

Can hand dexterity predict the disability status of patients with multiple sclerosis?

Masoumeh Ghandi Dezfuli¹, Malahat Akbarfahimi*², Seyed Massood Nabavi³
Afsoon Hassani Mehraban⁴, Ebrahim Jafarzadehpur⁵

Received: 16 September 2014

Accepted: 16 March 2015

Published: 30 August 2015

Abstract

Background: Multiple Sclerosis (MS) is the most common disabling neurological disease. Hand dysfunction is one of the main complaints of patients with MS. The present study aimed to compare hand dexterity of MS patients with low Expanded Disability Status Scale (EDSS) scores and healthy adults. It also sought to identify the predictors of disability status of patients with MS based on their manual dexterity and demographic characteristics.

Methods: In this cross-sectional study, 60 (16 male/44 female) patients with MS and 60 (19 male/41 female) healthy people, who matched in terms of age and sex, were recruited. Their hand dexterity was evaluated by the Purdue Pegboard Test. The disability status of the MS group was determined by the Expanded Disability Status Scale. The data were analyzed using SPSS15.

Results: The hand dexterity in MS group even with low EDSS score (1.5 ± 1.07) was weaker than control group. Moreover, the dexterity of dominant hand and alternating two hands coordination subtests of the PPT was a good discriminator between two groups ($p < 0.001$). The results of linear regression analysis suggested dominant hand dexterity and disease duration as predictors of disability status that predict 60.5 per cent of the variation in EDSS scores in patients with MS ($p < 0.001$).

Conclusion: Reduced dominant hand dexterity in patients with MS is a disabling factor. Further research is recommended to determine if early hand rehabilitation can reduce the severity of disability in Patients with MS.

Keywords: Multiple sclerosis, Hand, Disability.

Cite this article as: Ghandi Dezfuli M, Akbarfahimi M, Nabavi SM, Hassani Mehraban A, Jafarzadehpur E. Can hand dexterity predict the disability status of patients with multiple sclerosis? *Med J Islam Repub Iran* 2015 (30 August). Vol. 29:255.

Introduction

Multiple Sclerosis (MS) is a chronic disabling neurological disease with a progressive inflammatory course which damages the myelin sheath in the central nervous system. Myelin damage in discrete regions leads to heterogeneity of various features of MS (1). Onset usually occurs in the young and middle-aged people, indeed in the most productive years of career development and

family life (2) and adversely affects employment, social relationships and quality of life (3). Although in some studies factors such as decreased brain volume(4), slower nerve conduction, delayed evoked visual potential (5), cognitive impairments (4,6), illness duration (7), lack of physical fitness and ambulatory status (6), poor dynamic stability (8), and low contrast sensitivity (9) identified as an influential causes of disa-

¹. MSc of occupational therapy, Department of Occupational Therapy, School of Rehabilitation Sciences, Iran University of Medical Sciences, Tehran, Iran. Maghandi1388@gmail.com

². (**Corresponding author**) Assistant professor, Department of Occupational Therapy, School of Rehabilitation Sciences, Iran University of Medical Sciences, Tehran, Iran. Akbarfahimi.m@iums.ac.ir

³. Associate Professor, Department of Neurology, School of Medicine, Shahed Medical University, Tehran, Iran. seyedmassoodnabavi@gmail.com

⁴. Associate Professor, Department of Occupational Therapy, School of Rehabilitation Sciences, Iran University of Medical Sciences, Tehran, Iran. Mehraban.a@iums.ac.ir

⁵. Professor, Department of Optometry, Iran University of Medical Sciences, Tehran, Iran. Ejafarzadehpure@iums.ac.ir

bility and participation restriction in MS, there are many disability detectors among Patients with Multiple Sclerosis (PwMS) which are not still determined (10). Elucidating these possible underlying causes for activities limitation in MS would help suggesting effective treatment interventions (11) and remediation strategies for improving their quality of life and elimination disability.

One of the most common early neurological symptoms in PwMS is motor disorders (12). Upper limb dysfunction, experienced by nearly 75 per cent of PwMS, increases patients' dependence in their daily activities (13, 14). This neurological problem can be caused by sensory and/or motor deficits, muscle weakness (15,16), tremor, incoordination (1), spasticity, ataxia, and restricted range of motion (16). While loss of dexterity is common in 75 per cent of PwMS and can reduce or eliminate their fine motor skills such as picking things up, maintaining a hold on items, writing or buttoning clothing, controlling eating utensils (14), few studies have evaluated hand dexterity in MS (17) particularly with low Expanded Disability Status Scale (EDSS) score.

Dexterity is defined as fine, voluntary movements used to manipulate small objects during a specific task. It consists of two interconnected skills called manual dexterity (the ability of the hand to handle objects) and fine motor dexterity (18). In clinical and research setting, hand/upper extremity function and dexterity is generally measured through standardized ordinal scales or timed tests including Action Research Arm Test (19), TEMPA (20), Box & Block Test (19), Nine Hole Peg Test (9-HPT) (21), the Purdue Pegboard (PPT) and Jebsen-Taylor Test (20). The PPT assesses two types of dexterity using four subtests. It was initially designed to screen manual dexterity of industrial workers, but found application in rehabilitation fields as well. The PPT has two major advantages over other hand dexterity tests such as 9-HPT. Firstly, it measures upper extremity fine motor and fine fingertip dexterity along

with gross motor coordination. Moreover, while the 9-HPT only assesses the dexterity of one hand (22), the PPT can simultaneously examine the coordination between hands (23,24). The weakness of hand(s) and lack of dexterous manipulation skills in PwMS necessitate the investigation of function of the hands separately, alternatively, and simultaneously.

Despite the importance of the upper extremity function in independence, limited research has specifically evaluated the effects of hand dexterity on disability status in PwMS in low EDSS scores. Hence, the present study aimed to compare hand dexterity in PwMS and a healthy control group. It also sought to identify the predictors of severity of disability measured by the Expanded Disability Status Scale (EDSS).

Methods

Participants: This cross-sectional study recruited participants using convenience sampling and was conducted on 65 patients with definite MS and 65 healthy age- and sex-matched adults who presented to the neurology and MS clinic in Tehran (Iran) during April-June 2013 (Table 1). In order to confirm the diagnosis of MS, an expert neurologist assessed the patients using the 2010 revision of McDonald criteria (25). Individuals with any subtypes of MS with illness duration ≥ 2 years (based on the neurologist's diagnosis), time from the last relapse ≥ 3 months (26), and EDSS score < 6 (27) were included. The inclusion criteria for both groups were age between 18 and 40 years old, Mini-Mental Status Examination (MMSE) score > 21 (28), absence of acute or chronic mental illnesses and neurological disorders (except MS for the MS group), education level ≥ 5 years, normal or corrected-to-normal visual acuity, and ability to perform the PPT (ability to pick up a pin and putting it in the hole). Subjects with a history of hand and upper limb disorders, peripheral nerve disorders, and loss of consciousness due to a head injury were excluded.

Instruments

Purdue Pegboard Test (Tiffin, 1948):

Hand dexterity was measured using the PPT (model 32020, Lafayette Inc., USA). The instrument comprised 25 small metal pins, 20 collars, 40 washers, and a board with two sets of 25 holes and four concave cups in one horizontal row (21).

The test consisted of four subtests. In the first three subtests, the subjects had to remove the pins from the cup and place them vertically in the holes of the relevant column as rapidly as possible; they were supposed to complete the task by their dominant hand, non-dominant hand, and both hands at the same time, respectively. The number of pins placed in 30 seconds was scored. The fourth subtest, called the assembly subtest, involved picking up and placing the pins, washers, and collars using alternating hands in 60 seconds. The score represented the number of pieces assembled (21). The test-retest reliability of the PPT among PwMS has been reported as 0.85-0.90 for each subtest (22).

The Expanded Disability Status Scale (Kurtzke, 1983)

The EDSS is widely used to measure physical disability in PwMS. It was also applied in combination with a neurological examination in the present study (27).

Procedure: On admission, each of the 65 PwMS was examined with EDSS by an experienced neurologist. All participants, who were initially briefed about the overall procedure of the PPT, performed the test under the supervision of a trained occupational therapist. During the test (conducted at 3-8 pm), the subjects sat comfortably on a chair at a standard 75-cm tall test table in a quiet room. The study protocol was approved by the Ethics Committee of Iran University of Medical Sciences (Code: 92/d/320/213). Informed consent forms were also signed by all participants prior to enrollment.

Statistical analyses

Normal distribution of EDSS and hand dexterity scores was assessed with Kolmo-

gorov-Smirnov tests. Independent t-test and Pearson correlation coefficients were used to compare the mean scores of hand function skills between the two groups and to identify the relationships between the variables, respectively. Stepwise Discriminant Function Analysis (DFA) was applied to determine the best discriminator between the two groups. Regression analysis was performed to predict how the components of hand dexterity (score of the four subtests), age, and disease duration (independent variables) affected the EDSS score (dependent variable). Stepwise multivariate regression analyses were conducted to predict EDSS using only the variables that were significantly associated with the independent variables based on univariate analysis results (illness duration and Purdue dominant hand). Variables without significant relationships were removed from the model. All analyses were performed in SPSS for Windows 15.0 (SPSS Inc., Chicago, IL, USA) at a significance level of $p < 0.05$.

Results

Sample characteristics: Ten participants were excluded from the study. Five patients due to non-cooperation, and five control participants in order to better maintain the group matching by age ($p=0.120$) and sex ($p=0.344$). Finally, 60 PwMS (16 male/ 44 female) and 60 healthy adults (19 male/ 41 female) were included in the study (Table 1).

Most of the patients ($n=55$, 91.7%) had the relapsing-remitting type of the disease, while three patients (5%), and two patients (3.3 %) had the primary-progressive, and secondary-progressive types, respectively. The mean \pm SD of EDSS score of 40 PwMS was 0.93 ± 0.20 which was less than 1.5 and of 20 PwMS was 2.72 ± 1.12 (range: 2-5.5).

Most of the patients ($n=55$, 91.7%) had the relapsing-remitting type of the disease, while three patients (5%), and two patients (3.3 %) had the primary-progressive, and

Table 1. Characteristics of the Two Studied Groups (Patients with multiple sclerosis and Control Subjects)

Characteristics	MS Group(n=60)			Control Group(n=60)			Intergroup Difference	
	Range	Mean	SD	Range	Mean	SD	t	p
Age (years)	18-40	29.08	6.52	19-41	27.21	6.53	1.566	0.120
Education (classes, years)	6-24	13.53	3.83	6-16	13.01	2.28	0.886	0.337
Illness duration (years)*	0.5-19	4.20	3.68					
Total EDSS scores	0.5-5.5	1.53	1.07					
PPT* Dominant hand	6-18	13.45	2.34	15-21	18.21	1.56	13.09	< 0.001
PPT Non-dominant hand	4-18	12.35	2.67	13-20	16.66	1.50	10.89	< 0.001
PPT Both hands	4-16	10.41	2.38	8-17	13.58	1.82	8.16	< 0.001
PPT Assembly	10-40	24.50	5.91	17-58	39.18	6.57	12.86	< 0.001

* when MS was diagnosis by neurologist

**= Purde Pegboard Test (subtest score)

secondary-progressive types, respectively. The mean±SD of EDSS score of 40 PwMS was 0.93 ± 0.20 which was less than 1.5 and of 20 PwMS was 2.72 ± 1.12 (range: 2-5.5).

Based on the Independence T-test analysis (Table 1) the hand dexterity of MS group in all subtests were weaker than control group ($p < 0.001$).

Discriminant Function Analysis (DFA) with stepwise method was used to determine the most parsimonious way to distinguish between two groups using subtests of PPT. Significant mean differences were observed for all subtests of PPT. However only two PPT subtests; dominant hand and assembly subtests scores were reported by DFA for this parsimonious model. Therefore, the

predictive model is:

"DF = 0.295 dominant hand + 0.089 assembly -7.5"; with 65.12 per cent of explained variation.

The sensitivity and specificity were calculated, 88.3 per cent and 91.7 per cent, respectively. The predictive accuracy of the model for the analysis sample was 90.0 per cent and the cross validation classification showed that overall 90.0 per cent was correctly classified. Fig. 1 was shown the separation of two groups by using these two predictors.

Table 2 was shown the interrelationships between variables of the current study. The EDSS scores had a significant relationship with hand dexterity, age and illness duration. However, education had not correlated with other variables of this study.

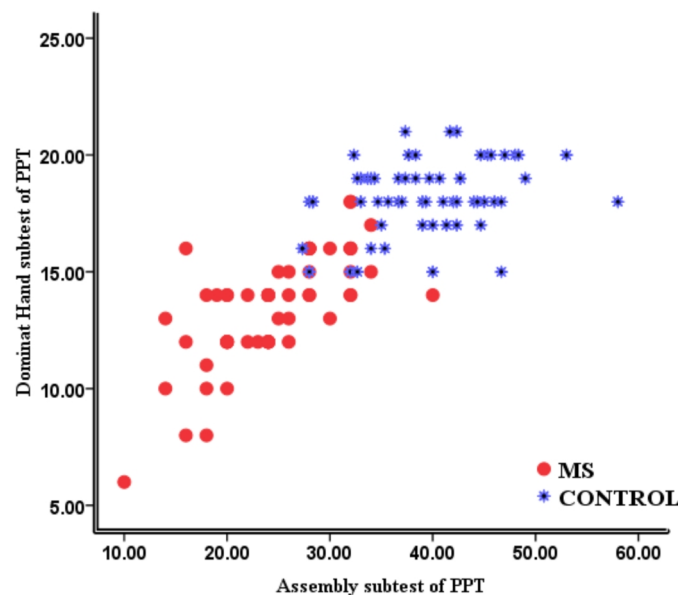


Fig. 1. Discriminant Function Analysis of two groups by dominant hand and assembly subtests scores of Purde Pegboard Test.

Table 2. Associations of demographic factors, disease severity and hand dexterity

Variables	1	2	3	4	5	6	7
Independent							
1. Dominant Hand	1						
2. Non-Dominant Hand	0.707**	1					
3. Both hands	0.640**	0.654**	1				
4. Assembly	0.699**	0.696**	0.574**	1			
5. Age (years)	-0.307*	-0.067	-0.188	0.294	1		
6. Education (classes, years)	-0.133	-0.043	0.086	-0.057	0.166	1	
7. Illness duration (years)	-0.457**	-0.125	-0.217	-0.325*	0.391**	0.184	1
Dependent							
8. EDSS scores	-0.742**	-0.475**	0.460**	-0.548**	0.412**	0.137	0.605**

*: significantly correlated at $p < 0.05$ **: significantly correlated at $p < 0.001$

Stepwise Multiple Regression analyses were performed to determine which set of the explanatory variables could serve parsimoniously as predictors of patients' disability status (EDSS) score. Two variables emerged as significant predictors: illness duration and dominant hand. Therefore, the final model for EDSS with two predictors is:

$$\text{EDSS}_{\text{prediction}} = 4.59 - 0.259* \text{ dominant hand PPT subtest} + 0.1* \text{ illness duration};$$

(with $R^2 = 0.605$).

Discussion

The first purpose of the present study was to compare hand dexterity of PwMS and healthy controls in addition to identifying the predictors of disability in PwMS. According to our findings, the PwMS (even those with low EDSS scores) had significantly weaker hand dexterity than healthy adults. Moreover, the dominant hand and assembly dexterity subsets of the PPT could discriminate the PwMS from the control group. This finding could be due to two reasons: temporal incoordination and eye-hand incoordination in MS. There are a numerous theories about how the information of both hands processed during bimanual tasks (i.e. assembly PPT's subtest) in the brain. Most of the evidence consensus on the tightly synchronization of the input/output signals of the both hands during performing the tasks. So such these inter-limb coordination tasks is highly dependent on the temporal coordination, it

means that the coordination signals are sent simultaneously to their effectors (29) including the premotor cortex, the parietal cortex, and particularly Supplementary Motor Area (SMA), the cingulated motor cortex, primary motor cortex (M1), and the cerebellum (30). Thus, any impairment of these centers and circuitries may cause the temporal incoordination in PwMS. In addition, accurate administration of the PPT, as a goal-directed movement, requires information about the retinal eye information and proprioceptors of the hands information should be integrated (31). Based on the biodemographic information of the PwMS in the current study, most patients suffering from one or more symptoms such as tremor, optic neuritis, and sensory disturbances might have caused the difference between these two groups. This finding is consistent with other records (11,15,32,33). Guclu-Gunduz et al.(15) and Kalron et al.(11) reported hand dexterity to be related with light touch-pressure. Meanwhile, Kamm et al. (32) and Poole et al. (33) suggested limb apraxia and visual perception disorders to have significant effects on hand dexterity in MS. Likewise, although sensory responses did not assess in current study, most patients had a history of at least one symptom (e.g. optic neuritis, hand paresthesia, and motor dysfunctions). However, further research is warranted to find the reasons for lack of hand dexterity in PwMS.

Based on the finding of the present study, dominant hand dexterity and illness duration could predict 60.5 per cent of the variation in EDSS scores (in terms of disability statuses) among PwMS. This finding is consistent with other studies (2,14,34, 35). Johansson et al. recorded the presence of hand dysfunction in PwMS, even those with low EDSS scores (14). Reddy et al. also confirmed the significant positive relationship between primary motor and premotor cortex (movement area of the fingers) deficits and severity of disability in MS (34). YozbatNran et al. (2) reported disability level and cognitive function correlated with upper extremity motor impairments and lack of hand dexterity. Chen et al. (35) established a strong relationship between finger strength and dexterity for performing various manual activities. While the International Classification of Functioning, Disability, and Health (ICF) defined disability as the impairment of body function/structure, activity limitations, and participation restrictions (36), obviously, the heterogeneous nature of MS involves the effects of various factors on disability (37). Therefore, may be hand dexterity assessment using the PPT could be used as a convenient method to predict disability in clinical practice.

Future research is recommended to investigate hand dexterity through other measures, e.g. MS Functional Composite (MSFC), which are more sensitive to upper extremity dysfunction. The current study had several limitations including a small sample size, using convenience sampling, and not measuring hand and finger sensations (which might have greatly affected the functional use of hands).

Conclusion

PwMS in this study had reduced hand dexterity. Therefore, weakness in the dominant hand and alternatively bimanual coordination could be good discriminators of PwMS from the control group. As dominant hand dexterity has an important role in disability status of PwMS, further research

is necessary to clarify the efficacy of compensatory or restorative interventions in improving hand function and independence in PwMS.

Acknowledgements

This study was a part of the first author's Master degree thesis in occupational therapy, conducted in 2012-2013 under the support received from School of Rehabilitation Sciences, Iran University of Medical Sciences, Tehran, Iran.

Conflict of Interests

The authors declare no conflict of interest in this study.

References

1. McDonald I, Compston A. The symptoms and signs of multiple sclerosis, in McAlpine's Multiple Sclerosis, A. Compston, G. Ebers, and H.L. Lassmann, Editors. Churchill Livingstone Elsevier Inc. 2006; 287-346.
2. YozbatNran N, Baskurt F, Baskurt Z, Ozakbas S, Idim E. Motor assessment of upper extremity function and its relation with fatigue, cognitive function and quality of life in multiple sclerosis patients. *Journal of the Neurological Sciences* 2006;246(1-2):117-122.
3. Sahraian MA, Pakdaman H, Harandi AA. Is it time to revise the classification of geographical distribution of multiple sclerosis? *Iran J Neurol* 2012. 11(2):77-8.
4. Weier K, Penner IK, Magon S, Amann M, Naegelin Y, Andelova, M, et al. Cerebellar abnormalities contribute to disability including cognitive impairment in multiple sclerosis. *PLoS One* 2014;9(1): e86916.
5. Schlaeger R, Schindler C, Grize L, Dellas S, Radue EW, Kappos L, Fuhr P. Combined visual and motor evoked potentials predict multiple sclerosis disability after 20 years. *Mult Scler* 2014 Sep; 20(10):1348-54.
6. Sandroff BM, Pilutti LA, Benedict RH, Motl RW. Association Between Physical Fitness and Cognitive Function in Multiple Sclerosis: Does Disability Status Matter? *Neurorehabil Neural Repair* 2015 Mar-Apr;29(3):214-23.
7. Khaleeli Z, Ciccarelli O, Manfredonia F, Barkhof F, Brochet B, Cercignani M, et al. Predicting progression in primary progressive multiple sclerosis: a 10-year multicenter study. *Ann Neurol* 2008;63(6):790-3.
8. Denomme LT, Mandalfino P, Cinelli ME. Strategies used by individuals with multiple sclerosis

sis and with mild disability to maintain dynamic stability during a steering task. *Exp Brain Res* 2014;232(6):1811-22.

9. Nunes AF, Monteiro PM, Vaz Pato M. Influence of multiple sclerosis, age and degree of disability, in the position of the contrast sensitivity curve peak. *Indian J Ophthalmol* 2014;62(2):180-5.

10. Baghizadeh S, Sahraian MA, Beladimoghadam N. Clinical and demographic factors affecting disease severity in patients with multiple sclerosis. *Iran J Neurol* 2013;12(1):1-8.

11. Kalron A, Greenberg-Abrahami M, Gelav S, Achiron A. Effects of a new sensory re-education training tool on hand sensibility and manual dexterity in people with multiple sclerosis. *Neuro Rehabilitation* 2013;32(4):943-8.

12. Gharagozli K, Poorsaadat L, Harandi AA, Pakdaman H, Kalanie H. Frequency distribution of the first clinical symptoms in the Iranian population with multiple sclerosis. *Iran J Neurol* 2012;11(3):118-20.

13. O'Hara L, Cadbury H, De S, Ide L. Evaluation of the effectiveness of professionally guided self-care for people with multiple sclerosis living in the community: a randomized controlled trial. *Clin Rehabil* 2002;16(2):119-128.

14. Johansson S, Ytterberg C, Claesson IM, Lindberg J, Hillert J, Andersson M, et al. High concurrent presence of disability in multiple sclerosis. Associations with perceived health. *J Neurol* 2007;254(6):767-73.

15. Guclu-Gunduz A, Citaker S, Nazliel B, Irkek C. Upper extremity function and its relation with hand sensation and upper extremity strength in patients with multiple sclerosis *NeuroRehabilitation* 2012;30(4):369-374.

16. Lamers I, Kelchtermans S, Baert I, Feys P. Upper limb assessment in multiple sclerosis: a systematic review of outcome measures and their psychometric properties. *Arch Phys Med Rehabil* 2014;95(6):1184-200.

17. Feys P, Romberg A, Ruutiainen J, Ketelaer P. Interference of upper limb tremor on daily life activities in people with multiple sclerosis. *Occup Ther Health Care* 2004;17(3-4):81-95.

18. Backman C, Cork S, Gibson G, Parsons J. Assessment of hand function: the relationship between pegboard dexterity and applied dexterity. *Can J Occup Ther* 1992;59:208-13.

19. Platz T, Pinkowski C, van Wijck F, Kim IH, di Bella P, Johnson G. Reliability and validity of arm function assessment with standardized guidelines for the Fugl-Meyer Test, Action Research Arm Test and Box and Block Test: a multicentre study. *Clin Rehabil* 2005;19(4):404-11.

20. Feys P, Dupontail M, Kos D, Asch PV, Ketelaer P. Validity of the TEMPA for the measurement of upper limb function in multiple sclerosis. *Clin Rehabil* 2002;16(2):166-173.

21. Wang YC, Magasi SR, Bohannon RW, Reu-

ben DB, McCreath HE, Bubela DJ, et al. Assessing dexterity function: a comparison of two alternatives for the NIH Toolbox. *J Hand Ther* 2011;24(4):313-20; quiz 321.

22. Yancosek KE, Howell D. A narrative review of dexterity assessments. *Journal of Hand Therapy* 2009;22:258-269.

23. Tiffin J. *Purdue Pegboard examiner manual*, in Science Research Associates. Chicago 1986.

24. Gallus J, Mathiowetz V. Test-retest reliability of the purdue pegboard for persons with multiple sclerosis. *American Journal of Occupational Therapy* 2002;57(1):108-111.

25. Polman CH, Reingold SC, Banwell B, Clanet M, Cohen JA, Filippi M, et al. Diagnostic criteria for multiple sclerosis: 2010 revisions to the McDonald criteria. *Ann Neurol* 2011;69(2):292-302.

26. Azimian M, Shahvarughi-Farahani A, Rahgozar M, Etemadifar M, Nasr Z. Fatigue, depression, and physical impairment in multiple sclerosis. *Iran J Neurol* 2014;13(2):105-107.

27. Kurtzke JF. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). *Neurology* 1983;33(11):1444-52.

28. Seyedian M, Falah M, Nourouziyan M, Nejat S, Delavar A, Ghasemzadeh HA. Validity of the Farsi Version of Mini-Mental State Examination. *Journal of Medical Council of I.R.I.* 2008;25(4):408-414.

29. Swinnen SP, Wenderoth N. Two hands, one brain: cognitive neuroscience of bimanual skill. *Trends Cogn Sci* 2004;8(1):18-25.

30. Swinnen SP, Vangheluwe S, Wagemans J, Coxon JP, Goble DJ, Van Impe A, et al. Shared neural resources between left and right interlimb coordination skills: the neural substrate of abstract motor representations. *Neuroimage* 2014;49(3):2570-80.

31. Feys P, Helsen WF, Lavrysen A, Nuttin B, Ketelaer P. Intention tremor during manual aiming: a study of eye and hand movements. *Mult Scler* 2003;9(1):44-54.

32. Kamm CP, Heldner MR, Vanbellinghen T, Mattle HP, Muri R, Bohlhalter S. Limb apraxia in multiple sclerosis: prevalence and impact on manual dexterity and activities of daily living. *Arch Phys Med Rehabil* 2012;93(6):1081-5.

33. Poole JL, Nakamoto T, McNulty T, Montoya JR, Weill D, Dieruf K, et al. Dexterity, Visual Perception, and Activities of Daily Living in Persons with Multiple Sclerosis. *Occupational Therapy in Health Care* 2010;24(2):159-170.

34. Reddy H, Narayanan S, Woolrich M, Mitsumori T, Lapierre Y, Arnold DL, et al. Functional brain reorganization for hand movement in patients with multiple sclerosis: defining distinct effects of injury and disability. *Brain* 2002;125 (Pt 12):2646-57.

35. Chen CC, Kasven N, Karpatkin HI, Sylvester

A. Hand strength and perceived manual ability among patients with multiple sclerosis. *Arch Phys Med Rehabil* 2007;88(6):794-7.

36. World Health Organization. 2001 (cited 2007 March 5); Available from: www.who.int/classification/icf

37. Ytterberg C, Johansson S, Andersson M, Widen Holmqvist L, von Koch L. Variations in functioning and disability in multiple sclerosis. A two-year prospective study. *J Neurol* 2008; 255(7): 967-73.