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***Title page with author details**

Participation restriction in people with multiple sclerosis: prevalence and correlations with cognitive, walking, balance and upper limb impairments

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Running title: Participation restrictions in MS

Participation, defined as involvement in life situations, is often considered to be associated with quality of life and has been proposed as one determinant of health status.[1] Indeed, participation is recently suggested as a primary outcome of interventions aiming to improve quality of life.[2 3] Participation restrictions, defined as 'problems an individual may experience in involvement in life situations,[4] can result from a combination of personal factors, impairments, activity limitations and environmental factors[5] that can differently impact on the execution of home, social and productive activities.

Although participation has its own definition and should be viewed as an independent construct, quality of life and independency in activity of daily living are often used to measure participation restriction. An early survey reported that two-thirds of 166 people with multiple sclerosis (PwMS) had limitations in performing activities without assistance and having an independent social/lifestyle.[6] A later study similarly revealed that 47% of 240 PwMS were not completely independent in their domestic life[7]. Finally, a study by Argento et al[8] reported differences between MS and healthy subjects in time spent at home with other people and use of domestic help.

Several studies have also been conducted to investigate the relationship between variables related with quality of life and activity limitation and multiple sclerosis (MS) related disorders. Mikula et al. found that health related quality of life is associated with disease severity and age in MS.[9] Ben Ari et al. found a correlation between activity limitation measured as restriction in outdoor activities and depression, cognitive disorders and leisure and domestic activities.[10] Finally, Yorkston et al. inquired on satisfaction with participation and found that participation is associated with fatigue, pain, depression, stress, anxiety, and well-being in MS[11]. Furthermore,

the frequency with which participants reported participating in active leisure, was associated with mobility impairments[12].

While it is known that gait impairments can lead to limitations in activity and potentially restrict participation, also balance disturbances[13], hand dexterity dysfunctions[14,15] and cognitive deficits[16] have a potentially deleterious effect on different domains of participation. However, the relationship between cognitive deficits, disorders at activity level and participation restrictions are not well understood. Moreover, physical and cognitive parameters have not been studied together in connection with participation in life domains, such as, home activities, social participation and work activities.

The study of the relation between participation restrictions and physical and cognitive factors is important since they are all modifiable factors that might respond to rehabilitation. Further, investigation of the magnitude of these relationships with tools commonly used in rehabilitation to measure attention and activity limitation might indicate their appropriateness as predictors of participation restrictions, Altogether, this may contribute to our developing more focused clinical rehabilitation protocols that can lead to improved participation in home and social situations, as well as better chances of participating in productive activities.

Until now participation restrictions have been mostly studied using scales addressing quality of life[9], amount of performed activities[10] or life satisfaction**Error! Bookmark not defined.** while a test specifically addressing participation might give a better picture of restriction in different domains of life participation. Furthermore the use of a standardized test on participation and the collection of data from a reference group of healthy subjects made it possible to calculate the true prevalence of participation restrictions.

The Community Integration Questionnaire (CIQ) was developed for people with traumatic brain injury.[17] It is a test specifically designed to assess participation restrictions, including home, social and productive activities and has also been used. [18, 19,2,20,21] for PwMS

The primary aim of this study was to use the home, social and productive activities domains of the CIQ to calculate the prevalence of global and domain specific participation restrictions in MS according to disability level and in relation to healthy persons. The secondary aim was to assess the relationship between participation restrictions in these three domains and activity disorders in terms of walking and balance disturbances, hand dexterity and cognitive deficits.

Method

A convenience sample of 105 people was recruited from inpatients and outpatients treated at the Rehabilitation and MS Center, Overpelt, Belgium; and the Department of Neurorehabilitation, Don Carlo Gnocchi Foundation Onlus, IRCCS, Milan, Italy. The inclusion criteria were: confirmed MS diagnosis (McDonald criteria[22]), age>18 year old, free from relapses or relapse-related treatments for one month before the study, and the ability to touch the chin at least with one hand. Subjects unable to follow test instructions or having other diseases interfering with the execution of tests were excluded, further information on the sample is available in Bertoni et al[15].

A convenience sample of twenty healthy subjects (HS) matched for age and gender were also tested to provide CIQ comparative data. We recruited all eligible subjects having the same age range and sex as PwMS in a two weeks window. Seven were men (35%), mean age (SD) was 51.9 (11.5) years with none of them reporting any musculoskeletal or neurological conditions.

All subjects received information regarding the study and were included after signing the informed consent forms. The study was approved by the ethical committee of each participating centre.

Descriptive variables

Expanded Disability Scale (EDSS), type of MS, disease duration, gender and age were retrieved from medical records as determined by the treating neurologist. Participants were asked for employment status.

Cognitive function and Activity predictors

The cognitive level and psychomotor speed was determined by the Symbol Digit Modalities Test (SDMT).[23] The SDMT requires individuals to identify nine different symbols corresponding to the numbers 1 through 9, and to practice writing the correct number under the corresponding symbol. Then they manually fill in the blank space under each symbol with the corresponding number. A score was calculated by totalling the number of correct answers over 90s.

Manual dexterity was measured with the Nine Hole Peg Test (NHPT);[24] The time needed to place and remove 9 pegs was recorded and averaged over 2 trials. Manual dexterity speed was calculated as pegs per second and used in the analyses.[14] Participants who were not able to place any peg within a time limit of 300 seconds received a score of 0 pegs per second.

Walking speed (seconds), was assessed with the Timed 25 foot walking test (T25FW).[25] According to standardized instructions an average of the 2 trials was computed.

Upright balance was assessed with Bohannon Standing Balance Test (BSBT)[26], ranging from 0 (unable to stand) to 6 (stand on one foot for 30’’).

Participation

The CIQ was used to assess participation. CIQ is scored to create a total score ranging from 0 to 29 representing from none to excellent community integration. It also provides scores from three subscales assessing:

Home Integration (10 points) that refers to participation in activities such as preparing the meal, doing house-work and planning social meeting in the home.

Social Integration (12 points), which refers to participation in outdoor activities including shopping, visiting friends and aspects of interpersonal relations.

Productive Activities (7 points). Including items inquiring employment, educational and volunteer activities.

Percentages of PwMS having CIQ scores lower than the 10^{th} percentile of those of HS were calculated for each sub scale of the CIQ to categorize the persons as having problem or no problem with participation.

Two physical therapists experienced in the assessment of PwMS performed all tests. To ensure standardization between centres an instruction booklet was used and two practice sessions in the two countries were held to minimize the differences between assessors. Data coming from

these preliminary assessments were analysed to verify if there were any statistically significant differences between the two centres.

Data Analysis

A T test (two-tailed) was used to calculate statistically significant differences between HS and PwMS.

Pearson's correlation coefficients were calculated to investigate the correlations between CIQ, demographic and clinical variables. T25WT and EDSS showed a high level of redundancy (Pearson's correlation coefficients>0.8), thus only EDSS was entered in the subsequent models.

For multivariate analysis statistical manuals suggest at least 10 subjects for each independent predictor[27]. We included 98 subjects in the model to account for missing data. Generalized linear models were used to assess the relationship between participation (dependent variable) and the other variables used as predictors. The first analysis containing demographic and clinical characteristics showed that only Type of MS and not age or disease duration was statistically significantly associated with the dependent variable thus only MS type and cognitive and activity deficits were entered in the final models.

We calculated Receiver Operating Characteristic curves to obtain cut off values for the statistically significant predictors that best distinguished participation restrictions in total CIQ or sub-domains of CIQ .Area Under the Curve (AUC) demonstrating accuracy of the cutoff value was calculated.

To manage and analyze the data, we used Statistica 8 with the significance level set at $p<0.05$.

Results

Seven subjects with incomplete data were excluded.

Table 1 shows the characteristics of the remaining 98 PwMS tested with all relevant tests. People with relapsing remitting, secondary progressive or primary progressive types of MS were: 32(33%), 56(57%) and 10(10%) respectively and 67 subjects (68.3%) used a walking aid. Out of the whole group 17 (16.2%) were retired, 46 (43.8%) stopped working prematurely, 18 (17.1%) had never been employed, 6 (5.7%) worked part time and 18 subjects (17.1%) worked full time.

Table 2 reports comparisons between HS and PwMS in terms of mean CIQ scores. As expected HS had statistical significantly higher level of participation compared to PwMS This was very evident in the productive activity domain where the score for HS were double compared to that of PwMS.

Table 3 reports the percentages of PwMS having a total CIQ scores below the 10^{th} percentile of HS scores from which to calculate proportion of participation restrictions according to disability level. Participation restriction increased with an increasing EDSS. Forty% of PwMS with EDSS <4 had scores below the cut-off, thus denoting participation restrictions, and up to 82% of the subjects with EDSS 6+ had scores below the cut off (Table 3). Noteworthy, 90% of wheelchair bound people (n=38) had scores below the cut-off.

Figure 1 depicts CIQ items and percentages of PwMS doing activities of daily living without help or more than 5 times/month. Less than 10% of PwMS did shopping alone and less than 25% of PwMS did shopping more than 5 times a month.

Table 4 shows bivariate correlations assessing the relationship between participation restrictions of the CIQ total score, its various domains and activity disorders. Highest correlations were observed between CIQ total score and SDMT(r=0.60) and between the home integration section of the CIQ and EDSS(r=-0.57) and NHPT(r=0.55).

Results from the multivariate analyses are reported in Table 5 to show the simultaneous relationship between participation restrictions, activity disorders and cognitive deficits. Models predicting overall participation restrictions (CIQ Total score) and home participation restrictions explained a larger proportion of variance than those predicting social integration and productive activities.

The SDMT was the best predictor in all participation domains and CIQ total score. Total CIQ scores were also negatively associated with BSBT and Type of MS (score of 14, 16 and 13 respectively for RR, PP and SP type). Meaning that people with higher cognitive and balance disorders and secondary progressive type of MS had higher participation restrictions compared to PwMS with primary progressive MS. Finally, decreased hand dexterity was positively associated with home participation restrictions.

The AUC (CI) and cut off scores for total CIQ for the SDMT were respectively 0.76 (0.64-0.87) and 34.5 points; BSBT were respectively 0.74 (0.63-0.84) and 2.5 points. AUC (CI) and cut off scores for home integration CIQ for the NHPT were respectively 0.73 (0.60-0.84) and 0.27 peg/s (around 33.3s to move 9 pegs).

Discussion

182 The aims of the study were to estimate the prevalence of participation restrictions in MS
183 according to disability level and to assess relationship between participation restrictions,
184 activity limitations and cognitive deficits.
185 This is the first study documenting that 77% of a sample of PwMS showed participation
186 restrictions, with integration in social participation tending to be more restricted than home
187 integration and providing test cut off scores that discriminate between PwMS with or without
188 restriction in participation. However, the results also highlight the fact that multiple sclerosis
189 does not restrict participation in the whole population and in all domains. PwMS with mild
190 involvement reported no or only mild participation restriction at home, while the vast majority
191 of PwMS with EDSS>7 show participation restrictions in all domains. In addition, participation
192 restrictions were less prevalent in the productive domain compared to the social domain.
193 Overall participation restrictions were found to be more correlated with cognitive deficits than
194 balance and gait limitations while hand dexterity was predominantly associated to participation
195 in home activities. Finally, even controlling for disorders at activity and cognitive level subjects
196 with a secondary progressive type of MS had a higher level of participation restrictions than
197 those with primary progressive type.

198

199 PwMS showed a substantial decrease in participation compared to age-matched HS.
200 Restrictions in social participation were the most prevalent, more than 70% of participants did
201 not perform outdoor activities such as shopping and visiting relatives on a regular basis. One-
202 third of the participants showed participation restrictions in home and productive activities
203 which have been linked to reduced self-esteem, life satisfaction, mental health status[28,29,30] and
204 perceived MS severity[31].

Participation restrictions also increased burden for family members with 91% of participants needing help for shopping and only 38% of them preparing the meal for themselves. Decreased number of activities may further impact on level of physical capacity leading to a further reduction in participation.[32] It is, however, important to point out that the comparison with healthy subjects scores and the analysis of subgroups showed that participation restriction are unevenly distributed. All participants having an EDSS score less than 4 had a normal level of participation in home activities and more than 60% of the sample reported normal levels of participation in productive activities irrespective of the EDSS score.

Cognitive deficits were the best predictor of participation restrictions in MS, results corroborated by Rao et al[33] that found that PwMS with cognitive deficits had restrictions in social, vocational, routine household activities and work. Huges et al[34] similarly found that cognitive impairment measured with a self-reported questionnaire was associated to a lower level of participation.

Our results and results from other studies[10,35] underscore the importance of neurocognitive assessment in MS and the use of cognitive tests preceding interventions aimed at improving community integration. We can also speculate that multimodal interventions, including treatments for cognitive disorders, might improve participation of PwMS.

Balance disorders were associated to participation restrictions. Balance disorders interfere with basic activities of daily living and may increase social isolation, fear of falling and consequent activity curtailment.[35] Petterson found that one third of PwMS were concerned about falling[35] with majority of them reporting activity curtailment. The above results underline the importance of considering fall risk factors such as balance and fear of falling in interventions to

enhance participation.[35]

Limited hand dexterity was associated with participation restrictions and in particular to restrictions in home activities, where upper limb control is essential for activities like dressing and cooking. Our results corroborate preceding studies that revealed a high percentage of bilateral hand dexterity deficits and correlations between the community integration Index and impairment in upper limb strength and sensibility.[15, 36]

In agreement with other studies[7,37] bivariate correlation was found between walking and participation restrictions but walking did not reach a significant threshold in the predictive model after controlling for other factors. Results did not change when gait speed was substituted by EDSS. Sample characteristics may have played a role since more than half used an assistive device and one quarter had severe walking restriction. The use of assistive device may aid in reducing participation restrictions even in participants with severe walking disturbances.

Social integration and productive activities were limited our sample; more than two/third of PwMS were retired and 43 % of them stopped working prematurely due to MS thus markedly increasing the burden on society. Association between functional status and social/protective activities was, however, unclear and deserves further studies. We found that a cognitive deficit was the only predictor associated with the social integration and productive domains of the CIQ. However, the explained variance was moderate, indicating that these domains cannot be explained solely by the deterioration of cognitive deficits and activity-related performances. It is known that interaction between cognitive disorders and social policy factors contributes to employment status[38]. This may have influenced our analysis since 16% of the sample was already of retirement age irrespective of activity limitations. Further, we did not evaluate social

support which has been reported as being important for quality of life in PwMS[39]. Results also imply that EDSS, NHPT and BSBT, cannot by themselves inform clinicians on potential participation restrictions in social and productive activities. It should be noted that the social integration and productive activities domains of the CIQ have been shown to have a low level of internal consistency and dimensionality[19] which may reduce the quality of information provided by these two subscales.

Finally PwMS with secondary progressive type of MS had increased participation restrictions compared to persons with the primary progressive form. This difference was consistent also when age, disease duration and clinical characteristics were controlled for. Several studies have revealed that depression, mood and anxiety are more prevalent in people with secondary progressive type of MS than primary progressive[40]. It is possible that these factors can explain observed differences between groups.

The results of the study underline the association of activity and cognitive deficits on participation, especially in moderately to severely disabled PwMS. This is important since they are factors that can potentially respond to intervention. Reducing activity limitations and cognitive deficits might thus lead to better participation. This, however, remains to be studied in future intervention studies. Further, the cut off scores can be used as guidance for the physician to detect PwMS having participation restrictions and thus reduce the impact of the deficits in order to improve their participation.

While the present study has strengths, such as, the number of participants and the inclusion of modifiable factors such as mobility, hand function and cognition that influence participation it

does have some limitations. First, recruitment of participants attending rehabilitation centers led to an overrepresentation of PwMS with moderate to severe disability. In addition, mildly cognitive disorders may have reduced the reliability of patient-reported outcomes. Second, this study featured a cross sectional design with correlation and regression analyses making definitive causation impossible.

Lastly, we did not measure specific factors that may have a direct impact on participation, such as depression, anxiety, fatigue, sensory disorders, presence of caregiver and internal-external barriers.

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