Mental Practice and Manipulative Skills Training in Multiple Sclerosis: A Pilot Study

Abstract

Introduction: Multiple sclerosis (MS) is a demyelinating disease of the central nervous system which produces both motor and cognitive dysfunctions. MS causes a decline in the performance of activities of daily living (ADL) due to impaired limb function.

Aim: This pilot study sought to determine whether the use of mental practice (MP) or MP combined with the training of manipulative skills would improve the manipulation motor skills and treatment satisfaction among people with MS.

Methods: The study participants were people with MS. Blinded evaluators performed three assessments for each patient (pre-treatment, post-treatment and at a three month follow up) with the Nine Hole Peg Test, Box and Block Test, the ABILHAND and The Canadian Occupational Performance Measure. Three groups were arranged with alternate allocation: (A) Mental practice, (B) Mental practice + skills training and (C) Control group.

Results: The sample included 35 patients. For the normally distributed quantitative variables, the mean and standard deviation were used (SD), and for non-normal quantitative variables, the median was used and the 25th and 75th percentiles (q1-q3). When comparing the three groups, there was no evidence of benefits in self-perceived performance of ADL in the gross and fine motor skills; however, there was an improvement in perceived satisfaction and in the performance of activities, independent of the treatment received.

Conclusion: The perceived performance and satisfaction in the performance of activities increases in people with MS when performing MP treatments, MP combined with skills training and conventional rehabilitation treatment.

Keywords: activities of daily living; manual dexterity; mental practice, motor image; multiple sclerosis.

Introduction

Multiple sclerosis (MS) is a demyelinating illness of the central nervous system (CNS), which leads to motor and cognitive dysfunctions (Tabrizi, Zangiabadi, Mazhari & Zolala, 2013). MS is the most common neurodegenerative illness among adults between the age of 18 and 50 years old (Khan & Amatya, 2017). Furthermore, MS is classified into the following subgroups: relapsing-remitting (RRMS, the most common subtype), progressive secondary (PSMS) and progressive primary (PPMS) (Tabrizi et al., 2013). This illness is characterized by a decline in muscle strength, loss of coordination in the execution of movements, tremor and fatigue (Pellegrino et al., 2015), with 66% of the motor alterations affecting the upper limbs (Jamali, Sadeghi-Demneh, Fereshtenajad & Hillier, 2017). In addition, 80% of people with MS display different degrees of sensory decline, as somatosensory afferents are essential for providing information on the motor activity, human mobility and motor learning (Jamali et al., 2017).

Activities of daily living (ADLs), such as eating, dressing and grooming, are defined by the level of functionality of the arms and hands. Even simple tasks, such as moving an object, are based on complex patterns of muscle activation which can be affected in subjects with MS. In addition, this group of factors leads to a decrease in motor manipulation skills, leading to a high level of disability and alterations of occupational performance, which negatively affect the quality of life of people affected by MS (Yu & Mathiowetz, 2014).

MS severely affects a high number of patients, causing a decline in activities and functionality (Jamali et al., 2017). This commonly leads to the need for intensive periods of rehabilitation (Bovend' Eerdt, Dawes, Sackley, Izadi & Wade, 2010). The complexity and intensity of multidisciplinary neurological rehabilitation is accompanied by elevated costs (Winser et al., 2019; Ma, Chan & Carruthers, 2014).

Although the general process of neurological rehabilitation is effective, there is scarce evidence for supporting the many specific therapeutic rehabilitation techniques. Currently, the intensive, task-oriented practice of activities is considered the basis of effective therapeutic techniques (Braun et al., 2013).

Mental practice (MP) is a training method, in which the internal reproduction of a specific motor act (mental simulation) is repeated many times, to promote learning or to improve motor skills (Machado et al., 2016). In this context, motor imagery (MI) involves the mental practice of a motor act without executing the movements involved. Thus, MI can be performed using different modalities (kinesthetic and visual) from a first or third person perspective (Tabrizi et al., 2013).

A limited number of studies have researched the differences in the MI capacities of people with MS, showing that patients attain significantly lower scores for the precision of their movements compared to controls for the correct execution of a hand rotation task (Tacchino et al., 2018).

Some studies (Harris & Hebert, 2015) show that MI activates brain regions related to motor function and provides an increase in the intensity of the practice, which can benefit patients with MS since this practice facilitates the adaptation of exercises in terms of safety and physical fatigue. Most studies published on MI state that use of the same improves levels of fatigue and the cognitive status in neurological pathologies, including MS (Braun et al, 2013; Park et al., 2018).

Although the systematic reviews available conclude that MI can be a potential tool for improving motor functions and activities, definitive conclusions cannot be extracted regarding the effects of MP, because the evidence available is relatively small (Park, Kim & Yang, 2018).

Considering the lack of studies on the use of MP to determine an improvement in motor manipulation skills and the performance of daily tasks in MS, additional research is necessary to further understand the effectiveness of this technique.

Aim

The aim of this study was to determine whether the use of MP or the combined use of MP together with the training of manipulation skills is able to improve both manipulative dexterity and the perceived performance satisfaction post-treatment of people with MS.

Material and Methods

Participants

Participants were subjects with MS from the MS associations of Móstoles (AMDEM) and Valdemoro (ADEMV) within the Community of Madrid, Spain and who volunteered to participate in the study.

Selection criteria

The inclusion criteria of this study were as follows: patients diagnosed with MS of the RRMS and SPMS subtypes, without the presence of flare-ups during the past three months and aged between 25 and 60 years; an Expanded Disability Status Scale (EDSS) score of ≤7, not presenting depressive symptoms (measured using the Beck Depression Inventory, BDI), not presenting cognitive decline, measured using the Montreal Cognitive Assessment (MoCA≥26) or Minimental Status Examination (MMSE≥24). In addition, they had to be regularly attending physical therapy and/or occupational therapy rehabilitation treatments.

Study procedure

All the participants signed the informed consent prior to beginning the study.

Three differentiated assessments were performed with each patient (pre-treatment, post-treatment and three-month follow-up). All assessments were conducted in the MS associations by a blinded assessor, who was not the person who administrated the treatment sessions. All data were gathered in a record sheet.

Immediately after performing the initial assessment, the participants were divided into three groups, with alternate allocation according to their order of inclusion in the study. The participants were allocated to one of three groups: (A) mental practice (B) mental practice combined with dexterity training or (C) a control group.

For groups A and B, a treatment protocol was designed with a six-week duration and involving a total of 12 sessions. Two half-hour sessions were performed each week, equaling a total of six hours of treatment. This intervention was agreed with the patients at the beginning of the treatment and was conducted in the participant's home. In addition to this intervention, all study groups continued to receive their usual physical therapy and/or occupational therapy sessions.

(A) Mental practice. During each of the 12 treatment sessions, the patient was asked to select two tasks from a list of MP activities designed by the authors, graded by level (for example, opening a drawer, opening a jar or washing a plate). Once the tasks were selected, patients received the specific visual or audio instructions and subsequently performed the tasks. The recording was viewed three times and the audio instructions were repeated two times. To listen to the audio instructions, the participants were requested to close their eyes in order to aid concentration. After listening to the recordings, the patient was asked to perform the tasks once again, practicing what had been learned. After the process was completed, the participant completed a questionnaire and scored each task.

(B) Mental practice + skill training. In this option, six sessions of MP were alternated with six sessions of skills training (ST). The MP protocol was the same as in group A: selecting, performing, visualizing, listening to and scoring the selected tasks. The activities performed in the skills training were based on the Kamm et al. (2015) protocol and bimanual tasks (for example, marker circles, nuts and screws or therapeutic putty). After the performance of each task, the patients were allowed to rest for 1 or 2 minutes to avoid the appearance of fatigue.

(C) Control group. The control group only received their usual physical therapy and occupational therapy treatments provided by their association. The treatment mainly consisted of the application of the Bobath concept (Ilett, Lythgo, Martin & Brock, 2015) and the Vojta method (Pavlikova et al., 2020), dry needling, myofascial induction therapy, passive mobilizations, training of gross and fine motor coordination of the upper limbs, resistance training and static and dynamic balance training.

Outcome measures

- Kinesthetic and Visual Imagery Questionnaire (KVIQ). It is a questionnaire that assesses both visual and kinesthetic components of MP. The patient must perform the movement with the dominant hand (failing that, with the non-dominant one) (Malouin et al., 2007). The KVIQ is a valid and reliable tool for assessing the participant's MP ability in MS patients (Tabrizi, Zangiabadi, Mazhari & Zolala, 2013). This measure was used to ensure the participants were able to complete MP treatment.
- Nine Hole Peg Test (NHPT). This test measures finger dexterity via the performance of an activity with the dominant hand followed by the non-dominant hand (Heller et al., 1987; Wang et al., 2011). NHPT has adequate reliability and its validity have been confirmed in patients with multiple sclerosis

(Carpinella et al. 2014; Gielen et al., 2014; Heldner et al., 2014; Hervault et al., 2017).

- Box and Block Test (BBT). This test measures gross motor dexterity with both the dominant hand and the non-dominant hand. (Slota, Enders & Seo, 2014). Adequate reliability and validity of the BBT have been reported in the assessment of patients with neurological disorders, including multiple sclerosis (Platz et al., 2005).
- The ABILHAND questionnaire. This tool measures the self-perception of manual skill, defined as the ability to perform ADLs, which require the use of the upper limbs without considering the strategies involved (Penta, Thonnard & Tesio, 1998). It is a reliable and valid method to assess patients with multiple sclerosis (Barrett et al., 2013).
- The Canadian Occupational Performance Measure (COPM). This measure is based on patient-centered care, by detecting changes in an individual’s perceived occupational performance and satisfaction, identifying any related problems (Law et al., 1990). Although the measurement properties of this measure in patients with multiple sclerosis is currently unknown, the COPM has been demonstrated to be a reliable and valid measure in patients with neurological dysfunctions such as stroke and spinal cord injury (Berardi et al., 2019;Yang et al., 2017).

Ethics committee

The present study was granted approval by the Ethics Committee of the Rey Juan Carlos University according to the ethical principles for medical research involving human subjects stated in the 2013 revision of the Declaration of Helsinki (World Medical Association, 2013).

Statistical analysis

Descriptive and statistical analyses were performed using the SPSS version 20.0 (Copyright © 2013 IBM SPSS Corp.). Normal distribution was verified by histograms and confirmed by the Shapiro-Wilk test. Descriptive data was represented by mean and the standard deviation (variables with normal distribution); median and interquartile range (quantitative variables without a normal distribution; and frequency and percentage (categorical variables).

For the analysis of clinical and demographic data characterizing the sample, the Chi-squared test was applied to compare proportions of categorical variables; the variance analysis test was used to compare the quantitative variables. Furthermore, linear models were used with mixed effects for repeated measures to assess the effects using the ABILHAND and the COPM, in its dimension on performance and satisfaction. For the mixed-model analysis, the fixed factors were “time” and “group” and the random factor was participants. The interaction between time and group was included in the model to compare the intragroup differences over time. Also,, the intragroup and intergroup differences of the BBT and NHP variables on the affected and non-affected side were verified using the Friedman test. The significance values of the pairwise comparisons were adjusted using the Bonferroni correction for several tests. The level of significance for the statistical analyses was set at 0.05.

Results

In total, 40 patients agreed to participate in the study, however, five were lost to follow-up due to the presence of a flare-up. The final sample therefore comprised of 35 participants ($n=35$), who were divided into three treatment groups: mental practice ($n=12$), mental practice + skills training ($n=13$) and control group ($n=10$). **Table 1** displays the sociodemographic and clinical characteristics of the sample, for which no statistically significant differences were found between the three groups.

The study results are presented below according to the outcome measures used.

ABILHAND

The effect of the time and group interaction was not significant for the ABILHAND ($F=1.657$, $p=0.19$), which indicates that there is no evidence of benefits in the self-perceived performance of ADLs when comparing the three groups (MP group, MP+ skills training and usual treatment). Separately, the time and group factors did not present any significant difference ($p>0.05$). This finding is displayed in **Table 2,** where no differences are observed in this variable over time and the groups are presented homogeneously.

COPM

According to the effects of the time and group interaction, no statistically significant finding was observed between the different interventions over time for the COPM both for the performance score ($F=2.124$, $p=0.11$) as well as for the satisfaction score ($F=0.701$; $P=0.60$). However, a significant increase in both scores was found between the pre-treatment and post-treatment period (COPM performance, $p=0.02$;

COPM satisfaction, p=0.04), indicating an improvement in the subject's perceived satisfaction and perceived improvement in the performance of activities, independent of the treatment received **[Table 2]**.

NHPT

No statistically significant differences were found in the NHPT scores of both upper limbs ($p>0.05$) indicating that there is no evidence of effectiveness or additional benefits for any of the tested therapeutic modalities, therefore, no improvement in fine manipulative dexterity was found in the subjects analyzed. **[Table 3]**.

BBT

Regarding the BBT scores on the affected side, no statistically significant results were found between both treatment modalities ($p>0.05$) **[Table 4]**. On the affected side, significant intergroup differences were found which have been identified using the Friedman test for the pre-treatment (p=0.045) and post-treatment periods (p=0.037). However, because of the correction for multiplicity, the only difference found was between the control group and the MP + dexterity group in the post-intervention period (p=0.032). During this period, the control group presented a median of 55.5 whereas in the MP + dexterity group, a median of 40.5 was found, which means that both groups have improved their gross motor coordination, although the control group revealed a greater improvement **[Table 4]**.

Discussion

The aim of this study was to determine whether the use of MP or the combined use of MP, together with training of motor manipulation skills, would improve the manipulative skills and improve perceived treatment satisfaction among patients with MS. The results of this study show that none of the interventions administered significantly improved the manipulation skills of participants when compared with conventional treatments.

Different studies reveal that MP may be an appropriate treatment method combined with conventional therapy, as it can adapt to a multitude of activities and provide greater functional benefits, besides improving the recovery of the upper limbs. However, previous reports fail to specify the type of treatment used in conventional treatments, nor the duration or frequency of the same (Park et al., 2018; Nielsen, Guillen & Gordon, 2010; Malouin, Jackson & Richards, 2013; Santos-Couto-Paz, Teixeira-Salmela & Tierra-Criollo, 2013; Park, Lee, Cho, Kim & Yang, 2015; García

Carrasco & Aboitiz, 2016; Bragado Rivas & Cano de la Cuerda, 2016; Braun et al., 2013; Harris & Herbert, 2015). Possibly, the lack of consensus in conventional treatment has influenced the lack of statistically significant results in our study. This may be due to the limited hours of conventional treatment received by the patients in our study. However, in a similar study, none of the scores significantly changed from the period directly after intervention to the 10 weeks (3 days per week, 1/2h of exercise) post-test period (Page, 2018).

During the isolated use of MP, as a substitute of conventional treatment, no statistically significant benefits have been found to support the technique. However, slightly positive changes have been reported with the implementation of this technique (Oh, Kim, Kim & Kim, 2016). This may be because there is no consensus among the authors regarding the ideal duration and the frequency of MP sessions (Nilsen et al., 2010; Malouin et al., 2013; Park et al., 2015; Page, Dunning, Hermann, Leonard & Levine, 2011) in the treatment of patients with neurological illnesses, including cerebrovascular accidents, Parkinson’s disease or MS. Additionally, there is a certain heterogeneity in the planning of interventions, which range from five to 54 weeks (García Carrasco & Aboitiz, 2016). However, the average duration generally varies between four to five hours, three times per week, during a period of four to six weeks, meaning a total average of 21 hours of treatment with MP (Bragado Rivas & Cano-de la Cuerda, 2016; Braun et al., 2013). This study has employed shorter time periods, which may explain the lack of significant positive outcomes, as the proportional increase for the implementation of MP was less than reported in previous studies. The protocol used in this study included independent work that the person was told to perform in their home setting, consisting of performing MP activities for 15 minutes each day during the 12 treatment sessions. In 2011, Ietswaart et al. (2011) also included independent MP (30 minutes per day, twice a week over four weeks), with similar results to our study, with no significant positive results in the implementation of the treatment and the motor recovery. However, in our study the subjects did perceive a subjective improvement in their performance and satisfaction, although not in the self-perception of the performance of the ADLs, as this was similar for all three treatments.

Few studies exist which are focused on improving the manipulation skills of people with MS (Kamm et al., 2015; AIAQS & FEM/Cemcat, 2012; Spooren, Timmermans & Seelen, 2012; Kalron, Greenberg-Abrahami, Gelav & Achiron, 2013;

Carpinella, Cattaneo, Bertoni & Ferrarin, 2012). In these, there is no consensus on the duration, the patient characteristics, the outcome measures, the techniques used and the observation of benefits in terms of functionality, skill, tremor, sensitivity or kinematics of the upper limb, among others. This lack of consensus regarding the duration of the treatment protocols, ranging from 15 to 29 sessions, during the interventions performed at the person's home or in the clinical environment, mean that the outcomes are unclear in terms of the improvements to the functionality of the upper limb, the sensitivity, and the techniques which offer the greatest benefits (Spooren et al., 2012; Bonzano et al., 2014; Gatti, Tettamanti, Lambiase, Rossi & Camola, 2015). The treatment protocols which increase this number of sessions and the treatment times have obtained statistically significant differences in manipulative dexterity or the performance of ADLs with the use of this dexterity (Kamm et al., 2015; Kalron et al., 2013; Waliño-Paniagua et al., 2019).

This pilot study attempted to carry out a treatment protocol to improve the manipulative skills of people with MS, performing an intervention at the person's home and thus facilitating the generalization of learning. The most significant aspect for the generalization of learning was that the patient was the one who selected the activity to be practiced from an extensive range of proposed activities, thus encouraging significant activities and active participation. Although statistically significant results were not found for the improvement of manipulation skills, the patient perceived an improvement in the performance of activity. This may be due to the low number of sessions dedicated to skills training (six sessions) compared to the articles revised which used an average of 20 sessions.

It is well known that persons with MS can experience a complex disability pattern. Studies that have evaluated the persons' own perception of their disability found that they experienced problems related to all areas of daily life activities. However, few investigations analyze how persons with MS perceive their performance and satisfaction with performance of daily activities following rehabilitation.

In our study, results indicated significant changes in self-perceived performance and satisfaction between the pre-treatment and post-treatment period (COPM performance, $p=0.02$; COPM satisfaction, $p=0.04$), indicating an improvement in the subject's perceived satisfaction and perceived improvement in the performance of activities, independent of the treatment received. This is also in agreement with similar studies (Lexell, Flansbjer & Lexell, 2014; Kos et al., 2016).

Future studies are necessary with a larger sample, as well as longer treatment times and a greater number of sessions, in order to further study the effectiveness of MP in the recovery of ADLs in patients with MS.

Study limitations

This study has several limitations. First, the failure to conduct a statistical power calculation may have resulted in low power for demonstrating the potential benefits of the implementation of MP alone or combined with the training of manipulation skills on manipulative dexterity and the perceived performance satisfaction post-treatment of people with MS. However, as a pilot study, it provides insights for future studies which should not only consider larger sample sizes with adequate power but also longer treatment times and a greater number of sessions, in order to further study the effectiveness of MP in the recovery of ADLs in patients with MS. Also, the level of kinesthetic and visual imagination which the participants presented was not considered despite the administration of a specific motor imagery scale.

Implications for occupational practice

- During occupational therapy treatments, training in mental practice may be considered a complementary tool in the rehabilitation of people with MS as it improves patient motivation and satisfaction with the performance of rehabilitation programs.
- Mental practice combined with conventional treatment could contribute to patients perceiving improved performance of ADLs.
- Mental practice requires a specific treatment protocol, as execution is highly variable.
- Self-reported outcome measures, such as the COPM, could provide highly valuable information about occupation performance that may not match the objective evidence.

Conclusions

The use of MP, and of MP combined with skills training does not lead to significant differences in the improvement of the manipulative dexterity skill in people with MS, compared with traditional rehabilitation treatment.

The performance and satisfaction in the performance of activities increases in people with MS when performing MP treatments, MP combined with skills training and conventional rehabilitation treatment.

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		Control group	Mental practice	Mental practice + skills training	Test; p value
Characteristics of the sample					
Age		47.00 (8.03)	42.33 (7.11)	47.77 (7.81)	F=1.786. p=0.184
Sex	Men	6 (60%)	3 (25%)	4 (31%)	X^2= 3.222. p=0.200
	Women	4 (40%)	9 (75%)	9 (69%)	
Level of studies	Basic	1 (10%)	0 (0%)	5 (38.5%)	X^2= 7.288. p=0.121
	High school	5 (50%)	6 (50%)	5 (38.5%)	
	University	4 (40%)	6 (50%)	3 (23%)	
Upper limb dominance	Right-handed	8 (80%)	12 (100%)	13 (100%)	X^2= 5.303. p= 0.071
	Left-handed	2 (20%)	0 (0%)	0 (0%)	
	Ambidextrous	0 (0%)	0 (0%)	0 (0%)	
KVIQ-10, median (q1-q3)		40 (21.5-45.25)	34 (27.75-41.75)	32.5 (24.75-38)	p=0.692
Characteristics of multiple sclerosis					
Subtype	Relapsing-remitting	5 (50%)	7 (58%)	6 (46%)	X^2= 0.887. p=0.926
	Primary-progressive	2 (20%)	2 (17%)	4 (31%)	
	Secondary-progressive	3 (30%)	3 (25%)	3 (23%)	
More affected side	Right	6 (60%)	3 (25%)	5 (38.5%)	X^2= 2.804. p=0.246
	Left	4 (40%)	9 (75%)	8 (61.5%)	
Duration (years)		11.40 (8.24)	8.88 (5.66)	11.88 (7.90)	F=0.590. p=0.560
Treatment duration (hours per week)	Occupational therapy	0.50 (0.62)	0.17 (0.39)	0.12 (0.42)	F=2.081. p=0.141
	Physical therapy	1.30 (0.62)	1.69 (0.89)	1.56 (0.42)	F=0.939. p=0.402

Table 1. Clinical and demographic characteristics of the sample.

Table 2. Changes observed in the intervention group in relation to self-perceived manual skill using the ABILHAND and concerning the identification of problems for performing ADLs using the Canadian Occupational Performance Measure (COPM).

	TIME						**linear model with mixed effects**			
	Pre		**Post**		**Follow-up**					
	Media	SD	**Media**	SD	**Media**	SD				
ABILHAND							**Factors**	**F**	**p value**	**pairwise comparison**
Control group	2.59	0.460	2.27	0.466	2.15	0.443	**Groups**	0.021	0.979	
Mental practice	2.25	0.420	2.24	0.438	2.25	0.418	**Time**	0.028	0.972	
Mental practice + skills training	1.94	0.404	2.27	0.427	2.47	0.407	**Time*groups**	1.657	0.188	
COPM Performance							**Factors**	**F**	**p value**	
Control group	4.189	0.533	4.178	0.453	4.451	0.562	**Groups**	0.322	0.727	
Mental practice	4.325	0.486	4.859	0.434	4.338	0.546	**Time**	4.255	0.027	pre<post, p=0.02
Mental practice + skills training	3.887	0.467	5.257	0.426	5.140	0.540	**Time*groups**	2.124	0.111	
COPM Satisfaction							**Factors**	**F**	**p value**	
Control group	3.806	0.745	4.378	0.704	4.218	0.631	**Groups**	0.357	0.703	
Mental practice	4.215	0.680	4.796	0.684	4.459	0.605	**Time**	3.586	0.043	pre<post, p=0.04
Mental practice + skills training	3.817	0.653	5.677	0.676	4.986	0.595	**Time*groups**	0.701	0.599	

Table 3. Changes observed in the intervention groups in terms of upper limb function according to the Nine Hole Peg Test (NHPT).

		Control group			Mental practice			Mental practice+skills training			Intergroup comparison
		Median	**Q1**	**Q3**	**Median**	**Q1**	**Q3**	**Median**	**Q1**	**Q3**	**(p value)**
NHPT affected	**Pre**	28.9	25.4	40.0	29.0	20.9	33.4	30.0	24.0	36.1	0.59
	Post	26.7	26.0	35.2	27.1	24.5	33.8	27.6	23.4	34.8	0.95
	Follow-up	29.1	27.7	31.8	26.7	24.0	33.5	34.2	21.7	40.0	0.91
Intragroup comparisons (p-value)		0.37			1.00			0.26			
NHPT non-affected	**Pre**	23.3	19.5	27.3	25.6	21.0	30.0	25.5	22.7	35.0	0.23
	Post	22.9	20.0	26.2	28.9	22.1	32.5	26.2	21.4	37.0	0.15
	Follow-up	23.6	20.8	24.4	29.1	23.1	31.0	26.7	22.1	47.9	0.30
Intragroup comparisons (p-value)		0.64			0.25			0.46			

Table 4. Changes observed in the intervention groups regarding the coordination of the upper limbs according to the Box and Block Test (BBT).

		Control group			Mental practice			Mental practice+skills training			Intergroup comparison	pairwise comparison
		Median	**Q1**	**Q3**	**Median**	**Q1**	**Q3**	**Median**	**Q1**	**Q3**	**(p-value)**	**(adjusted p-value)**
BBT affected side	**Pre**	46.5	36.0	61.0	38.5	29.5	48.0	41.0	34.0	46.0	0.19	
	Post	44.0	41.0	55.0	40.5	33.0	55.0	37.5	29.0	49.0	0.49	
	Follow-up	45.0	39.0	47.0	46.5	35.5	52.5	38.0	30.0	54.0	0.74	
Intragroup comparisons (p-value)		0.06			0.28			0.77				
BBT non-affected side	**Pre**	52.5	45.0	66.0	41.5	35.0	51.0	46.0	37.0	49.0	0.045	control vs MP: 0.06; control vs MP+skills: 0.12; MP vs MP+skills:1.00
	Post	55.5	48.0	60.0	49.0	37.0	58.0	40.5	34.0	49.0	0.037	control vs PM: 0.41; control vs PM+skills: 0.032*; PM vs PM+skills:0.86
	Follow-up	51.0	50.0	56.0	51.0	42.5	53.5	41.0	34.0	48.0	0.15	
Intragroup comparisons (p-value)		0.05			0.39		0.32					
pairwise comparison (adjusted p-value)		Pre vs post: 1.00; Pre vs follow-up: 0.10; Post vs follow-up: 0.10										