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The impact of cognitive rehabilitation on quality of life in multiple sclerosis: A pilot study

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Abstract

Background: Cognitive impairment in people with multiple sclerosis (pwMS) negatively impacts daily function and quality of life (QoL). Prior studies of cognitive rehabilitation in pwMS have shown limited benefit but many focused on cognitive function scores rather than QoL measures. Studies using QoL metrics primarily evaluated group cognitive rehabilitation, which may be less appropriate due to variable cognitive profiles in pwMS. This study assesses the impact of an individualized cognitive rehabilitation approach on QoL in MS.

Methods: We performed a retrospective chart review of NeuroQoL assessments done by pwMS ($n = 12$, mean age 47.9 ± 4.0 years, 75% female, 100% White, 75% RRMS) before and after participation in an individualized compensatory cognitive program. We used a comparison group of pwMS who were candidates for the program but did not participate ($n = 9$, mean age 48.9 ± 4.4 years, 88.9% female, 100% White, 66.7% RRMS)

Results: PwMS who participated in the rehabilitation program saw improvements in Sleep Disturbance (50.5 from 55.5, $p = 0.005$), Fatigue (52.5 from 57.0, $p = 0.024$), Anxiety (49.8 from 55.4, $p = 0.011$), and Cognitive Function (39.3 from 36.7, $p = 0.049$).

Conclusions: Individualized compensatory cognitive rehabilitation appears effective for improving QoL measures in pwMS with cognitive complaints, supporting the need for further randomized controlled prospective analysis of this intervention.

Keywords: Multiple sclerosis, quality of life, rehabilitation, outcome measurement

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Introduction

Multiple sclerosis (MS) is a neurodegenerative disease characterized by relapsing events of inflammatory demyelination, as well as chronic progressive insidious white matter and grey matter atrophy. Cognitive impairment often manifests as a result of the progressive aspect of the disease. The prevalence of cognitive impairment in people with MS has been reported to be between 40-70%.[1] Cognitive challenges affect daily functions such as employment, errands and chores, medication adherence, symptom management, and coping skills. Limitation in daily function can increase caregiver burden and have a negative impact on quality of life.[1]

Cognitive rehabilitation is a therapy designed to help patients with cognitive challenges. Rehabilitation approaches include restitution strategies to retrain cognitive skills and compensation strategy training to improve coping mechanisms for existing cognitive deficits.[2] There are a variety of cognitive rehabilitation programs around the world, and their measured efficacy and perceived benefit is similarly varied. Many studies use cognitive domain scores for their primary outcome measures.[3] However, it may be more appropriate to look at outcomes of quality of life, especially in rehabilitation programs that use compensation strategy training.

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The compensation strategy programs aim to improve function, not cognitive deficits. Quality of life scores may improve despite a lack of improvement in cognitive domain scores.

Our institution offers an Integrated Cognitive Rehabilitation Program (ICRP) for patients with mild to moderate cognitive impairment. Specialists from occupational therapy, speech language pathology, and neuropsychology work together to evaluate patients and develop function-based compensatory interventions to help them work around their functional deficits.[4] The program begins with an evaluation process, in which each patient is assessed through a discipline specific lens to create a comprehensive view of the patients current cognitive and functional profile. Patients then work individually with the therapists to address identified patient specific goals rather than in a group setting. Intervention is patient specific and tailored. This study seeks to characterize changes in quality of life measures associated with participation in individualized cognitive rehabilitation in people with MS (pwMS).

Methods

We performed a single center retrospective observational study of patients with MS seen at the University of Rochester Multiple Sclerosis Center. The goal of the study was to quantify changes in quality of life measures obtained before and after participation in the ICRP. In an attempt to account for test-retest bias, we also looked at a comparison group composed of candidates for ICRP who did not participate in the program due to travel barriers.

Outcome measures

NeuroQoL (Quality of Life in Neurological Disorders)[5] assessments were used as primary outcome measures, specifically the domains of Sleep Disturbance, Fatigue, Anxiety, Depression, Stigma, Cognitive Function, Social Role Participation, and Social Role Satisfaction. Patients seen at our MS center have the opportunity to participate in the Multiple Sclerosis Partners Advancing Technology & Health Solutions (MS PATHS)[6] program. As part of this program, at every routine visit, subjects complete a series of functional assessments and questionnaires. One evaluation generates a t-score for each Neuro-QoL domain, in relation to a normal population distribution. The Processing Speed Test (PST), a 120 second Symbol Digit Modality Test (SDMT) included in the MS PATHS evaluation, was used as a secondary outcome measure. NeuroQoL and PST scores become available in the electronic medical record at the time of each visit.

Cognitive rehabilitation program

During routine clinical follow up visits in our MS Center, providers screen patients for subjective cognitive complaints as part of the MS related review of systems. If this screen is positive, providers discuss possible secondary causes of cognitive impairment with patients such as depression, poor sleep, and metabolic abnormalities. If these are addressed and patients continue to report subjective difficulties (such as memory difficulties, attention difficulties, slowed processing speed, difficulty with abstract reasoning, or word finding difficulties) they are offered referral to the ICRP. If patients are interested in the ICRP and able to attend, they are referred and scheduled for an intake evaluation. During intake, a patient is evaluated by a neuropsychologist, speech language pathologist, and occupational therapist to identify the individual's cognitive and functional deficits. If the neuropsychiatric evaluation suggests that mood disturbance is a substantial source of their cognitive complaints, patients are turned away from the cognitive rehabilitation program and given resources for mental health services. Patients accepted into the program return for an average of 3-4 treatment sessions of SLP and/or OT to develop compensatory and adaptive strategies to improve daily function.

Patient selection

Intervention Group – We used referral documentation to identify subjects who participated in the ICRP from the MS Center between January 1 2017 and December 31st, 2019. One of the authors (KCM) conducted manual chart reviews to confirm the diagnosis of multiple sclerosis and to abstract subject demographics, NeuroQoL scores, and PST scores. Subjects were excluded if they were not enrolled in MS PATHS, did not complete MS PATHS evaluations both before and after participation in the ICRP, or if they had documentation of an MS relapse or steroid use within three months of referral to the ICRP. To reduce variability, the MS PATHS evaluations were required to be within the 6 months prior to starting the ICRP, and within 6 months after completing participation in the ICRP.

Comparison Group – We used an informatics query available from our Clinical and Translational Science Institute to identify patients with a diagnosis of MS (ICD-10: G35) and any mention of "ICRP" or "Cognitive Rehabilitation" in their chart after January 1st, 2017. This date was chosen because

MS PATHS was launched at our site in early 2017. As with the intervention group, manual chart review was used to confirm the diagnosis of MS and to abstract demographics and scores. The manual chart review was also used to confirm via clinician documentation that the subject was an appropriate candidate for the ICRP. For example, patients would be excluded if a clinician documented that referral to the ICRP would be considered if their cognition worsened. Potential subjects were also excluded if they were not enrolled in MS PATHS, if they did not have an MS PATHS evaluation within 6 months pre- and post- documentation of candidacy for ICRP, or if they participated in the ICRP.

Statistical analysis

Results were reported descriptively. Differences by groups were assessed using two sample t-tests for continuous variables and Fishers Exact test for categorical variables. Differences between scores within groups were assessed with the repeated measures t-test. No corrections were performed for multiple testing. Data analysis was conducted using Microsoft Excel and SAS software (University Edition 3, SAS Institute Inc).

Data availability

Due to the potential for loss of patient confidentiality, complete individualized data cannot be made publicly available; however, anonymized data may be shared at the request of qualified investigators.

Results

Of the 74 patients referred from the MS Center who participated in the ICRP, 12 subjects met inclusion criteria for the ICRP intervention group. Of the 232 subjects identified from the CTSI informatics query, 9 subjects met inclusion criteria for the comparison group (Figure 1). 5 of those 9 subjects were unable to participate due to travel barriers. Demographics and baseline scores are depicted in Table 1. Characteristics of age, sex, race, MS type, and baseline timed 25-foot walk were similar across groups. Baseline NeuroQoL domain scores did not differ between the two groups. The mean baseline processing speed test (PST) score was higher in the comparison group compared to the ICRP group (53.2 vs 36.0, $p = 0.018$).

NeuroQoL domains were separated into Function Domains and Symptom Domains for ease of interpretation (Figure 2). Higher Function Domain scores indicate better function, and higher Symptom Domain scores indicate more severe symptoms. Mean Cognitive Function scores improved following participation in ICRP (39.3 from 36.7, $p = 0.049$). There was no change in Cognitive Function scores over time in the comparison group. There were no changes in either group seen in Social Role Participation or Social Role Satisfaction scores.

Sleep Disturbance scores improved after participation in the ICRP (50.5 from 55.5, $p = 0.005$), as did Fatigue scores (52.5 from 57.0, $p = 0.024$) and Anxiety scores (49.8 from 55.4, $p = 0.011$), while no significant changes were seen over time for these domains in the comparison group. No changes were seen in Depression scores (48.8 from 50.4, $p = 0.238$) after participation in the ICRP; in the comparison group, Depression scores did improve over time (43.5 from 47.2, $p = 0.046$). No significant changes were seen over time in Stigma scores in either group.

PST scores did not change over time in the ICRP group (36.0 to 39.2, $p = 0.113$) nor in the comparison group (53.2 to 55.2, $p = 0.232$).

Discussion

This study provides preliminary data suggesting that individualized compensatory cognitive rehabilitation is effective at improving quality of life measures in pwMS and cognitive complaints. Although the sample size was small, the subjects that participated in the ICRP saw improvement in 4 quality of life domains—Anxiety, Fatigue, Sleep Disturbance, and Cognitive Function—as compared with the comparison group. It should be noted that while PST scores in the ICRP group did not improve, this was an expected outcome as the goal of this program was to improve function using adaptive strategies, not to improve the cognitive deficits per se.

The comparison group did see improvement in their Depression quality of life scores as compared with the ICRP group. Depression can manifest as cognitive changes; it is possible that patients who did not pursue ICRP elected to focus on primarily addressing mood concerns. While we did not necessarily expect Depression scores to improve in the ICRP group, because there is not a mental health treatment focus of the program, the improvement in anxiety scores may reflect education regarding individual deficits and lessened uncertainty about ability to function. It is also possible that the comparison group Depression score improvement represents an aberrant result due to limited scale sensitivity or the multiple comparisons made within this study. As a

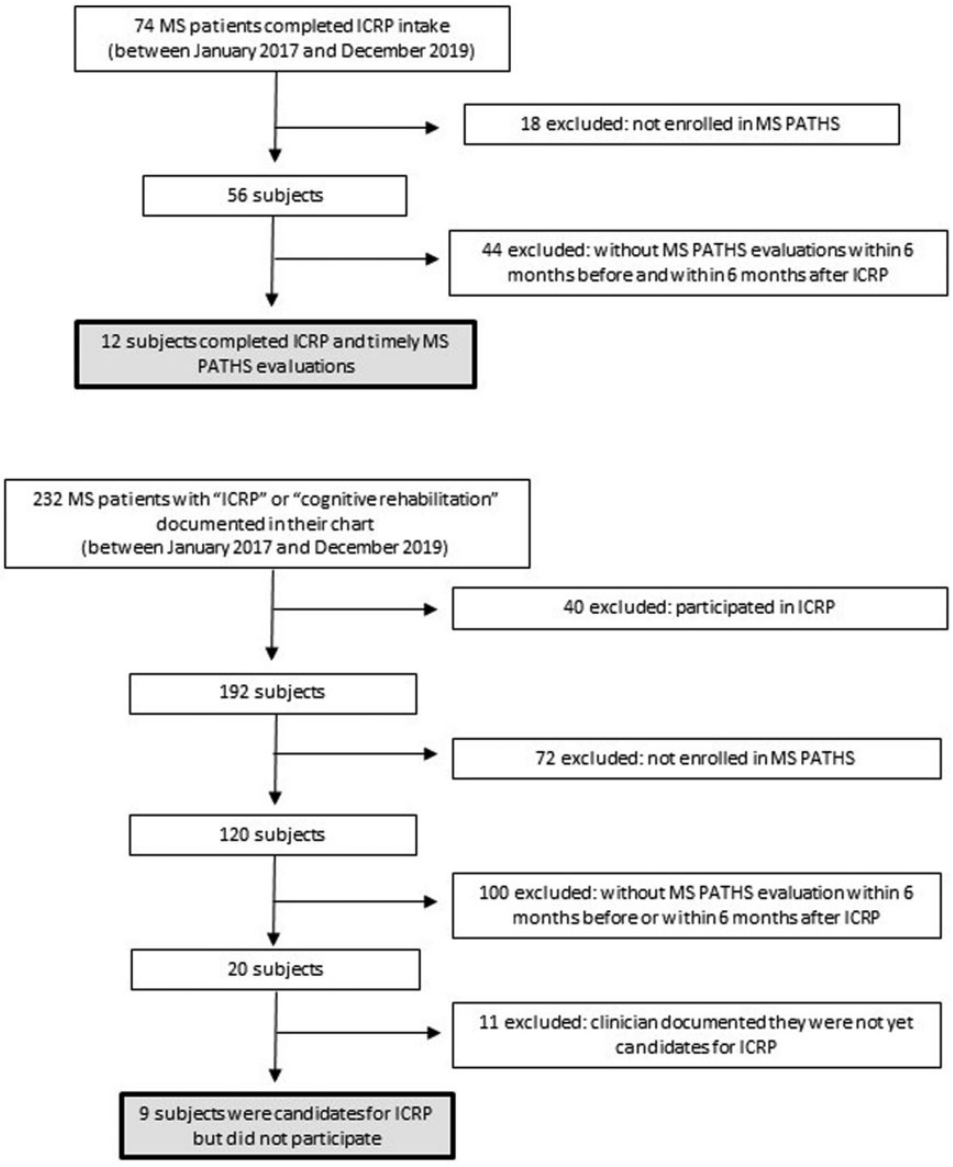

Figure 1. Patient selection methods for the ICRP intervention and comparison groups.

result, these findings are interpreted with caution; future studies with a larger sample size are indicated to reduce the risk of type 2 error.

Prior studies have used quality of life measures as their primary outcome measure with mixed results.[7–10] Notably these studies used group cognitive rehabilitation sessions rather than individual therapy sessions. The authors noted a need for additional studies to see if the benefit identified in some of the studies was due to the supportive group setting rather than any cognitive retraining or adaptation. Individual compensatory rehabilitation has been studied quantitatively in psychiatric disorders such as schizophrenia, bipolar, and depression[11] and qualitatively in stroke survivors;[12] however, it appears that no two programs are precisely alike. Individualized cognitive rehabilitation may be more appropriate for people with MS because cognitive profiles and adaptive strategy preferences within this population vary greatly.

The authors acknowledge multiple limitations of the study. While the comparison group was created in order to address test-retest bias, this was not a true control group because of the retrospective nature of the study. This was reflected in the differences seen in baseline PST scores. The better baseline scores

Table 1. Demographic characteristics and baseline mean [±SE] scores comparing the group that participated in the Integrated Cognitive Rehabilitation Program (ICRP) and the group that did not participate in the ICRP.

	ICRP Group (n = 12)	No ICRP Group (n = 9)	p-value
Age (years)	47.9 [±4.0]	48.9 [±4.4]	0.87
Sex (% Female)	75%	88.9%	0.60
Race (% White)	100%	100%	
MS Type (% RRMS)	75%	66.7%	1.00
Timed 25 Foot Walk (seconds)	7.0 [±0.8]	6.4 [±0.5]	0.53
PST Score	36.0 [±4.4]	53.2 [±5.0]	0.02
NeuroQoL domain: Sleep Disturbance	55.5 [±1.8]	50.9 [±2.7]	0.158
NeuroQoL domain: Fatigue	57.0 [±1.9]	52.0 [±3.0]	0.151
NeuroQoL domain: Anxiety	55.4 [±2.2]	51.1 [±3.1]	0.266
NeuroQoL domain: Depression	50.4 [± 2.5]	47.2 [±2.8]	0.409
NeuroQoL domain: Stigma	54.4 [±1.6]	48.8 [±2.9]	0.088
NeuroQoL domain: Cognitive Function	36.7 [±1.7]	43.4 [±4.1]	0.115
NeuroQoL domain: Social Role Participation	43.9 [±2.4]	47.3 [±2.2]	0.336
NeuroQoL domain: Social Role Satisfaction	43.1 [±1.6]	46.5 [±2.5]	0.244

Note: Age, Time 25 Foot Walk, Processing Speed Test (P ST), and NeuroQoL domains were compared using a two sample t-test. Categorical variables of Sex and MS Type were compared using Fishers Exact Test. The bolded p-value indicates the significant difference between baseline PST scores.

may indicate that this group did not feel impaired enough to try to overcome the travel barriers that were cited as the reason for not participating in the ICRP.

The racial representativeness of the two groups is not ideal, as we note that all of the subjects identified as White. In our electronic medical record system, nearly 90% of patients who carry a diagnosis of MS identify as White, suggesting that 2-3 subjects identifying as non-White would be expected in this study. The lack of racial diversity in this small study sample may be attributable to sampling error. However, it limits generalizability of the study results to under-represented populations. More importantly, it stands as a reminder to identify and correct potential reasons that under-represented populations may be less likely to be referred to the ICRP or enrolled in research.

It is also difficult to know whether the statistically significant findings correspond with clinically meaningful findings. To recap, a score of 50 represents the z-score of 0, and 10 points represents one standard deviation. It seems reasonable to hypothesize that the half standard deviation improvement in the Anxiety, Fatigue, and Sleep Disturbance quality of life domains could be both clinically and statistically significant. While this remains unclear, this study contributes to discussions about what constitutes a clinically significant change in NeuroQoL scores.[13,14]

An area for additional study is longer follow up. We only evaluated the first post-rehabilitation quality of life measures. A few subjects had repeat NeuroQoL evaluations, but not enough to complete a meaningful statistical analysis. Because of this, it is unclear whether there was lasting benefit beyond the first 6 months. Lastly, the sample size was not large enough to identify subgroups of subjects that derived the most benefit from the ICRP. In the future, with a larger sample, it would be helpful to look at changes in scores by MS phenotype (relapsing vs progressive), by age, and by baseline PST and NeuroQoL scores.

In spite of the study limitations, the preliminary benefit shown in multiple quality of life domains following the ICRP program is encouraging regarding the use of individual compensatory rehabilitation strategies in people with MS. This is particularly important given the lower likelihood of true improvement in cognitive scores due to the neurodegenerative nature of the disease. Future directions for this work include analysis of qualitative data to better assess the subjective clinical impact of the objective improvement in quality of life measures. This qualitative evaluation may also give insight into what strategies from the program are most beneficial

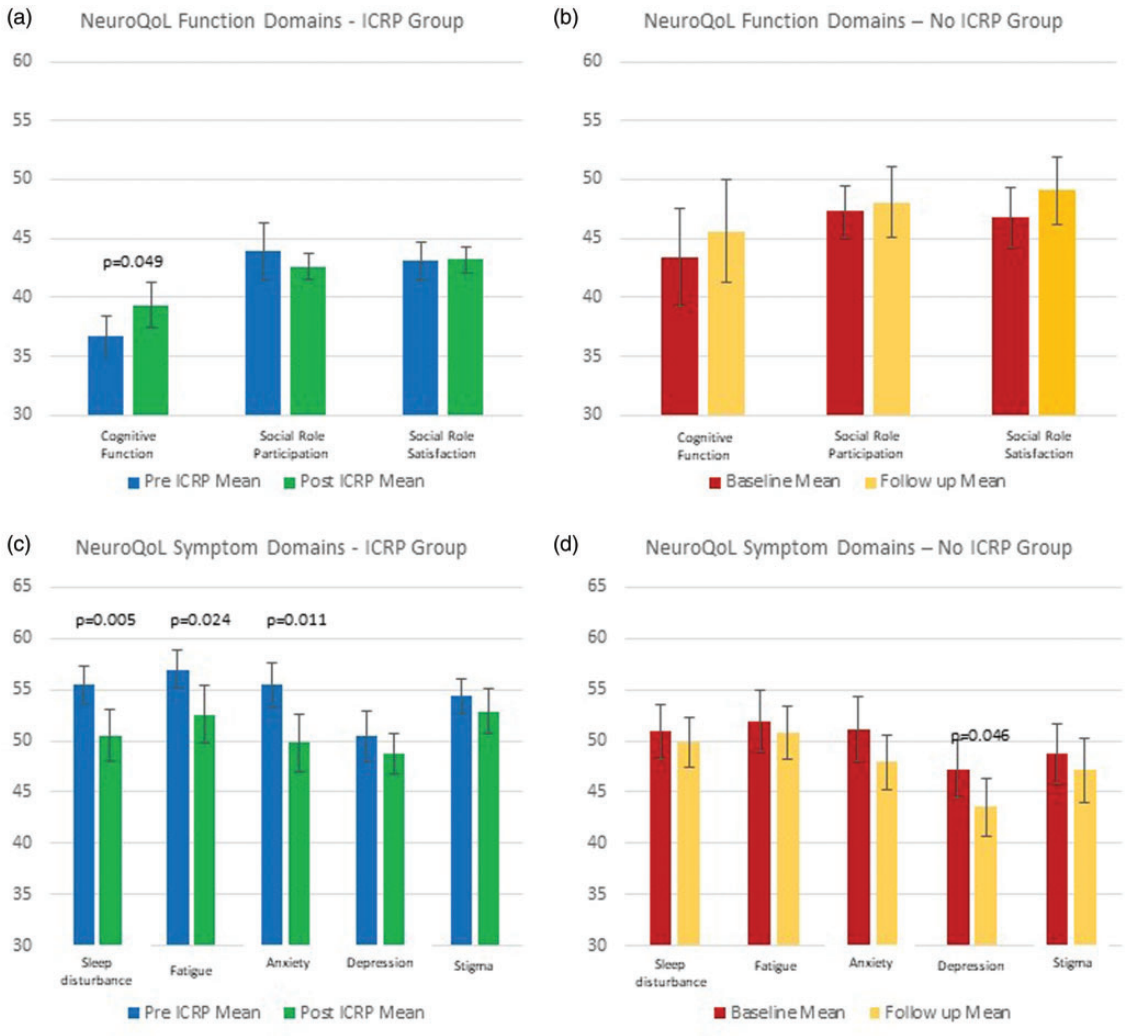

Figure 2. NeuroQoL mean group scores before and after participation in ICRP. Error bars represent standard error. [a] Mean function domain scores before and after cognitive rehabilitation. Higher scores represent better quality of life related to function. Quality of life related to cognitive function significantly improved. [b] Mean function domain scores where ICRP was recommended but not completed. [c] Mean symptom domain scores before and after cognitive rehabilitation. Lower scores represent better quality of life related to function. Quality of life related to sleep disturbance, fatigue, and anxiety significantly improved. [d] Mean symptom domain scores where ICRP was recommended but not completed. Quality of life related to depression significantly improved .

to people with MS. Data from this study may be used to design a prospective study randomizing potential ICRP candidates to either ICRP or an active control group. A larger prospective study should allow for the additional desired subgroup analyses.

Conflict of Interests

Author MH receives research support from Biogen and PCORI. Author AM has no disclosures to report.

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