it captures what a participant actually did, rather than what he or she was asked to do. This adjustment necessitates a similar adjustment to *ID*, yielding an **Effective Index of Difficulty (ID_e)**:

$$ID_e = \log_2\,(D/\,W_e + 1) \tag{5}$$

Calculated using the adjustment for accuracy, *TP* is a human performance measure that embeds both the speed and accuracy of responses. *TP* is most useful as a dependent

variable in factorial experiments using user groups, pointing devices or pointing techniques as independent variables.

Based on the above McKenzie et al. [20] proposed an extension of the performance and accuracy measures used, and we will briefly describe each additional parameter, along with an explanation of how it is calculated. All measures used are shown in Table I.

A **Missed Click (*MC*)** is performed when the user fails to make a selection (click) on the target but chooses a point off target instead. The Missed Click is a quantitative metric and counts how many times per move or per trial the user selects a point off target.

A **Targer Re-Entry (*TRE*)** occurs when the cursor enters the target area and exits without the user being able to click like it happens once in Fig. 2. Target Re-Entry incidents are calculated during each trial and the final number (sum) of TRE incidents per trial is registered at the end of the experiment.

Fig. 2. Target Re-Entry (*TRE*) example.

For instance, if the above phenomenon is observed 2 times in a 20-trial session, *TRE* will be 0.1 per trial for this session.

A **Task Axis Crossing (*TAC*)** occurs every time the cursor crosses the line joining the centers of the start target and the end target. In Fig. 3 there is one incident.

Fig. 3. Task Axis Crossing (*TAC*) example.

The TAC metric is recorded as an average score per trial for every session.

A **Movement Direction Change (*MDC*)** occurs when the tangent of the path is parallel to the line joining the centers of the start button and the target button, which is demonstrated by the following algorithm: First, we calculate the difference ($y_i - y_{i+1}$) of all the (x, y) samples and then we multiply the results per two mutually $(y_i - y_{i+1})*(y_{i+1} - y_{i+2})$. The MDC value is equal to the number of times a sign swap appears in the products. 3 *MDCs* occur in Fig. 4.

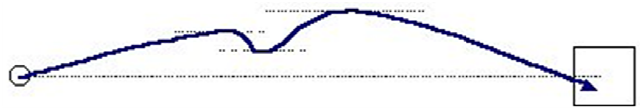

Fig. 4. Movement Direction Change (*MDC*) example.

An **Orthogonal direction change (*ODC*)** occurs along the axis orthogonal to the task axis, like it happens twice in Fig. 5. The algorithm to calculate *ODC* is similar to the one used for *MDC*, with the difference that we use the x coordinates instead of the y.

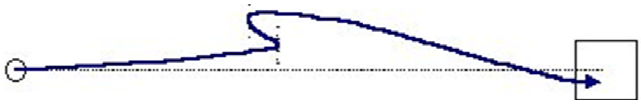

Fig. 5. Orthogonal Direction Change (*ODC*) example.

The five measures above introduced by McKenzie et al. [20] characterize the pointer path by logging discrete events, and they don't have units of measurement (*scalar*). They are presented as average values per session, and the average is calculated as the number of total incidents per session divided by the number of trials per session. Three continuous measures complete the set of parameters, and these have *pixels* as a unit of measurement. Their presentation is again an average per session, accumulating all pixels from all trials and dividing the sum by the trial count.

The **Movement Variability (*MV*)** parameter calculates the average distance value of the path followed from the axis joining the start point and final point. If y_i is the cursor distance from the straight movement line, (the straight line between the start of the movement to the center of the target) and is the average distance of points from the straight line, then the *MV* is calculated by the formula:

$$MV = \sqrt{\frac{\sum(y_i - \bar{y})^2}{n - 1}} \tag{6}$$

where n is the number of (x, y) samples. A move is considered 'perfect' when $MV = 0$.

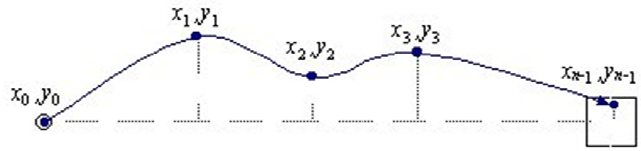

Fig. 6. The coordinates of a cursor trajectory.

The **Movement Error (*ME*)** parameter calculates the absolute value per move of the cursor orbit distance from the straight line joining the start point and the final point regardless of whether the cursor is above or below this line.

The *ME* value is calculated by the formula:

$$ME = \frac{\sum|y_i|}{n} \tag{7}$$

where n is the number of samples of each move and y_i is the distance of each cursor point from the straight line between the start point and the final point. The calculation of the distance of each point from a straight line is made similarly to the Movement Variability metric: after retrieving the portion of the

samples corresponding to the particular movement, we calculate the distance of each sample from the ideal line, and then we calculate the average of the distances' absolute values. A move is considered 'perfect' when $ME = 0$.

The **Movement Offset (*MO*)** parameter calculates for every move the total average distance of the cursor's track from the line joining the centers of the start button and the target button. The *MO* value is calculated by:

$$MO = \quad _i \tag{8}$$

where y_i is the distance of each cursor point from the line joining the centers of the start button and the target button. The calculation of each point's distance from the line is made similarly to the Movement Variability and the Movement Error metric mentioned above. Particularly, after retrieving the samples corresponding to the specific move, we calculate the distance of each sample from the ideal line, and then we calculate the distances' average value. A move is considered 'perfect' when $MO = 0$.

TABLE I. THE TEN PERFORMANCE AND ACCURACY MEASURES

Abbreviation	**Measure**
MT	Movement time
TP	Throughput
MC	Missed click
TRE	Target re-entry
TAC	Task axis crossing
MDC	Movement direction change
ODC	Orthogonal direction change
MV	Movement variability
ME	Movement error
MO	Movement offset

III. IMPLEMENTATION

We studied patients who had been hospitalized in Demyelinating Diseases Section of the Neurological Clinic of Eginition Hospital of Athens for the first episode of multiple sclerosis, and compared the patients' results to the results of a group of healthy volunteers. An IDEA test station was installed at the Nursing Section, where the experiments took place. The medical protocol we used is shown below:

A. Medical Protocol

All study participants must be of age between 18 and 55 and have a short mental status examination with MMSE $\geqslant$ 24 [21]. The experimental process was explained in detail to all subjects and their written consent for their participation was asked.

Patient selection criteria:

- There was diagnosis of at least two focuses on brain MRI.
- No clinically apparent locomotor deficit at the upper limbs.

Exclusion criteria:

- Use of benzodiazepines, antidepressants, neuroleptics, alcohol for a period of 6 months prior to the study.
- Presence of psychiatric, metabolic, endocrine or other serious organic disease.
- Presence of depression or anxiety.
- History of loss of consciousness, head injury or epilepsy.
- Taking corticosteroids on the previous month.
- Receipt of immunomodulatory or immunosuppressive treatment.
- Relapse one month before the examination.
- Disturbance of visual acuity ($\leq$4/10), or color perception, or hearing.

The medical protocol is separated into four parts. The first part consists of a clinical assessment of the patient, based on EDSS (Expanded Disability Status Scale) score [22] and the 9 Hole Peg Test (assessment of the upper limbs' functionality). The second part consists of several tests including FSS (fatigue), Zung (depressive symptoms), CDS (derealization), Eysenck (extraversion, neuroticism, psychotism), Sifneos (alexithymia), LCB (control site scale), and SCL-90 (scale of psychosomatic burden). The third part consists of several executive control and function tests: Stroop, Wisconsin test, Action Program Test, Key Search Test, Zoo Map Test, the executive control questionnaire (DEX) and CANDEX. The last part includes the IDEA System experiment.

The clinical evaluation of patients with EDSS scale took place during the incident and at the stage of remission before performing the trials. Measurements were made at the stage of remission, at least one month after the complete discontinuation of treatment with corticosteroids. Before the psychophysiological study, we administered questionnaires for recording personality structure and actual psychological condition. Subsequently, the motor performance evaluation test with the IDEA system followed.

B. Processing Results

The IDEA system produces ASCII files containing the coordinates of the cursor's position on the screen, acquired every 10 ms. Except these raw data, the resulting .txt files also contain useful flags and metadata used to compute the movement parameters. MATLAB helps to process data and compute results.

IV. STATISTICAL ANALYSIS TOOLS

The normality of the distributions of age and the measures of the experiment based on the IDEA system was tested with

the Kolmogorov-Smirnov test. In case of normality all measures will be presented with their mean values together with their standard errors and their corresponding 95% confidence intervals (CI). The matching of the control with the patient group with regards to age and sex distribution was performed with the t-test and chi-square test (Fisher exact test) correspondingly. The ten measures (Table I) of the test were subjected to multivariate analysis of covariance (MANCOVA) with group and sex as the fixed factors and age as the covariate. This was followed by univariate between group comparisons with the necessary adjustments for multiple comparisons, while the effect of age on the measures (Table II) was reported through the corresponding Pearson correlation coefficient (r). Finally, in order to test the predictive value of the test with regard to the two groups, the test measures (except MO) were entered as independent predictors in a hierarchical logistic regression model with group as the dependent variable. The independency of the variables used in the regression model was verified using Pearson correlation, and additionally using the Rank-Score Characteristic (RSC) function that measures "cognitive diversity" as proposed in [23]. For the correlation method the level of significance was set at 0.05. All analyses were performed with the statistical tool SPSS Statistics v20 [24].

V. Results

The Kolmogorov-Smirnov test revealed that the distributions of age and all the measures with the exception of Movement Direction Change did not deviate from normality. This justifies the use of parametric statistical procedures. The two groups were matched for age (controls: 30.2±1.4, patients: 30.9±1.7 years, t_{53}=0.29, p=0.771) and sex (females/males 20/6 in controls and 21/8 in patients, χ_{21}=0.15, p=0.76). As shown in Table II, the MANCOVA procedure revealed significant correlations (p<0.01) of age with Movement Time (r=0.407) and Throughput (r=-0.357). The sex effect was focalized on differences in Movement Offset (p<0.01), where women demonstrated a negative average of Movement Offset (-2.3, 95% CI -3.9 to -0.6), while men had a positive average of Movement Offset (1.8, 95% CI 0.4 to 3.2). Sex also exhibited statistically important differences in Orthogonal Direction Change, where males had higher score than females.

TABLE II. AGE-MEASURES CORRELATION

	ODC	MT	TP	MC	TRE	TAC	MDC	MV	ME	MO
r	0.087	0.407	-0.357	-0.080	0.052	0.132	-0.013	0.129	0.162	-0.203
p	0.526	0.002	0.007	0.563	0.708	0.338	0.923	0.349	0.238	0.137

The significant effect of group spread to four test measures, namely Movement Variability (p=0.017), Movement Offset (p=0.019), Movement Error (p=0.030) and Task Axis Crossing (p=0.030). As the patterns in the following Figures show, patients had significantly higher mean values than controls in Task Axis Crossing, Movement Variability and Movement Error, and significantly lower values in Movement Offset. Actually the mean Movement Offset in the patient group was by itself significantly lower than zero (one-sample t-test, p=0.013).

The results of the hierarchical logistic regression model revealed that the inclusion in the logistic regression equation of just two predictors, namely Movement Variability and Orthogonal Direction Change could correctly predict the group membership of 18/26 controls and 20/29 patients, giving a total of correct classifications 38/55=69.1%, which significantly greater than the 50% that would be achieved by chance. We must note that before conducting the regression model calculations, a Pearson correlation analysis between all measure pairs excluded MO from the calculations as it had a significant correlation with MV (p=0.015), and MC (p=0.035). The same analysis gave a p=0.08 for the two predictor variables (MV and ODC) showing no significant correlation between them. On the other hand, the RSC analysis [23] of the measures did not conclude to be more precise than the score analysis, so it did not affect the Pearson correlation results.

In Figs. 7 to 11 the results are illustrated and the significant differences between the two subject groups are shown. Specifically, the black stars on the diagrams of *TAC*, *MV*, *MO*, and *ME* denote that these parameters have statistically important differences between the two groups.

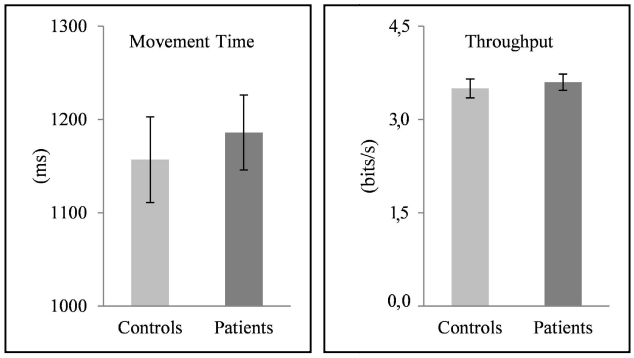

Fig. 7. Movement Time (*MT*) and Throughput (*TP*) between patients and healthy subjects.

VI. Conclusions

Observing our results we derive to the conclusion that there were significant correlations between the variables of interest. Specifically, the correlation of age with Movement Time and Throughput signifies that as people get older they require on average more time to perform each move and have a reduced throughput. Moreover, a significant difference of mean values between controls and patients in Task Axis Crossing, Movement Variability, Movement Error as well as Movement Offset is apparent. This result reveals that patients make greater effort to move the cursor from the start point to the target point in a straight line compared to healthy subjects.

Consequently, taking into consideration that the logistic regression equation predicted correctly the 69.1% of the classifications and the fact that the examined patient sample has no apparent clinical motor deficits, we can assume that the

IDEA system can be potentially used as a reliable prediction tool with notable sensitivity.

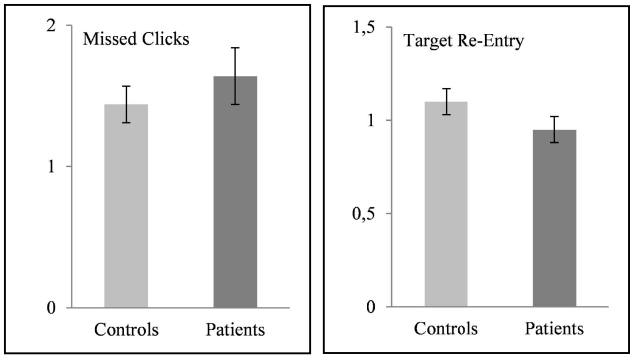

Fig. 8. Missed Clicks (*MC*) and Target Re-Entry (*TRE*) between patients and healthy subjects.

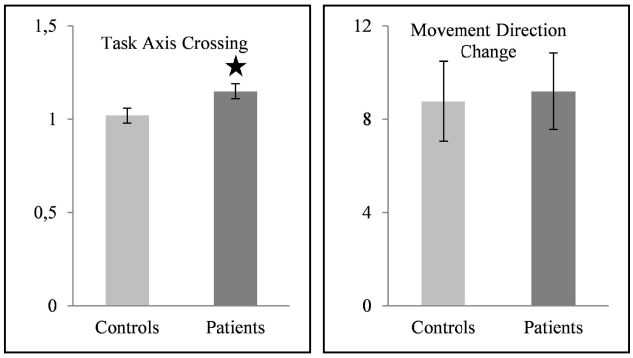

Fig. 9. Task Axis Crossing (*TAC*) and Movement Direction Change (*MDC*) between patients and healthy subjects.

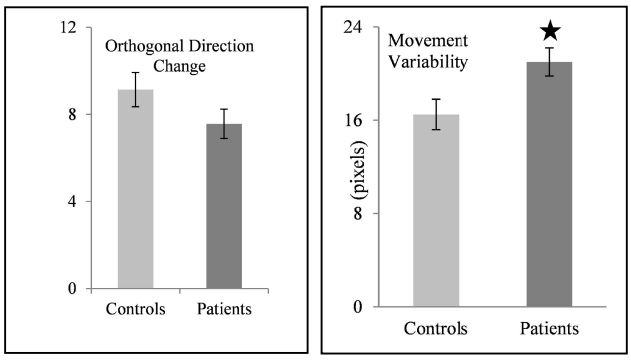

Fig. 10. Orthogonal Direction Change (*ODC*) and Movement Variability (*MV*) between patients and healthy subjects.

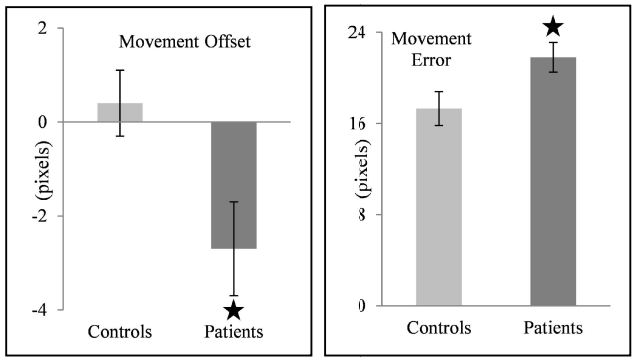

Fig. 11. Movement Offset (*MO*) and Movement Error (*ME*) comparison between patients and healthy subjects.

Based on the additional capabilities of the IDEA system (e.g., various input devices, multidimensional tests, and flexible user interface) we expect that it could become an effective tool for the rehabilitation in multiple sclerosis. In accordance with several other relative studies on rehabilitation robotics of the upper limbs [25-29] specific muscles of the upper limbs could be tested and trained by implementing certain repetitive visual tasks on the screen besides the 1D trials discussed above, (e.g., 2D, 3D, labyrinths, paths) and additionally provide haptic feedback information, depending on the programmable input device [10].

Based on the above, the research could be performed to a greater extent if, as our next step, we incorporate the results of the psychometric measurements and the corresponding questionnaires' analysis. This way, it would be possible to look at the correlation between personality characteristics (e.g., extraversion, neuroticism, etc.), elements of psychopathology, and cognitive functions (memory, executive control, attention) [30-32] in conjunction with the kinetic performance of both groups (healthy subjects and patients with multiple sclerosis). Our next study will conclude whether the correlation patterns differ between the two groups, when we enrich our data sets with all this new input that we have already acquired from our complete protocol. The findings of such a study can be used for the assessment of the underlying pathology in early stages of the disease in order to allow effective treatment and rehabilitation of patients in the future.

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REFERENCES

[1] G. Kouroupetroglou (Ed.), Disability Informatics and Web Accessibility for Motor Limitations, Information Science Reference Press - IGI Global, Pennsylvania, Hershey PA, USA, 2013.

[2] G. Kouroupetroglou (Ed.), Assistive Technologies and Computer Access for Motor Disabilities, Information Science Reference Press - IGI Global, Pennsylvania, Hershey PA, USA, 2013.

[3] M. Pugliattia, G. Rosatia, H. Cartonc, T. Riiseb, J. Drulovicd, L. Ve´cseie and I. Milanovf, "The epidemiology of multiple sclerosis in Europe", European Journal of Neurology, vol. 2006, pp. 700–722, 2006.

[4] M. Kellor, J. Frost, N. Silberberg, I. Iversen and R. Cummings, "Hand strength and dexterity", Am. J. Occup. Ther., vol. 25, no. 2, pp. 77-83, 1971.

[5] D. Goodkin, D. Hertsgaard, J. Seminary, “Upper extremity function in multiple sclerosis: improving assessment sensitivity with box-and-block and nine-hole peg tests”, Arch Phys Med Rehabil., vol. 69, no. 10, pp. 850-854, 1988.

[6] G. Earhart, J. Cavanaugh, T. Ellis, M. Ford, K. Foreman and L. Dibble, “The 9-Hole Peg Test of Upper Extremity Function”, J. Neurol. Phys. Ther., vol. 35, no. 4, pp. 157-163, 2011.

[7] V. Mathiowetz, K. Weber, N. Kashman and G. Volland, “Adult Norms for the Nine Hole Peg Test of Finger Dexterity”, OTJR: Occupation, Participation and Health, vol. 5, no. 1, pp. 24-38, 1985.

[8] K. Oxford Grice, K. Vogel, V. Le, A. Mitchell, S. Muniz and M. Vollmer, “Adult Norms for a Commercially Available Nine Hole Peg Test for Finger Dexterity”', Am. J. Occup. Ther., vol. 57, no. 5, pp. 570-573, 2003.

[9] A. Pino, E. Kalogeros, I. Salemis, and G. Kouroupetroglou, “Brain Computer Interface Cursor Measures for Motion-impaired and Able-bodied Users”, Proceedings of the 10th International Conference on Human-Computer Interaction, Crete, Hellas, 2003, vol. 4, pp. 1462-1466, Mahwah, NJ, Lawrence Erlbaum Associates, Inc.

[10] G. Kouroupetroglou, A. Pino, A. Balmpakakis, V. Golematis, D. Chalastanis, N. Ioannou and I. Koutsoumpas, “Performance Evaluation of Gesture-based 2D and 3D Pointing Tasks”, Proceedings of GW2011: The 9th International Gesture Workshop - Gesture in Embodied Communication and Human-Computer Interaction, May 25-27, 2011, Athens, Greece, pp. 10-15.

[11] G. Kouroupetroglou, A. Pino, A. Balmpakakis, V. Golematis, D. Chalastanis, N. Ioannou and I. Koutsoumpas, “Using Wiimote for 2D and 3D Pointing Tasks: Gesture Performance Evaluation”, Lecture Notes in Artificial Intelligence, vol. 7206, pp. 13-23, 2012.

[12] A. Pino, E. Tzemis, N. Ioannou and G. Kouroupetroglou, “Using Kinect for 2D and 3D Pointing Tasks: Performance Evaluation”', Lecture Notes in Computer Science, vol. 8007, pp. 358-367, 2013.

[13] ISO 9241-9:2000 Ergonomic requirements for office work with visual display terminals (VDTs) -- Part 9: Requirements for non-keyboard input devices.

[14] X. Zhang and I. MacKenzie, “Evaluating Eye Tracking with ISO 9241 - Part 9”, Human-Computer Interaction. HCI Intelligent Multimodal Interaction Environments, pp. 779-788, 2007.

[15] P. Fitts, Human engineering for an effective air-navigation and traffic-control system. Washington: National Research Council, Division of Anthropology and Psychology, Committee on Aviation Psychology, 1951.

[16] P. Fitts, “The information capacity of the human motor system in controlling the amplitude of movement”, J. Exp. Psychol., vol. 47, no. 6, pp. 381-391, 1954.

[17] I. MacKenzie, “Fitts' Law as a Research and Design Tool in Human-Computer Interaction”, Human–Computer Interaction, vol. 7, no. 1, pp. 91-139, 1992.

[18] R. Soukoreff and I. MacKenzie, “Towards a standard for pointing device evaluation, perspectives on 27 years of Fitts’ law research in HCI”, Int. J. Human-Computer Studies, vol. 61, no. 6, pp. 751-789, 2004.

[19] P. Fitts and J. Peterson, “Information capacity of discrete motor responses”, J. Exp. Psychol., vol. 67, no. 2, pp. 103-112, 1964.

[20] I. MacKenzie, T. Kauppinen and M. Silfverberg, “Accuracy Measures for Evaluating Computer Pointing Devices”, in Proceedings of the ACM CHI 2001 Human Factors in Computing Systems Conference, Seattle, Washington, 2001, pp. 9-16.

[21] M. Folstein, S. Folstein and P. McHugh, “Mini-mental state”, J. Psych. Res., vol. 12, no. 3, pp. 189-198, 1975.

[22] J. Kurtzke, “Rating neurologic impairment in multiple sclerosis: An expanded disability status scale (EDSS)”, Neurology, vol. 33, no. 11, p. 1444, 1983.

[23] D. F. Hsu, B. S. Kristal, and C. Schweikert, “Rank-score characteristic (RSC) function and cognitive diversity”, Lecture Notes in Computer Science, vol. 6334, pp. 42-54, 2010.

[24] IBM. (2011). IBM SPSS Statistics 20 Algorithms [Online]. Available FTP: public.dhe.ibm.com Directory: software/analytics/spss/documentation/statistics/20.0/en/client/Manuals File: IBM_SPSS_Statistics_ Algorithms.pdf

[25] D. Gijbels, I. Lamers, L. Kerkhofs, G. Alders, E. Knippenberg and P. Feys, “The Armeo Spring as training tool to improve upper limb functionality in multiple sclerosis: a pilot study”, J. Neuroeng. Rehabil., vol. 8, no. 1, p. 5, 2011.

[26] I. Carpinella, D. Cattaneo, S. Abuarqub and M. Ferrarin, “Robot-based rehabilitation of the upper limbs in multiple sclerosis: Feasibility and preliminary results”, J. Rehabil. Med., vol. 41, no. 12, pp. 966-970, 2009.

[27] R. Riener, T. Nef and G. Colombo, “Robot-aided neurorehabilitation of the upper extremities”, Med. Biol. Eng. Comput., vol. 43, no. 1, pp. 2-10, 2005.

[28] A. Bardorfer, M. Munih, A. Zupan and A. Primozic, “Upper limb motion analysis using haptic interface”, IEEE/ASME Trans. Mechatron., vol. 6, no. 3, pp. 253-260, 2001.

[29] J. Beebe and C. Lang, “Relationships and Responsiveness of Six Upper Extremity Function Tests During the First Six Months of Recovery After Stroke”', J. Neurol. Phys. Ther., vol. 33, no. 2, pp. 96-103, 2009.

[30] A. Peresedova, R Konovalov, M. Krotenkova, I. Zavalishin, and O. Trifonova, “Cortical reorganization in multiple sclerosis with movement disorders detected by functional MRI (own observations and literature data)”, Zh. Nevrol. Psikhiatr. Im. S. S. Korsakova., vol. 109, no. 2, pp. 38-43, 2009.

[31] A. Ternes, J. Fielding, P. Addamo, O. White and N. Georgiou-Karistianis, “Concurrent Motor and Cognitive Function in Multiple Sclerosis”', Cogn. Behav. Neurol., vol. 27, no. 2, pp. 68-76, 2014.

[32] G. Koutsis, P. Kokotis, A. Papagianni, E. Andreadou, M.E. Evangelopoulos, P. Davaki, N. Karandreas , “The spectrum of facial nerve dysfunction in multiple sclerosis: a clinical and EMG study”, Mult. Scler. J., vol. 16, no. 10, p. 361, 2010.