PERFORMANCE AND PARTICIPATION OUTCOMES FOR INDIVIDUALS WITH NEUROLOGICAL CONDITIONS

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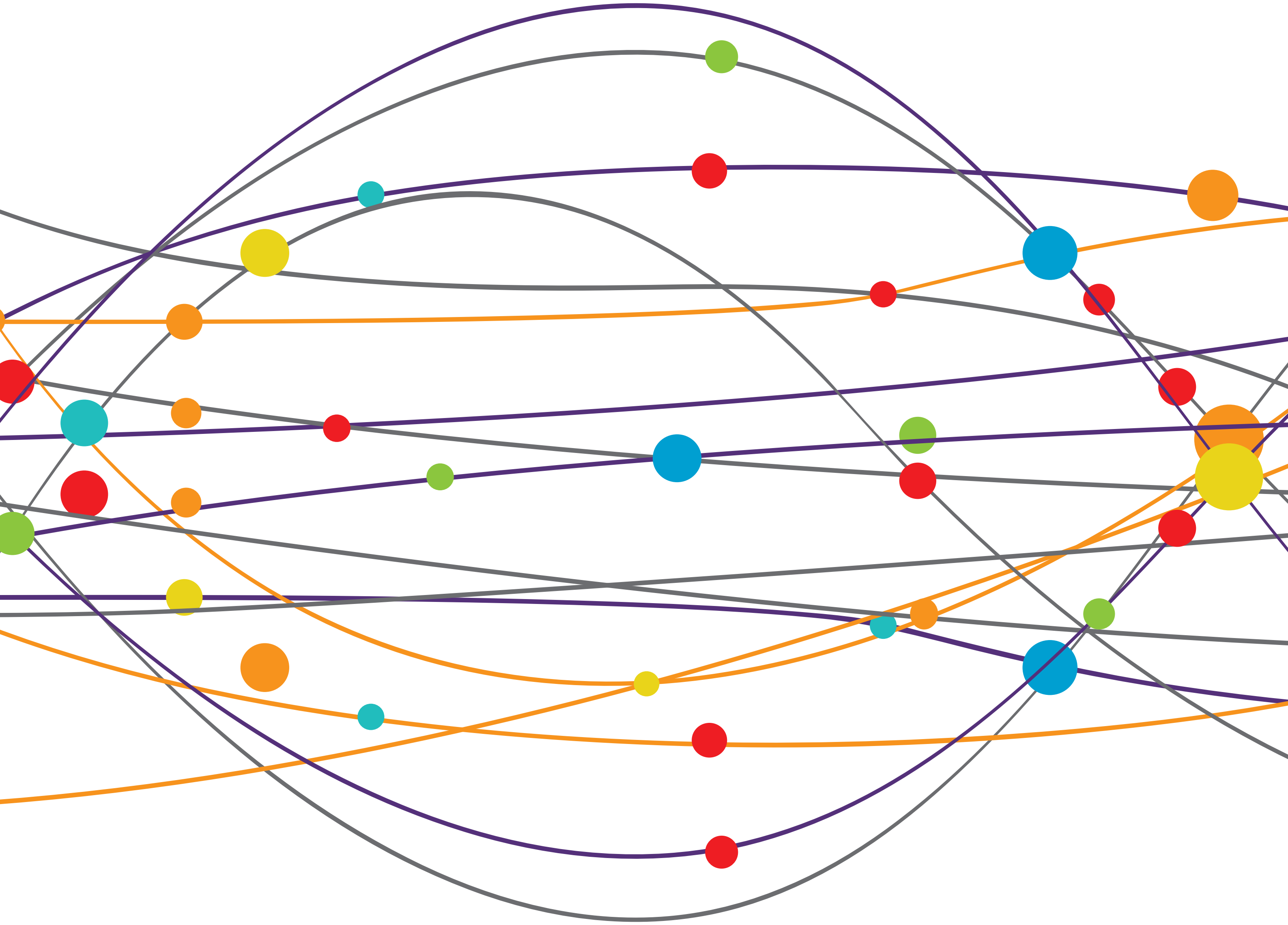

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PERFORMANCE AND PARTICIPATION OUTCOMES FOR INDIVIDUALS WITH NEUROLOGICAL CONDITIONS

Topic Editors:
Naomi Josman, University of Haifa, Israel
Lisa Tabor Connor, Washington University in St. Louis, United States
David Jing-Piao Lin, Massachusetts General Hospital, Harvard Medical School
Boston, United States

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EDITORIAL
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Editorial: Performance and Participation Outcomes for Individuals With Neurological Conditions

Naomi Josman[1]*, *Lisa Tabor Connor*[2] *and David J. Lin*[3,4]

[1] Department of Occupational Therapy, Faculty of Social Welfare & Health Science, University of Haifa, Haifa, Israel, [2] Program in Occupational Therapy, Departments of Neurology & Social Work, Washington University School of Medicine, St. Louis, MO, United States, [3] Department of Neurology, Center for Neurotechnology and Neurorecovery, Massachusetts General Hospital and Harvard Medical School, Boston, MA, United States, [4] Division of Neurocritical Care and Emergency Neurology, Department of Neurology, Massachusetts General Hospital, Boston, MA, United States

Keywords: central nervous system deficits, neurorehabiliation, cognition, neurorecovery, neuroplasticity, stroke recovery

Editorial on the Research Topic

Performance and Participation Outcomes for Individuals With Neurological Conditions

People suffering from neurological conditions such as Parkinson's disease, stroke, and brain injury encounter and endure numerous situations in their daily lives that cause excess disability and restrict full participation in their meaningful activities.

Neuroscience and rehabilitation science are complementary disciplines, engaged in the exploration of the human Central Nervous System (CNS) and the amelioration of functional disability. There is often, however, a lack of discourse between these disciplines, which precludes opportunities for meaningful exchange and synergistic collaboration to improve the lives of people who suffer from a disability.

The goal of this current theme issue was to foster original research papers in neuroscience and rehabilitation science that may serve to address the existing disconnect between disciplines. This platform offered an opportunity for a meaningful exchange of ideas, findings, and practices toward ultimately promoting knowledge, improving clinical practice, and reducing performance deficits and participation restrictions for people with neurological ailments and diseases. This broader, biopsychosocial approach to understanding rehabilitation and recovery from neurological deficits, embraces the concept that true understanding of recovery and living with a chronic condition, goes beyond knowledge of disease mechanisms. Social determinants and secondary disease sequelae may have a significant impact on functional performance and participation.

The initial call for papers invited researchers and practitioners to submit research papers on the topic of "Performance and Participation Outcomes for Individuals with Neurological Conditions." This focused topic recognized the need for a more comprehensive and integrative perspective in research and practice to address this disconnect between neuroscience and rehabilitation. This perspective should thus reveal neglected key domains, as well as incorporate a range of components intricately involved in human performance, such as motor, sensory, cognitive, and emotional components. Such integration may serve to significantly enhance the functional outcomes for persons suffering from any of the range of neurological conditions.

The theme call aimed at addressing these respective issues by soliciting original research papers, review articles, or meta-analyses, covering topics ranging from basic research to translational studies anchored in neuroscience or rehabilitation.

Edited and reviewed by:
Giorgio Sandrini,
University of Pavia, Italy

****Correspondence:***
Naomi Josman
njosman@univ.haifa.ac.il

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The encouraging response to our call yielded 22 submitted papers that underwent a peer-review process. Ultimately, 16 papers were adjudged to favorably meet the theme call objectives and scientific standards. As this special issue was designed to organize our thinking around outcome, rather than disease, we provide a classification of the articles by their primary outcome focus. We categorized the papers as addressing prognostic indicators of recovery (4 articles), performance (4 articles), or participation (8 articles). Schliep et al.; Valè et al.; Wang, Wang et al.; and Sul et al. addressed the need for greater understanding of prognostic indicators of recovery such as lesion location, behavioral characteristics, EMG assessment in motor disorders, and the initiation of swallowing in disorders of consciousness. Performance outcomes and their contributors was the focus of Fasoli and Adans-Dester, Ranford et al., Yael et al., and McCambridge et al.. The vast majority of the papers included in this special issue cluster around the multifactorial outcome of participation: Rotenberg et al., Malone et al., Yosef et al., Wang, Chan et al., Toglia et al., Erler et al., Nicholas et al., and Cattaneo et al..

The breadth of neurological conditions and methodological approaches in this issue is astounding. Although broad in scope, our focus on the larger outcomes of people with neurological conditions, we believe, enables us to glean principles for maximizing performance and participation at the highest conceptual level. One of the most striking themes that emerged from this collection, for example, is that cognitive and emotional factors are of utmost importance for the performance of motor-intensive activities and participation in life activities that are motorically-demanding in diseases classically thought of as diseases of the motor system. Moreover, social support is a major predictor of resumption of pre-disease activities.

Of course, putting the focus on outcome introduces factors that are outside the purview of neurological science and will not replace studies focused on disease mechanisms that foster new treatment approaches aimed at treating or curing disease. The vast majority of the patients living with these neurological conditions will be doing just that—living with their chronic conditions. Our hope is that a more holistic scientific treatment of factors predicting outcome will advance our rehabilitation attempts to promote better living for people with neurological conditions.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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ORIGINAL RESEARCH
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Association of Lesion Location With Long-Term Recovery in Post-stroke Aphasia and Language Deficits

Bomi Sul[†], *Kyoung Bo Lee*[†], *Bo Young Hong, Joon Sung Kim, Jaewon Kim, Woo Seop Hwang and Seong Hoon Lim*[*]

Department of Rehabilitation Medicine, St. Vincent's Hospital, College of Medicine, The Catholic University of Korea, Seoul, South Korea

Background: Recovery from post-stroke aphasia is important for performing the activities of daily life, returning to work, and quality of life. We investigated the association between specific brain lesions and the long-term outcome of four dimensions of aphasia: fluency, comprehension, naming, and repetition 12 months after onset in patients with stroke.

Methods: Our retrospective cross-sectional observational study investigated the relationship between the Korean version of the Western Aphasia Battery scores in 31 stroke patients 1 year after the onset of stroke and stroke lesion location. Brain lesions were assessed using voxel-based lesion symptom mapping (VLSM) in conjunction with magnetic resonance imaging.

Results: Damage to the Rolandic cortex, Heschl's gyrus, the posterior corona radiata, supramarginal cortex, superior longitudinal fasciculus, superior temporal gyrus, and insula was associated with a low total AQ score. Lesions in the inferior triangularis and inferior operculum of the frontal cortex, supramarginal cortex, and insula were associated with a poor fluency outcome. Damage to the parietal cortex, angular cortex, temporal middle cortex, sagittal stratum, and temporal superior cortex was associated with poor recovery of comprehension skills. Lesions in the angular cortex, supramarginal cortex, posterior corona radiata, superior longitudinal fasciculus, internal capsule, temporal superior cortex, and temporal middle cortex were associated with poor recovery of naming in patients with stroke. Damage to the superior temporal cortex, posterior corona radiata, and superior longitudinal fasciculus was associated with poor recovery of repetition component.

Conclusions: We identified specific brain lesions associated with long-term outcomes in four dimensions of aphasia, in patients with post-stroke aphasia. Our findings may be useful for advancing understanding for the pathophysiology of aphasia in stroke patients.

Keywords: stroke, aphasia, K-WAB, prognosis, outcome, brain imaging, VLSM

Edited by:
Lisa Tabor Connor,
Washington University in St. Louis,
United States

Reviewed by:
Alessandro Giustini,
Consultant, Arezzo, Italy
Carlo Cavaliere,
Institute of Research and Medical
Care (IRCCS) SDN, Italy

***Correspondence:**
Seong Hoon Lim
seonghoon@catholic.ac.kr

[†] *These authors have contributed equally to this work*

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INTRODUCTION

Aphasia is a language disorder typically caused by stroke-related damage to the dominant hemisphere. Post-stroke aphasia is associated with mortality, disability, and the use of health services. The long-term outcomes for post-stroke aphasia vary widely. Recovery from aphasia is important for performing the activities of daily life, returning to work, and quality of life in patients with stroke (1).

Several studies have investigated the prognosis of speech and language after stroke. Factors predicting post-stroke aphasia recovery include lesion size and location, aphasia severity, and the type of speech deficit (2). Additionally, stroke severity at onset and the Western Aphasia Battery (WAB) score 72 h after onset (3, 4), and the specific brain regions damaged, affect the long-term prognosis of post-stroke aphasia (2, 5–8). The involvement of Broca's area, the superior temporal gyrus, arcuate fasciculus, and superior longitudinal fasciculus are associated with a poor prognosis in patients with chronic post-stroke aphasia at 4–6 months after onset (5, 6, 8). However, the timing of 4–6 months after onset might be less sufficient to reflect full functional recovery, further neurological recovery is thought to be likely (9). Knowledge of the role or specific brain lesions may facilitate the understanding of the pathophysiology of aphasia and could then be used as basis for neuromodulation strategies for aphasia, such as repetitive trans-magnetic stimulation or trans-cranial electric stimulation (10–12).

Thus, we investigated the roles that specific brain lesions play in recovery of deficits in fluency, comprehension, naming and repetition of language, using lesion symptom mapping methods that included analyses of brain magnetic resonance imaging (MRI) scans and clinical language test, in patients with first-ever supratentorial strokes 12 months after stroke onset.

METHODS

Study Design and Participants

Our retrospective observational study included the data of 31 post-stroke aphasia, right-handed patients with first-stroke patients recruited from a single inpatient/outpatient center between January 2011 and December 2017. The inclusion criteria were: (1) first-ever supratentorial stroke, (2) a single ischemic or hemorrhagic left hemisphere lesion confirmed by magnetic resonance imaging (MRI), (3) right handedness, (4) native Korean speaker, (5) at least 9-years of education, (6) no prior history of psychiatric or neurological disorders, (7) absence of central or peripheral paretic dysarthria, and (8) completion of a language assessment using the Korean version of the Western Aphasia Battery (K-WAB) 1 year after the onset of stroke (6). No restrictions were placed on the type or severity of the aphasia. Subjects were excluded if they had any other functional or structural brain disorder. Similarly, to previous studies for brain lesion analysis, we included the patients with stroke, regardless of type; ischemic and hemorrhagic (13–15). Of the 214 individuals who underwent language assessment for aphasia after stroke, 31 qualified for the study. All subjects received speech therapy and other rehabilitation therapy; physical or occupational therapies as needed. The rehabilitation program of all subjects had started within 5 days after onset. The speech therapy continued up to 12 months after onset, and consisted of with 0.5–2 h per week, respectively.

Demographic characteristics and language assessments were obtained for all subjects. High-resolution 1.5T anatomical MRI scans with 5-mm slice thickness were used to determine the precise location of the brain lesion (16). All participants underwent the same MRI scanning protocol. We used a 1.5-Tesla Philips MR scanner (ACHIEVA, Philips, Netherlands). The MRI protocol included whole-brain, three-dimensional, T1-weight images (TR/TE = 527.4/13, Slice thickness 5 mm, GAP 1.5 mm, flip angle 90', Refocus angle 180', FOV 230*230, Matrix 304*222, Voxel size 0.75*1.02*5 mm, NEX 2), T2-weight images (TR/TE = 4500/100, Slice thickness 5 mm, GAP 1.5 mm, flip angle 90', Refocus angle 160', FOV 230*230, Matrix 384*233, Voxel size 0.6*0.86*5 mm, NEX 2), and fluid-attenuated inversion-recovery (FLAIR) axial images (TR/TE = 6000/100, Slice thickness 5 mm, GAP 1.5 mm, flip angle 90', Refocus angle 150', FOV 230*230, Matrix 304*222, Voxel size 0.75*1.02*5 mm, NEX 2). The study protocol was reviewed and approved by the Institutional Review Board of The Catholic University, College of Medicine (Registry No. VC18RESI0112). The requirement for informed consent was waived by the board.

Language Test

The validated K-WAB was administered to all patients on admission by a single speech language pathologist; however, only data from cases of aphasia caused by first-ever stroke were subjected to analysis. The K-WAB assessment consists of four subsets: fluency, comprehension, repetition, and naming (7, 17). The severity of aphasia was quantified using the aphasia quotient (AQ; range, 0–100), which was calculated using the formula developed by Kertesz (fluency score + comprehension score/20 + naming score/10 + repetition score/10) ×2 (17). The data of K-WAB measured at 1 year after onset were used for outcome of language recovery.

Lesion Analysis and Statistical Analysis

Lesion locations and sizes were assessed using MRIcron software (http://www.mricro.com/mricron). T2 images were co-registered with each participant's T1 MRI, and then, the T1

TABLE 1 | Patient demographic and clinical characteristics.

Demographics (n = 31)	
Gender, M/F (%)	51.6/48.4
Age, years*	55.5 ± 11.5
Time from onset of stroke to speech evaluation, days*	725.9 ± 233.4
Stroke pathology, hemorrhage/infarction (%)	51.6/48.4
Brain injury location (*n*, %)	
Cortex	14 (45.2)
Subcortex	6 (19.3)
Mixed (cortex and subcortex)	11 (35.5)
Lesion Volume voxels (*n*)*	55482.16 ± 43109.30

**Mean ± SD. M, male; F, female.*

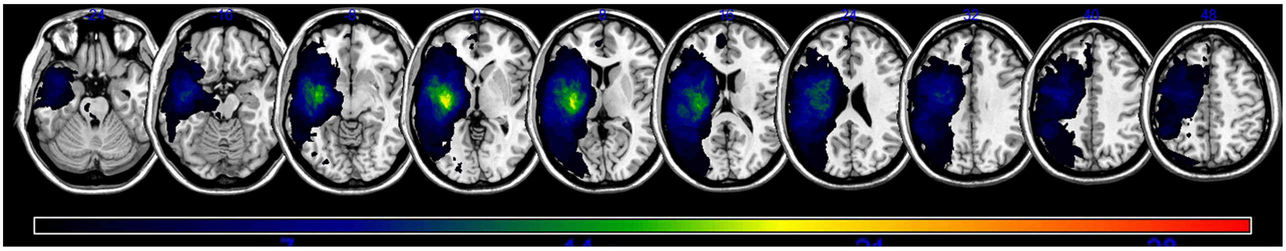

FIGURE 1 | A lesion overlap map of all subjects ($n = 31$). The color spectrum indicates the frequency of overlap.

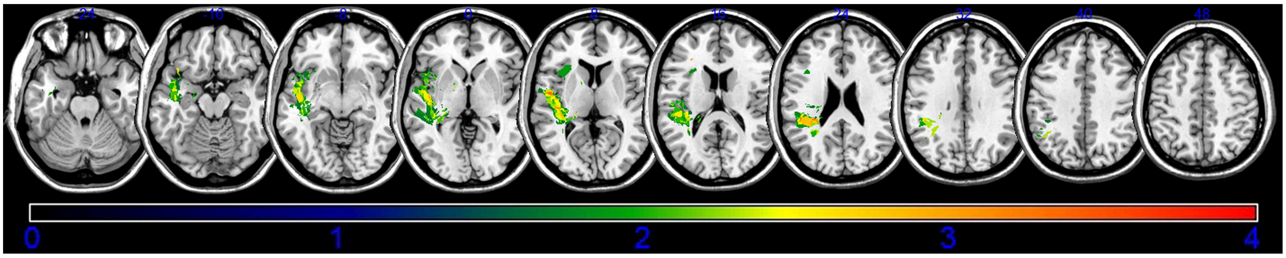

FIGURE 2 | Voxel-based lesion-symptom mapping of the total aphasia quotient after application of the non-parametric Brunner–Munzel test. The color scale indicates Brunner–Munzel rank order z statistics. Only voxels significant at $p < 0.05$ are shown. The statistical map shows voxels with a minimum Z score of 1.89797 and maximum range of 4, which was the maximum brightness.

and lesion maps were normalized to the Montreal Neurologic Institute (MNI) template using statistical parametric mapping 8 software (SPM8, http://www.fil.ion.ucl.ac.uk/spm/software/spm8) and non-parametric mapping (NPM) software (18–20). The number of MRI voxels in each stroke lesion was calculated, and the lesions were traced by a trained image analyst and confirmed by an experienced physiatrist (a neurorehabilitation specialist), who was blind to all clinical data. Only voxels indicating that at least 10% ($n = 3$) of the patients had lesions were included in the final analysis. The non-parametric Brunner–Munzel test for continuous data was used (15). Colored VLSM maps representing the z statistics were generated and overlaid onto the automated anatomical labeling and Johns Hopkins University white matter templates provided with the MRIcron software (18, 21).

RESULTS

The study included 31 patients (mean age, 55.5 ± 11.5 years; 15 females and 16 males). The mean time from the onset of stroke to the language assessment was 725.9 ± 233.4 days, and the mean brain lesion volume was 55482.16 ± 43109.30 voxels. Patient clinical and demographic data are shown in **Table 1**. The language assessment findings are shown in **Supplementary Table 1**.

An overlap map of the 31 lesions was created (**Figure 1**). The VLSM analyses using NPM revealed that lesions of the Rolandic cortex, Heschl's gyrus, posterior corona radiata, supramarginal cortex, superior longitudinal fasciculus (SLF), superior temporal gyrus, and insula were associated with a low total AQ (**Table 2**, **Figure 2**). The frontal inferior triangularis, frontal inferior operculum, supramarginal cortex, and insula were associated with fluency; the parietal cortex, angular cortex, temporal middle cortex, sagittal stratum, and temporal superior cortex were associated with comprehension; the angular cortex, supramarginal cortex, posterior corona radiata, SLF, internal capsule, temporal superior cortex, and temporal middle cortex were associated with naming; and the temporal superior cortex,

TABLE 2 | Total aphasia quotients associated with stroke lesions.

MNI coordinates (X, Y, Z)	BM *Z* max	*n* Voxels	Anatomical brain lesion
−49, −5, 8	2.71638	101	Rolandic cortex
−38, −25, 8	2.9998	110	Heschl
−29, −37, 24	3.03567	111	Posterior corona radiata
−46, −35, 28	2.94784	114	Supramarginal cortex
−37, −39, 25	2.77033	111	Superior longitudinal fasciculus
−45, 31, 16	2.5758	87	Temporal superior
−39, −15, 12	1.89797	85	Insula

Montreal Neurological Institute (MNI) coordinates of voxels using lesion overlay map of 31 subjects that were significant based on the Brunner–Munzel (BM) Z score and the number (n) of clustering voxels that survived the false discovery rate-corrected threshold of P < 0.05. Anatomical regions were identified using the automated anatomical labeling and Johns Hopkins University white matter templates.

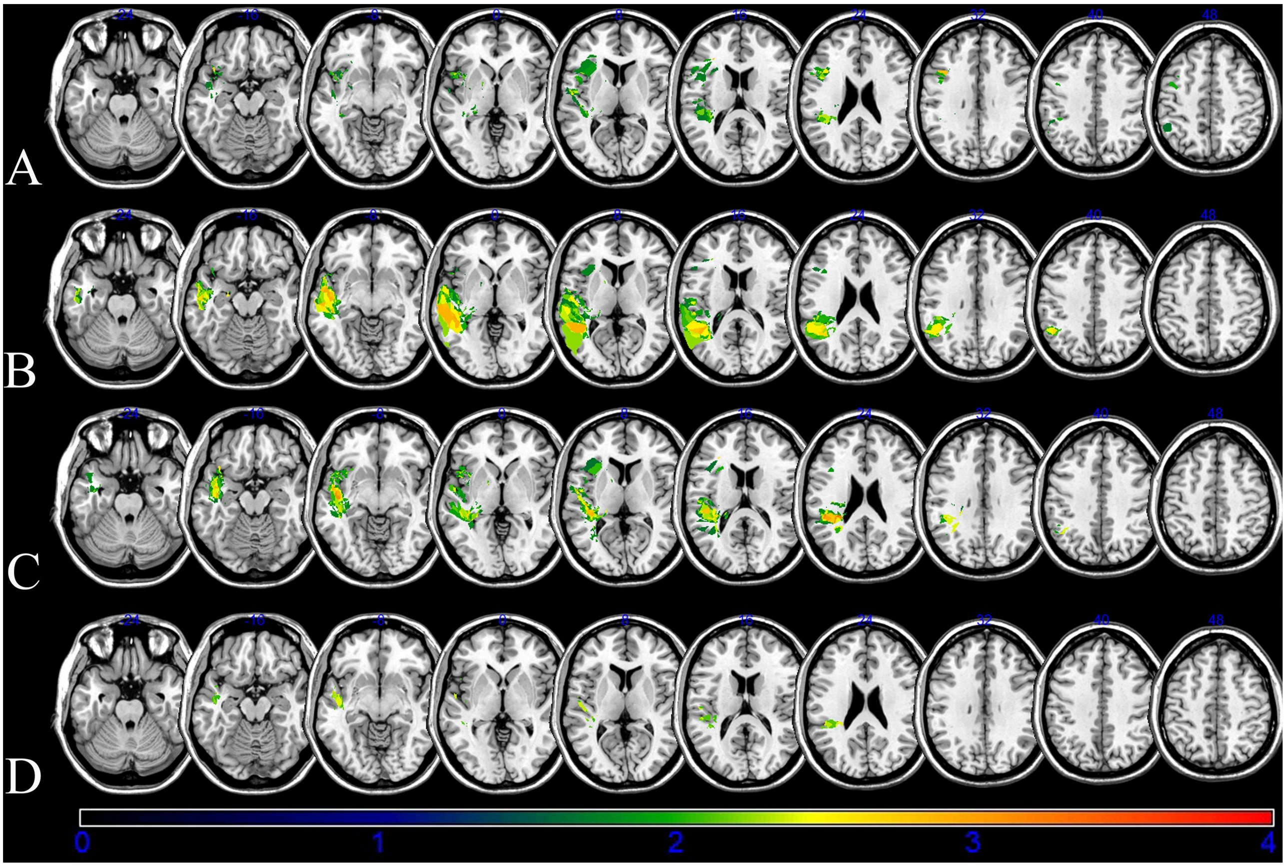

FIGURE 3 | Voxel-based lesion-symptom mapping (VLSM) of the language deficits after the non-parametric Brunner–Munzel statistical analysis. The color scale indicates Brunner–Munzel rank order z statistics. Only voxels significant at $p < 0.05$ are shown. The maximum range of the z score was set at 4, which was the maximum brightness. **(A)** VLSM for fluency with a minimum z score of 2.32076. **(B)** VLSM for comprehension with a minimum Z score of 2.50055. **(C)** VLSM for naming with a minimum Z score of 2.38888. **(D)** VLSM for repetition with a minimum Z score of 3.19465.

posterior corona radiata, and SLF were associated with repetition (**Table 3**, **Figure 3**).

The damage of supramarginal cortex affected fluency and naming. The temporal middle cortex and angular cortex related with recovery of comprehension and naming. The SLF and posterior corona radiata may affect the recovery of repetition and naming. The damage of the temporal superior cortex may affect outcome of comprehension, naming and repetition.

DISCUSSION

We found that lesion location was associated with long-term outcomes in fluency, comprehension, naming, and repetition in patients with aphasia at 12 months after stroke onset. Damage to the Rolandic cortex, Heschl's gyrus, posterior corona radiata, supramarginal cortex, superior longitudinal fasciculus, superior temporal gyrus, and insula were associated with overall poor outcomes. Lesions in the inferior triangularis and inferior operculum of the frontal cortex, supramarginal cortex, and insula were associated with poor fluency. Damage to the parietal cortex, angular cortex, temporal middle cortex, sagittal stratum, and temporal superior cortex was associated with poor comprehension skills. Lesions in the angular cortex, supramarginal cortex, posterior corona radiata, superior longitudinal fasciculus, internal capsule, temporal superior cortex, and temporal middle cortex were associated with poor recovery of naming ability, and damage to the superior temporal cortex, posterior corona radiata, and superior longitudinal fasciculus was related to poor recovery of repetition skills. These findings suggest that specific lesion sites are predictors of aphasia recovery in patients with first-ever stroke 12 months after onset.

Nowadays, neuromodulation with repetitive magnetic stimulation or trans-cranial electric stimulation for stroke patients has been widely investigated (12, 22–25). For neuromodulation, determining target specific brain lesion is important (10, 24, 26). Thus, the functions of specific brain lesions for stroke have been uncovered; motor of upper limb, gait, balance, and language (6, 13, 19, 27). These investigations would be useful for understanding of functional deficit of stroke, itself, and also for determining target brain lesion in neuromodulation therapy. Our findings may contribute to the understanding of aphasia itself, and further to usage of neuromodulation therapy of aphasia.

Previous studies have shown that the language network involving Broca's complex, including the inferior prefrontal

TABLE 3 | Stroke lesions associated with the aphasia dimensions.

Sub-quotients	MNI coordinates (X, Y, Z)	BM *Z* max	*n* Voxels	Patients with lesion (*n*)	Anatomical brain lesion
Fluency	−36, 15, 31	3.23888	83	11	Frontal inferior triangularis
	−37, 14, 30	3.23888	85	11	Frontal inferior operculum
	−43, −35, 26	2.32076	113	7	Supramarginal cortex
	−35, 12, 2	2.48052	98	12	Insula
Comprehension	−47, −46, 40	2.50055	113	6	Parietal cortex
	−47, −48, 35	2.50055	113	6	Angular cortex
	−44, −48, 6	2.88614	107	5	Temporal middle cortex
	−43, −29, −6	2.90267	114	11	Sagittal stratum
	−54, −4, −10	3.35279	107	7	Temporal superior cortex
Naming	−42, −55, 39	2.38888	102	5	Angular cortex
	−44, −37, 28	2.43480	116	5	Supramarginal cortex
	−28, −37, 23	3.15591	108	5	Posterior corona radiata
	−38, −40, 25	2.77023	111	6	Superior longitudinal fasciculus
	−36, −37, 13	2.78821	109	10	Internal capsule
	−45,−12,−9	3.10543	116	12	Temporal superior cortex
	−44, −1, −17	2.55562	110	7	Temporal middle cortex
Repetition	−46, −10, −10	3.61530	117	12	Temporal superior cortex
	−30, −38, 23	3.61530	110	5	Posterior corona radiata
	−37, −37, 26	3.19465	111	6	Superior longitudinal fasciculus

Montreal Neurological Institute (MNI) coordinates of voxels using lesion overlay map of 31 subjects that were significant based that were significant based on the Brunner–Munzel (BM) Z score and the number (n) of clustering voxels that survived the false discovery rate-corrected threshold of $p < 0.05$. Anatomical regions were identified using the automated anatomical labeling and Johns Hopkins University white matter templates.

gyrus, insular cortex, Wernicke's complex, premotor cortex, and superior temporal gyrus play a major role in language (6, 28, 29). Moreover, white matter including the arcuate fascicle, SLF, uncinate fascicle, and the extreme capsule fiber system play a functional role in language processing (5, 7, 29). Another recent study showed that the damage to the arcuate fasciculus related to the recovery of aphasia, and damage to the external capsule also affected the recovery of aphasia (14). Our finding that lesions in the supramarginal cortex, superior temporal gyrus, insula, and SLF were associated with a low AQ score in patients with stroke is consistent with that of previous studies. A previous case report wrote that the Rolandic cortex is the cause of transcortical motor aphasia (30), the Heschl's gyrus is involved in the comprehension of syntax (31), and posterior corona radiata lesions are associated with poor recovery from aphasia (32). These lesions had not been considered as the main cause for aphasia (8). Our findings suggest that the Rolandic cortex, Heschl's gyrus, and posterior corona radiata may be new causative lesions for post-stroke aphasia. Taken together, these findings suggest that the Rolandic cortex, Heschl's gyrus, and posterior corona radiata play roles in the recovery of post-stroke aphasia via the lesion itself, or in disruptions of language network (7).

The role of the Broca's complex in verbal fluency is well-known (28); however, our findings suggest that the inferior triangularis and inferior operculum also play significant roles in mediating fluency. Moreover, the insula cortex has been shown to support fluency as a syntax-specific process (33). A recent lesion-symptom correlational analysis found that the posterior supramarginal gyrus played a role in the processing of concrete and abstract verbs related to fluency (34). We found that damage to the inferior triangularis and inferior operculum of the frontal cortex, supramarginal cortex, and insula were associated with poor fluency. Language fluency is a complex process involving phonation, motor function, syntax synthesis, and semantic meaning; thus, it is not surprising that it is mediated by a network of brain regions. The recent repetitive transcranial magnetic stimulation was consistent with the inhibition of contra-lesional pars triangularis and pars opecularis (24, 35, 36). Our results support the rationale of the target for neuromodulation.

The results that parietal cortex, angular cortex, temporal middle cortex, and temporal superior cortex lesions were associated with poor recovery of comprehension is consistent with previous findings (37–39). Moreover, our finding that the sagittal stratum pathway may mediate language comprehension supports that of a previous study showing that sagittal stratum damage, including the geniculostriate pathway and inferior longitudinal fasciculus, impaired access to orthographic word forms and semantics (40). A recent study of post-stroke aphasia found that the posterior superior temporal gyrus, intraparietal sulcus, and pars triangularis were involved in naming ability (41). We found that the superior temporal cortex, temporal middle cortex, angular cortex, supramarginal cortex, posterior corona radiata, superior longitudinal fasciculus, and internal capsule were associated with poor recovery of naming in stroke patients with aphasia. Naming is higher-order function involving comprehension, semantic, syntax, phonation, and speech. Thus, several lesion sites may affect naming ability.

We found that damages to the superior temporal cortex, posterior corona radiata, and SLF were associated with poor repetition outcomes in post-stroke aphasia patients. A previous study found that the left inferior fronto-occipital fascicle and uncinate fascicle were associated with repetition (42). Another study, which had a small sample (11 aphasic subjects), found that impaired repetition was associated with lesions in the central operculum, angular gyrus, supramarginal gyrus, and Heschl's gyrus in the acute phase of stroke (43). Taken together, these findings indicate that the brain regions involved in repetition deficits were related to those in fluency and comprehension and the white matter connecting them.

The supramarginal cortex, temporal superior and middle cortex, angular cortex, SLF, and posterior corona radiata contributed to two or more functions. Possible explanations were as follows. First, these areas would contribute to several roles, indirectly. Thus, influence from a distinct area might affect our results. Based on the brain network, the studies for a specific brain lesion may be not sufficient to explain all pathogenesis of aphasia. Second, four subsets of aphasia have developed, based on clinical phenotype. The mismatch between the process in brain and clinical phenotype would contribute to our results. However, the diagnosis and treatment should be reliant on clinical phenotype. Our results revealed the specific brain lesion on long-term outcome of aphasia with four subsets; fluency, comprehension, repetition, and naming, in patients with stroke. These results would be useful in the clinical setting. For example, for the planning of non-invasive neuromodulation therapy, our results may have merit for the decision of the target area individually, based on the patient's MRI findings and K-WAB results.

Our study has two major limitations. First, our small sample size and cross-sectional design may limit the interpretation of our findings. Second, our sample may have been affected by selection bias because we excluded the data of subjects who died 12 months post-stroke; thus, the study included relatively well patients who would not normally undergo the K-WAB test 12 months post-stroke. Nonetheless, we identified specific brain areas associated with four language deficits in patients with first-ever stroke 12 months after onset. Our study differs from those conducted previously in that we investigated lesion locations associated with four aphasia deficits using VLSM, and we used data obtained 12 months after stroke onset when further neurological recovery is thought to be unlikely (6, 42, 43).

In conclusion, we identified specific brain lesions associated with long-term outcome with K-WAB and acute MRI data in four language deficits 12 months after onset in stroke patients with aphasia using VLSM. Our findings may be useful for the development of treatment strategies and for advancing understanding of the pathophysiology of aphasia in stroke patients.

DATA AVAILABILITY

All datasets generated for this study are included in the manuscript and/or the **Supplementary Files**.

ETHICS STATEMENT

The study protocol was reviewed and approved by the Institutional Review Board of The Catholic University, College of Medicine (Registry No. VC18RESI0112). The requirement for informed consent was waived by the board.

AUTHOR CONTRIBUTIONS

BS and KL: making concept, analysis of results, and writing draft. JSK and BH: providing subjects and review of draft. JK: analysis of results and acquisition of data. WH: acquisition of data. SL: making concept, analysis of results, writing draft, review, and finalize of draft.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2019.00776/full#supplementary-material

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Educational and Exercise Intervention to Prevent Falls and Improve Participation in Subjects With Neurological Conditions: The NEUROFALL Randomized Controlled Trial

Davide Cattaneo[1]*, Elisa Gervasoni[1], Elisabetta Pupillo[2], Elisa Bianchi[2], Irene Aprile[1], Isabella Imbimbo[1], Rita Russo[3], Arianna Cruciani[1], Andrea Turolla[4], Johanna Jonsdottir[1], Michela Agostini[4], Ettore Beghi[2] and NEUROFALL Group

[1] Fondazione Don Carlo Gnocchi Onlus (IRCCS), Milan, Italy, [2] Istituto Di Ricerche Farmacologiche Mario Negri, Milan, Italy, [3] San Carlo Borromeo Hospital, Milan, Italy, [4] IRCCS Fondazione Ospedale San Camillo, Venice, Italy

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Lisa Tabor Connor,
Washington University in St. Louis,
United States

Reviewed by:
Marco Iosa,
Fondazione Santa Lucia (IRCCS), Italy
Maw Pin Tan,
University of Malaya, Malaysia

***Correspondence:**
Davide Cattaneo
dcattaneo@dongnocchi.it

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Background: Falls, mobility impairments and lack of social support lead to participation restrictions in people with neurological conditions. The aim of this multicenter, single blinded randomized controlled trial was to test whether an educational program focusing on fall prevention and safe mobility reduces falls and increases social participation among people with neurological conditions.

Methods: Ninety people with Stroke ($n = 25$), multiple sclerosis ($n = 33$) and Parkinson disease ($n = 32$), median age 63 (31–89), were randomized. A permuted block algorithm stratified by field center was used to allocate participants to an education group (EG, $n = 42$) consisting of an educational program focused on fall prevention and tailored balance exercises and a control group (CG, $n = 48$) receiving usual treatments. After baseline assessment, each participants was followed for 6 months with telephone contacts by blinded interviewers. Being fallers (>1 fall) and time to become a faller were used as primary outcomes. Community Integration Questionnaire (CIQ) and Instrumental Activities of Daily Living (IADL) scales assessed treatment effects on social integration and daily living activities.

Results: Over a median (Interquartile Range) follow-up of 189 (182–205) days, [EG = 188 (182–202), CG = 189 (182–209)] fallers were 10 in the CG and 11 in the EG (hazard ratio 0.95, 95% confidence interval (CI) 0.45 to 2.5; $P = 0.94$). At follow-up the EG scored significantly better than CG on the CIQ (+1.7 points, CI: 0.1 to 3.3) and IADL (+2.2 points, CI: 0.4 to 4.0).

Conclusions: This educational program did not reduce the risk of falls but it improved the ability to carry out activities of daily living and decreased participation restrictions in people with neurological conditions.

Keywords: prevention, falls, participation, neurological disease, rehabilitation

INTRODUCTION

People with neurological disorders are often characterized by motor dysfunction and imbalance leading to risk of falls and impacting on participation in activities of daily living.

Parkinson disease (PD), multiple sclerosis (MS) and stroke carry high risk of falls. Among people with PD, 45–68% are reported to be fallers each year and two-thirds of them fall repeatedly (1). More than 50% of people with MS are fallers (2) and about 14–65% of participants with stroke fall at least once while in hospital and 37–73% fall during the 6 months after discharge (3).

In a recent observational study, falls, mobility impairments and lack of social support led to participation restrictions in 77% of participants with MS (4). This is in keeping with other studies showing lower level of participation in PD (5) and stroke (6) and difficulties in the execution of home, social and productive activities. Although participation has recently been suggested as a primary outcome of interventions (7), little is known of the effects of rehabilitation on participation restrictions and the relationship between participation in social activities and falls.

A published report investigating the risk of falls and fall predictors in 299 people with PD, MS, and stroke (8) showed that 47.1% of participants fell at least once in the 6 months following baseline assessment and 31.7 and 17.0% of the sample reported repeated and, respectively, injurious falls.

These results are in line with previous studies showing high proportion of fallers among these three conditions often leading to injuries and impairments in activities of daily living (1, 9, 10). A second study inquired on pathology-specific mobility and balance disorders associated with falls and participation restrictions (11). However, there is insufficient evidence on the effects of rehabilitation on fall prevention (12) and even less on the effects of a combined educational and exercise program to reduce fall frequency (13).

Here we report results associated with the hypothesis that a combined educational and exercise program focusing on fall prevention and safe mobility reduces the risk of falls and increases social participation among subjects with PD, MS, and stroke with functional limitations.

METHODS

Our study was a multicenter, single blinded randomized trial conducted in three Italian field centers between January 2015 and March 2016 by the NEUROFALL group. This group comprised researchers and clinicians (physiotherapists and medical doctors) involved in studies on fall prediction and prevention in neurological disorders.

Participants were included if they had PD, MS or stroke, were able to walk 10 m independently with or without a mobility aid, were willing to commit to the educational program, and were able to give written informed consent. A patient was excluded if he/she had: (1) Major depression; (2) Severe joint/bone disorder interfering with mobility; (3) Aphasia if interfering with understanding the aims of the study and self-administered tests; (4) relapses in the previous 3 months (MS); (5) Stroke occurred in < 4 weeks before study entry; (6) Cognitive impairment (Minimental State Examination score <21); To increase generalizability of findings we did not exclude subjects with a MMSE lower than 24. However, we asked caregivers to interact with assessors to check for data consistency in participants with MMSE scores from 21 to 24. The institutional review boards at all participating sites approved the study protocol (FDG_10.12.2014), and written informed consent was obtained from all participants. The study was registered in ClinicalTrials.gov (NCT03570268).

Randomization

Participants were randomized 1:1 to an education or control group (see **Figure 1**) using a computer generated randomization list generated before commencement of the study and stratified by field center and pathology. Randomization sequence was created with SAS 9.2 (SAS Institute, Cary, NC, USA) using random block sizes of 4.

Interventions

Participants in the experimental intervention group (education group) received an educational program and tailored home exercises. From a theoretical point of view the educational intervention drew upon educational group theory, and the delivery of recently published papers investigating the effect of educational programs (14, 15).

From a practical point of view the educational program consisted of a mix of peer to peer and clinician led session, lasting 1 h. The session consisted of multiple, interacting components fostering brainstorming, problem-solving and action planning activities (16) and was supported by a handbook and audio-video material designed to promote sharing of strategies used to prevent falls and to improve social participation and activity of daily living among participants. We also provided videos of falls to foster discussion among participants on causes, circumstances and behaviors leading to falls.

The 1 h session was led by a trained physical therapist who delivered information to small groups ranging in size from two to four people with the same pathology. Regarding the contents, we focused on increasing knowledge of pathology-specific types of falls, behavioral and environmental fall risk factors such as internal and external barriers. Participants were asked to provide examples of falls reporting their feelings and the strategies they used to modify their behaviors and environment to reduce fall risk factors. We provided information on participation restrictions and its effects on eventually increasing deconditioning and falls and then asked the participants to comment on the trade-off between falls prevention (e.g., restricting activities of daily living when fatigue) and independence in activity of daily living. Finally, we asked participants to share their strategies to maintain an active lifestyle while reducing risk of falling. At the end of the session the therapist moderating the group provided information on techniques and strategies for preventing falls and increase social participation and engagement

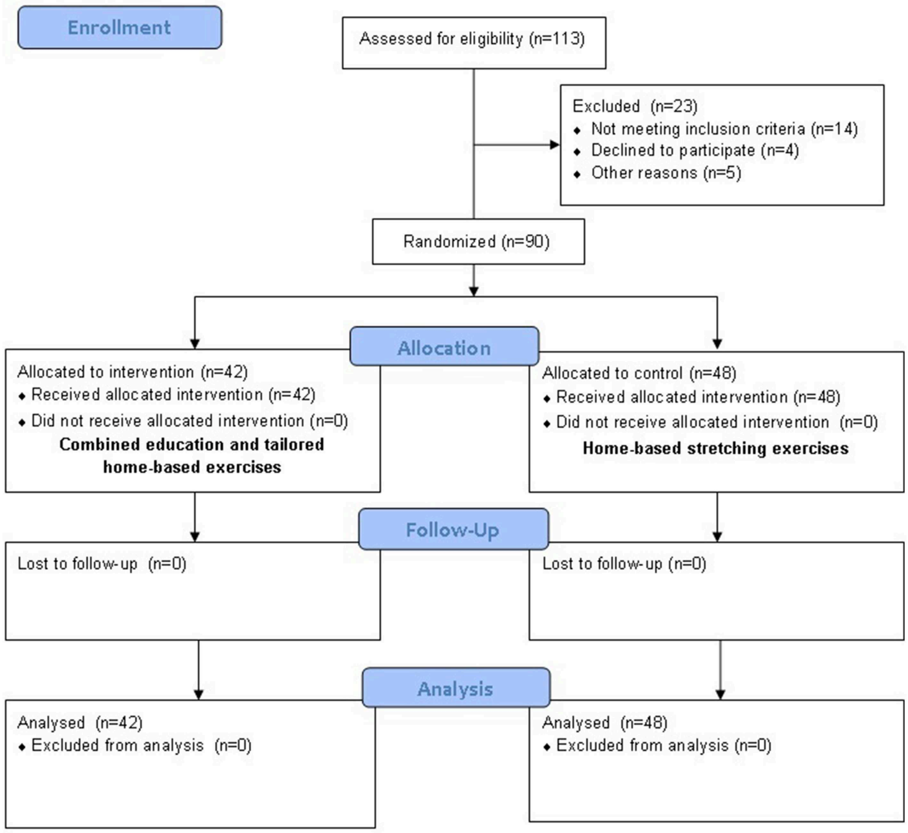

FIGURE 1 | CONSORT flow chart.

in activities of daily living that were not covered during the session.

After the educational session we provided two 1 h exercise sessions to teach the exercises and 1 h follow up session 2 days after the last exercise sessions.

The exercise sessions were spent to teach tailored mobility and balance exercises developed on existing evidence (17), our previous research (18–20) and clinical experience. In the follow-up session participants discussed issues from the preceding session, they were asked if they had understood the study procedure and the tasks they needed to carry out at home and were supervised while they performed the prescribed exercises in order to correct eventual errors.

Participants were invited to perform the exercises at home 2–3 times a week for 2 months.

Participants allocated to the control group received ongoing usual treatments. In addition, two 1 h sessions were spent to teach stretching exercises that the patient was invited to perform at home for 2 months.

Subjects in both groups were asked not to discuss the intervention with other participants to avoid patients in the usual care group integrating components of the intervention into their routine.

Data Collection

After releasing written informed consent, each participant was invited to a baseline visit to collect demographic and clinical characteristics including age, sex, disease type and duration, use of walking aids, incontinence, and history of falls in the preceding 6 months. A number of clinical scales were used to test functional disability only at baseline, balance (Berg Balance Scale, BBS) (21), walking abilities (Timed Up & Go, TUG, Ten Meter Walking Test) (22). and self-confidence with balance (Activity Balance Confidence Scale, ABC) (23). Questionnaires on performance during daily living activities (Instrumental Activities of Daily Living, IADL) (24), and social integration (Community Integration Questionnaire, CIQ) (25) were applied at baseline and at follow up. Each patient was given a fall diary and was followed for 6 months with telephone contacts approximately at 2, 4, and 6 months. At each contact, the patient was inquired on targeted mobility and balance rehabilitation programs received during the follow up, use of walking aids, and any incurred falls, with date, circumstances, underlying cause and related injuries. A fall was defined as an unexpected event where the person inadvertently came to rest on the ground or other lower level (26). Subjects with >1 fall in the 6 months follow up were categorized as "fallers."

Percentage of fallers and time to second fall were used as primary outcomes.

CIQ and IADL scales were rated at last follow up to assess the effects of intervention on changes in social integration and daily living activities. Data were collected by trained interviewers blinded to the intervention not located in the clinical centers where the assessments were made. Data was uploaded in an *ad-hoc* database and was not available until the end of the study.

Statistical Analysis

We assessed the impact of education on the cumulative time-dependent probability of falls with percentage of fallers as our primary outcome variable. A subject was categorized as a faller at the time of the second fall occurring after randomization. Event time was defined as the time from first assessment until participant was categorized as faller, and censoring times were defined as the time from first assessment until the fall assessment. Kaplan–Meier estimator was used to obtain cumulative incidence curves for the education and control group. For group comparison, we estimated hazard ratios with 95% confidence intervals and used likelihood ratio tests from Cox proportional hazards regression models. A multivariable analysis was also performed controlling for pathology, falls number at baseline, age, disease duration, treatment received during the FU and use of walking aid.

For the clinical outcomes, we focused on participation (CIQ) and activities of daily living (IADL). For each measure, we used multivariable linear models to compare the specific intervention effect on total scores, for subjects in the education and control group, adjusting for baseline score, pathology, falls number at baseline, age, disease duration, treatment received during the FU and use of walking aid. The covariates were selected as they represented main fall risk factors in participants with neurological conditions (2, 27, 28). The effect of intervention was assessed on a two-tailed significance of 0.05 using the intention to treat approach.

In a previous study conducted in a similar population, about 40% of patients experienced at least one fall over a 6 month period, and about 25% experienced at least two falls over the same period (25). Assuming that the percentage of patients experiencing at least one fall would decrease to 15% in the education group, we planned to include 48 patients per group to have 80% power to detect this difference with a 5% level of significance. With this planned sample size, the study also had sufficient power (80%) to detect a reduction of 5% in the percentage of patients experiencing at least two falls in the education group.

As only five (5.5%) patients were categorized as "injurious fallers" (i.e., fallers experiencing injuries) at the follow-up (3 education group, 2 control group) in this study we did not report results for this variable.

RESULTS

A total of 113 patients were assessed for eligibility (**Figure 1**). Ninety cases (MS = 33, PD = 32, Stroke = 25) were randomized to the education group ($n = 42$) or to the control group ($n = 48$). The planned number (48 patients in each arm) could not be achieved because the recruitment rate was increasingly slow, preventing the enrolment of the six additional patients within an acceptable time frame. With 42 patients enrolled in the experimental group, instead of the 48 originally planned, the power for the primary endpoint is reduced to 76%. The baseline characteristics of the two intervention groups were comparable (**Table 1**).

Thirty participants (33%) reported more than 1 fall in the past 6 months and 71 (79%) received rehabilitation during the follow-up. Patients with history of falls were slightly more frequent in the experimental group (18.42%) compared to the control group (12.25%). However, no statistically significant between group differences were found for percentage number of fallers (Educatio$n = 25.60\%$; Control $= 12.25\%$; $p = 0.12$) and number of subjects receiving other treatments (Educatio$n = 35.85\%$; Control $= 36.75\%$, $p = 0.48$), (**Supplementary Figure 1**).

Over a median (IQR) follow-up of 189 (182–205) days, [Education = 188 (182–202), Control = 189 (182–209)] 10 participants (24%) in the education group were fallers (had fallen

TABLE 1 | Clinical and demographic characteristics of the sample.

	Education group ($n = 42$)	**Control group ($n = 48$)**
Variable	**Demographic characteristics**	
Age in years mean (SD)	61 (15)	63 (11)
Women *N* (%)	16 (38)	17 (35)
	Clinical characteristics	
Pathology		
Multiple sclerosis *N* (%)	16 (38)	17 (35)
Parkinson *N* (%)	15 (36)	17 (35)
Stroke *N* (%)	11 (26)	14 (29)
Incontinence *N* (%)	14 (34)	11 (25)
Disease duration in years mean (SD)	9 (7)	9 (7)
Falls in past six months median (IQR)	1 (0-3)	0 (0–2)
	Walking aid	
Walking Aid		
None *N* (%)	14 (34)	20 (42)
Unilateral *N* (%)	8 (19)	13 (27)
Bilateral *N* (%)	16 (38)	9 (19)
Wheelchair *N* (%)	10 (4)	6 (13)
	Functional characteristics	
BBS median (IQR)	42 (37–47)	42 (35–48)
TUG (seconds) median (IQR)	26 (26)	24 (25)
10m Walking Test (second) mean (SD)	20 (31)	17 (29)
IADL median (IQR)	14 (10–17)	13 (9–17)
ABC median (IQR)	45 (33–69)	48 (25–70)
CIQ median (IQR)	12 (9–15)	13 (10–15)

BBS, Berg Balance Scale; TUG, Timed up and go Test; IADL, Instrumental Activity of Daily Living; ABC, Activities Balance Confidence; CIQ, Community Integration Questionnaire; SD, Standard Deviation; IQR, Interquartile range, (Q_1-Q_3).

twice) and 11 (23%) in the control group were fallers (adjusted hazard ratio 0.95, 95% confidence interval (CI) 0.45 to 2.5; $P = 0.94$, **Figure 2**). The results were unchanged when the number of falls at baseline, age, disease duration, treatment received during the follow-up and use of walking aid were accounted for (adjusted hazard ratio 0.61, 95% CI 0.57 to 4.6; $P = 0.35$).

A clinically meaningful relationship was observed between number of falls, CIQ and IADL (**Figure 3**) suggesting that number of falls in the education group were evenly distributed at baseline, while post treatment a high number of falls was present only in subjects with higher level of participation and independence in activities of daily living.

Based on linear models, the education group averaged 1.7 (CI: 0.1 to 3.3) more points on the CIQ than the control group ($P = 0.04$). Subjects using walking aids scored lower than subjects walking without support.

Figure 4 reports CIQ post-scores adjusted for pre-scores, treatment received during follow-up, and walking aid for the education and control group. Similarly, the adjusted IADL scores during follow-up (**Figure 4**) were greater for the education group than for the control group with a mean between group difference of 2.2 (CI: 0.4 to 4.0, $P = 0.02$) and, with subjects walking without support showing best scores.

DISCUSSION

Several studies have investigated the effects of exercise on falls prevention with negative results (12, 13). However, few reports investigated the combination of multifactorial interventions (29). Our hypothesis was that the combination of educational sessions and home exercises could reduce falls without a concomitant reduction in activities daily living and participation. However, we found no difference in the risk of falls for an educational intervention vs. a usual care program among participants with neurological conditions with gait and balance limitations and high risks of falling. The results were consistent across several subgroups, including pathology and history of falls. On the other hand, the education program improved ability to carry out activities of daily living and decreased participation restrictions without a concomitant increase of number of falls.

Our sample was at high risk of falls as evidenced by 33% of participants reporting one or more falls in the 6 months before assessment. The participants had functional limitations, with a mean BBS score of 42 points at baseline that is below the expected score of 55 (SD 2.5) points for healthy people of similar age (30) and below the cut-off score of 45 points for the occurrence of balance disorders (31).

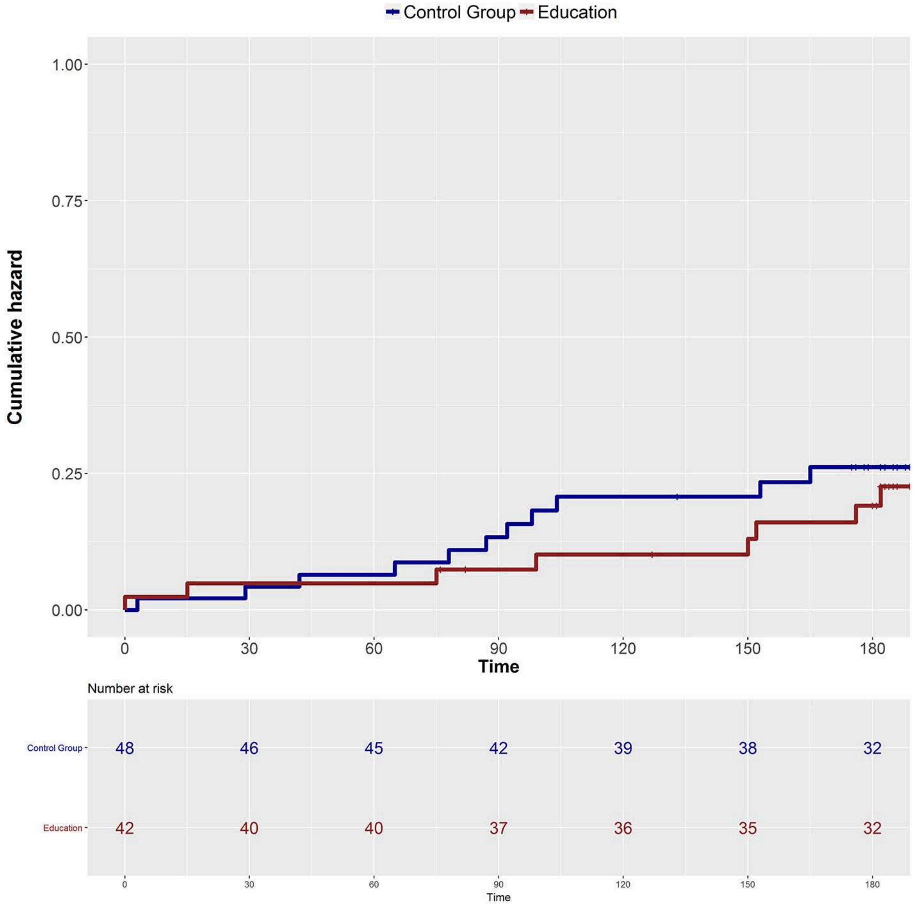

FIGURE 2 | Cumulative hazard of falling over time in the two groups.

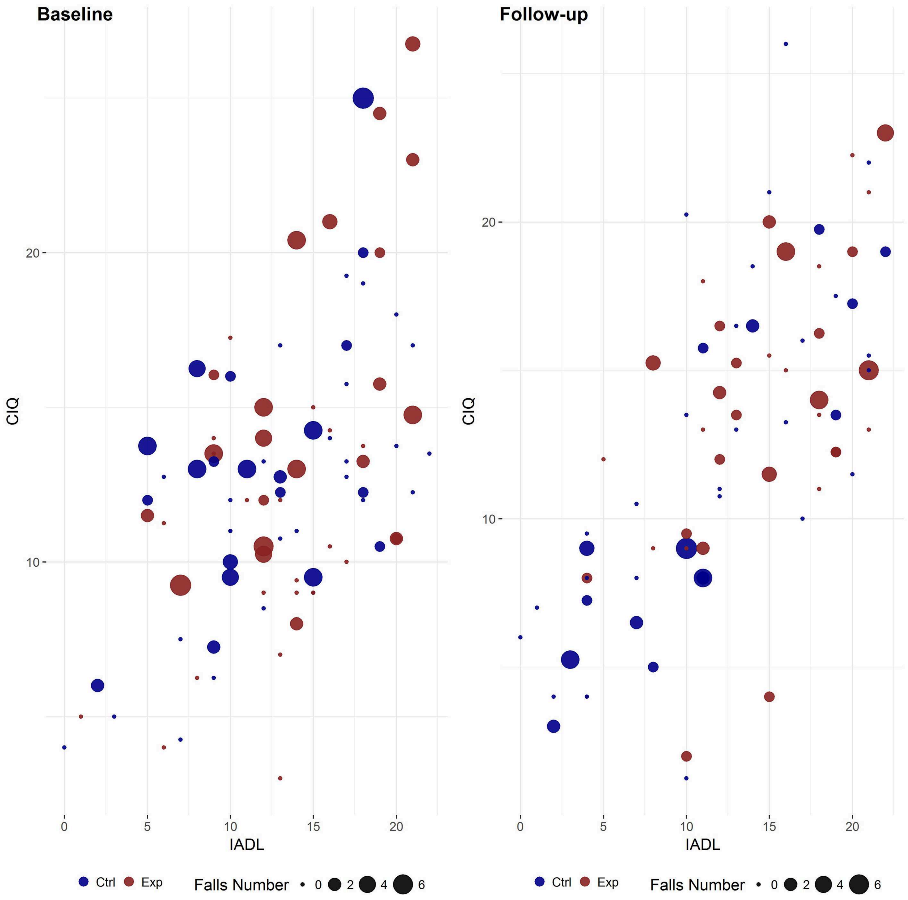

FIGURE 3 | Relationship between participation, activity of daily living and number of falls in education and control group at baseline and during follow-up. IADL, Instrumental Activity of Daily Living; CIQ, Community Integration Questionnaire; Exp, Experimental Group; Ctrl, Control Group.

Despite this being a fairly large trial of education in subjects with neurological conditions we did not find a reduction in the proportion of fallers after the intervention. This is in keeping with previous studies showing that well-designed approaches comprising only exercises can enhance mobility in stroke (32, 33) but their effects on falls are still unclear (10). A recent review comprising seven studies reporting exercise intervention did not show a significant reduction in the rate of falls in the acute and subacute stages after stroke (12).

Mixed results were also reported for PD since the only two trials showing reductions in fall frequency (34, 35) were fully supervised. Fall prevention in MS also showed mixed results with some studies showing 22–35% reduction of fallers in the experimental groups while others reported no effects (14, 20).

There may be several explanations for the lack of effects of our combined education and exercise program on falls. Firstly, at endpoint people in the educational group showed higher levels of daily activities and participation than those in the control group. It is thus possible that the risk abatement was in part compensated by an increase in risk behavior in the education group.

Secondly, we used falls diaries to assess the number of falls in the 6 months after baseline assessment, after having explained to participants at recruitment how to complete the diaries. Unlike more sophisticated devices, the diaries are inexpensive and easy to complete. Nevertheless, it is possible that misreporting falls may have occurred differently in the two groups.

Furthermore, it was impossible for ethical and practical reasons to restrain rehabilitation treatments in our cohort for 6 months. These activities were monitored during the follow up period and almost 80% of the sample received treatment to improve balance and gait. Although between group differences in treatment received should be controlled by random allocation of subjects and were included as covariate in cox models, their effects may have biased the results of our intervention.

Nonetheless, the education improved scores on CIQ, a measure of home and social integration, and productive activities and on activities of daily living. This is of importance since reduction of falls after interventions might otherwise have been attributed to restricted participation in activities of daily living. Moreover, improvement in participation may ultimately prove to be beneficial by

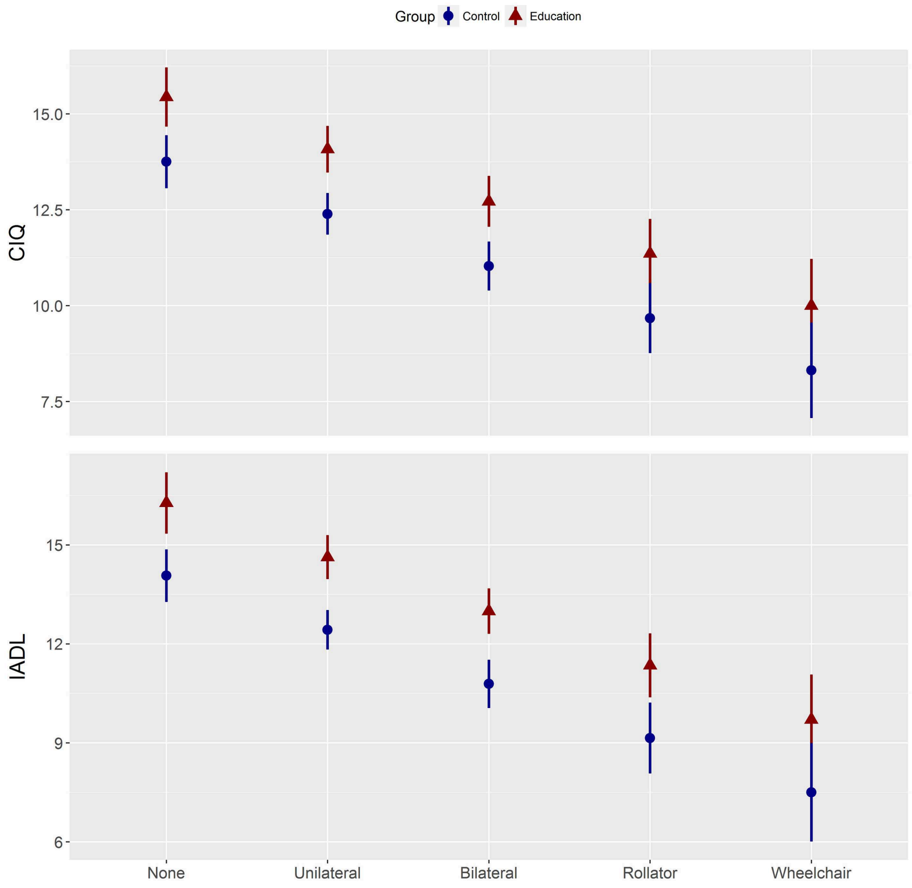

FIGURE 4 | Participation and activity of daily living post-scores adjusted for pre-scores. CIQ, Community Integration Questionnaire; IADL, Instrumental Activities of Daily Living; Control, home-based stretching exercises group; Education, combined education and tailored home-based exercises (experimental) group.

leading to functional improvement and decreasing falls in the long term.

The effects of rehabilitation on participation and activities of daily living are still unclear with some reviews and studies showing no effects (36) while others report improvements after occupational therapy and functional electrical stimulation (37). Our results corroborate findings from a recent review suggesting that self -management programs can improve quality of life in people with neurological conditions. Further studies are needed to understand if new more complex multidisciplinary, personalized, and patient-centered approaches with an efficient involvement of caregivers and family members can have stronger impact on participation in people with neurological conditions (38).

Study Limitations

The first limitation is the selection of the study population since this is not a population-based study. Second, we selected prevalent rather than incident participants in need of rehabilitation. The exclusion of participants who were not proposed for rehabilitation programs might have resulted in a selected sample. Third, the collection of data on falls was dependent on the compliance of the participants and, although they were provided with fall diaries, the 2 month intervals between our assessments might have been too long to prevent recall bias. Fourth, the follow-up was perhaps too short for a precise detection of fallers. Fifth, although the total sample is large, the participants affected by each disease were perhaps too few for the detection of disease-specific differences in the rate of falls after intervention. Last, the planned number of patients to be randomized could not be achieved due to an increasingly low recruitment rate. However, given the 1% difference in the percentage of fallers between the two treatment arms, a statistically significant difference in favor of the educational arm could not be obtained even in the unlikely event that all cases had been randomized to the experimental arm and none of them became fallers during follow-up.

Even with these limitations, our study documents that the combined education program improved the ability to carry out activities of daily living, decreasing participation restrictions without a concomitant increase of number of falls. Further studies with a better methodology are needed to fully exploit the effect of the combination of educational and balance training program on fall reduction in the different neurological groups.

First, according to Finlayson et al. (14) a delivered group program lasting several weeks may result in better outcomes. Moreover, the provision of more group activities, lectures and take-home exercises might better reinforce program contents. Periodical supervising of home exercises should be introduced to tailor treatments according to participant improvements, deliver better scheduling of treatment sessions, motivate subjects and provide feedback of performance. Finally, environmental assessments, prescription of appropriate mobility aids, and the involvement of the caregiver should be considered to reduce fall frequency.

ETHICS STATEMENT

This study was carried out in accordance with, and the protocol approved by, the recommendations of Fondazione Don Gnocchi.

AUTHOR CONTRIBUTIONS

DC, EG, and EBe drafted the manuscript. EBi conducted the statistical analysis. IA, II, AC, RR, AT, MA, and the NEUROFALL Group collected the data. DC, EG, JJ, and EBe participated in project conception, organization and execution. All the authors reviewed and critiqued the manuscript.

NEUROFALL GROUP MEMBERS

Angelo Montesano, MD, Marco Rovaris, MD, Gianluca Iacobone, Alessandra Rodano, Silvia Romi, Francesca Tettamanzi (Milano), Andrea Polli, PT (Venezia).

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2019.00865/full#supplementary-material

Supplementary Figure 1 | Hazard ratios for time to fall for education vs. control group according to subgroups.

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Social Support as a Predictor of Community Participation After Stroke

Kimberly S. Erler[1]*, Virginia Sullivan[1], Sarah Mckinnon[1] and Rebecca Inzana[2]

[1] Department of Occupational Therapy, MGH Institute of Health Professions, Boston, MA, United States, [2] Department of Communication Sciences and Disorders, MGH Institute of Health Professions, Boston, MA, United States

Participation is a primary goal of neurorehabilitation; however, most individuals post stroke experience significant restrictions in participation as they attempt to resume their everyday roles and routines. Despite this emphasis on participation, there is a paucity of evidence-based interventions for optimizing this outcome and a limited understanding of factors that contribute to poor participation outcomes. Caregiver support at discharge from inpatient rehabilitation positively influences physical and psychological outcomes after stroke but more research is needed to understand the association between social support and participation. This study aimed to examine the independent contribution of perceived social support to participation 3 months post discharge from inpatient stroke rehabilitation. This study was a secondary analysis of the Stroke Recovery in Underserved Populations 2005–2006 data. Participants were adults $\geq$55 years old, living in the community 3 months post discharge from inpatient rehabilitation for ischemic stroke ($n = 422$). Hierarchical linear regressions were performed. The primary variables of interest were the PAR-PRO Measure of Home and Community Participation and the Duke–University of North Carolina Functional Social Support Questionnaire. Perceived social support at discharge from inpatient rehabilitation for ischemic stroke contributed uniquely to the variance in participation 3 months later ($\beta = 0.396$, $P < 0.001$) after controlling for race, sex, age, years of education, comorbidities, stroke symptoms, depression, FIM Motor, and FIM Cognitive. Social support accounted for 12.2% of the variance in participation and was the strongest predictor of participation relative to the other independently significant predictors in the model including FIM Motor and depression. There is already a focus on caregiver training during inpatient rehabilitation related to basic self-care, transfers, and medical management. These findings suggest the need for rehabilitation professionals to also address social support during discharge planning in the context of promoting participation. Given the findings, expanding caregiver training is necessary but novel interventions and programs must be carefully developed to avoid increasing caregiver burden.

Keywords: neurological rehabilitation, stroke, social support, social participation, community integration

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Tamara Tse,
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***Correspondence:**
Kimberly S. Erler
kerler@mgh.harvard.edu

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INTRODUCTION

Stroke is the leading cause of disability in the United States with almost 800,000 people experiencing a new or recurrent stroke each year (1). Stroke can result in a complex matrix of physical, communication, cognitive, and emotional impairments that limit a person's ability to perform basic activities of daily living or participate in the community. The World Health Organization (WHO) International Classification of Functioning, Disability and Health (ICF) provides a scientific basis for examining disability and functioning in the context of a health condition (2). The ICF describes three domains impacted by a health condition: body structures and functions (impairments) which capture functioning at the level of the body, activities which capture functioning at the level of the individual, and participation which captures functioning at the societal level.

Neurorehabilitation aims to minimize disability and restore function after stroke, primarily focusing on the restitution of impairments and compensation for activities of daily living (3). Many rehabilitation professionals expect that an impairment-based or activity-based approach will lead to improvements in community participation (4); however, research indicates that this secondary gain in participation may not always occur. The majority of stroke survivors experience restrictions in participation as they attempt to resume their everyday lives (5–8). Determining modifiable factors that contribute to successful community participation after stroke has the potential to advance clinical practice by informing novel interventions and program development.

Participation is a valued outcome post stroke and often used as a metric of successful rehabilitation (9–12). Participation occurs at the intersection between the person, the activity, and the environment (13, 14). Obembe and Eng (15) suggest that recovery from stroke should be considered successful if the individual resumes the level of community participation similar to his pre-stroke baseline. In samples of healthy adults and adults with chronic conditions, participation has been linked to better overall health and well-being (16–19). Previous research has shown that poor participation after stroke is associated with increased older age (6), worse stroke severity (20), worse physical function (21), worse cognition (22), more comorbidities (21), and increased rates of depression (7); however, the directionality of these relationships remain unknown.

Social support is an environmental factor that has been shown to be a positive prognostic indicator for physical and psychological outcomes after stroke (23–27). Social support can come from a wide range of sources such as family, friends, significant others, social networks, religious organizations, or community groups. Social support can also be the actual assistance a person receives from others or the perceived support that results from the confidence of the availability of support for physical or emotional needs. There is limited evidence to suggest the existence of a positive relationship between social support and participation; however, this relationship needs to be further elucidated. The relationship between perceived social support and participation is particularly important to understand since it is a potentially modifiable factor. A recent systematic review (28) that aimed to determine the relationship between social support and participation post stroke yielded only six articles that met the inclusion criteria, and only one article that included participants in the United States. Norlander et al. (29) found that in addition to driving status and walking distance, the extent of one's social network at 16 months after the first stroke was predictive of more frequent social and leisure activities. Further studies (30, 31) found that both the quality and quantity of social support is associated with participation, but that functional limitations were more strongly related to participation.

Participation is a valued outcome after stroke, and social support has been shown to positively impact other meaningful outcomes. Given the limited evidence in general, and the cultural and health system differences amongst countries, there is a need to better understand the association between participation and the perceived social support after stroke in a sample representative of the United States. The availability of a dataset with a large sample size and the primary predictor and outcome variables of interest as well as many other important confounding variables provides the unique opportunity to test our hypothesis about the relationship between perceived social support and participation to determine feasibility for future prospective research in this area. Hence, the purpose of this study was to determine the unique contribution of perceived social support at discharge from inpatient rehab to participation at 3 months post discharge among individuals with first time ischemic stroke. We hypothesized that, after controlling for other demographic, health, and functional factors, perceived social support at discharge from inpatient rehabilitation would be associated with better participation 3 months later among community dwelling adults with for first time ischemic stroke.

METHODS

Participants

This study was a secondary analysis of the publicly available dataset, Stroke Recovery in Underserved Populations (SRUP) 2005–2006 database (32). SRUP was an observational cohort study of individuals with first time stroke who received inpatient rehabilitation at one of 11 rehabilitation hospitals in various regions of the country including New Jersey, New York (2), Iowa, California, Illinois, Texas (2), Washington D.C., Kentucky, and Florida. Inclusion criteria required participants to have a diagnosis of first time stroke, be ≥ 55 years old, and demonstrate the ability to respond to basic questions about orientation. After consent to participate in the study, nursing staff collected demographic and clinical information within 72 h of discharge from the rehabilitation facilities, and trained nurse researchers collected follow up data via telephone at 3 months post-discharge. Further inclusion criteria for our study required participants to have a diagnosis of ischemic stroke (vs. hemorrhagic stroke), be living in a community setting (vs. institutional setting) at the 3-months follow up, and have complete participation and social support data.

Instruments

Age, sex, race, years of education, number of comorbidities (including arthritis, cancer, respiratory disease, diabetes, heart disease, other circulatory diseases, kidney disease, obesity, mental health diagnoses, or fractures), and number of stroke symptoms (including hemiplegia or hemiparesis, speech difficulties, swallowing difficulties, or neuromuscular symptoms) were derived from demographic and stroke characteristic variables in the SRUP database. Participation, social support, depression, physical function, and cognitive function were assessed with the following measures.

Participation

The primary outcome of interest, community participation, was measured with the PAR-PRO Measure of Home and Community Participation (33). The PAR-PRO was developed to complement the FIM, measuring more complex areas of performance (33). Participants were asked the frequency of participation on four items in the domains of socializing inside the home, socializing outside of the home, recreation and leisure activities, and religious or spiritual activities. Response options included no participation in the past month, 1–2 times in the past month, several times in the past month, every week over the past month, and more than once per week. Summary PAR-PRO scores ranged from 0 to 16 with higher scores indicating more community participation. The PAR-PRO has been shown to have good psychometric properties in populations with neurological impairments, including individuals with stroke (33). The PAR-PRO was administered via telephone at 3 months post discharge from inpatient stroke rehabilitation.

Social Support

The 11-item Duke–University of North Carolina Functional Social Support Questionnaire (DUFSS) is a measure of perceived social support (34, 35). The DUFSS consists of 11 items (e.g., I have people who care what happens to me) that are scored on a five-point Likert scale with responses ranging from "as much as I would like" to "much less than I would like." Summary scores range from 11 to 55 with a higher score indicating higher perceived social support. The measure includes items that This DUFSS score was assessed at discharge from inpatient rehabilitation.

Depression

The Center for Epidemiologic Studies Depression Scale (CES-D), a 20-item scale with response options ranging from 0 (none of the time) to 3 (most of the time), measured depression (36). Item scores are summed for a total score ranging from 0 to 60 with higher scores indicating more depressive symptoms. This study followed previously established criteria to dichotomize those with and without clinically significant depression using a cutoff score of ≥16 (36, 37). Depression was assessed in person at discharge from inpatient rehabilitation.

Physical and Cognitive Function

The FIM Motor and FIM Cognitive subscales measured physical and cognitive disability, respectively (38). The FIM cognitive has five items, and the FIM Motor has 13 items, each rated on a seven-point scale ranging from total assistance (1) to complete independence (7). Higher scores indicate better cognitive and physical function. The FIM Motor and FIM Cognitive were assessed at discharge from inpatient rehabilitation.

Statistical Analyses

All analyses were performed in IBM SPSS Statistics 25.0 for Windows (39). We conducted hierarchical linear regressions for the dependent variable of participation (PAR-PRO) scores at 3 months post discharge from inpatient rehabilitation for ischemic stroke. Model 1 included the predictors of race, sex, age, years of education, number of comorbidities, number of stroke symptoms, depression, FIM Motor, and FIM Cognitive. Model 2 included all of the predictors in the first model with the addition of social support (DUFSS) scores at discharge from inpatient rehabilitation. The R^2 change between the two models represents the unique contribution of social support to participation after controlling for all other variables in the model. Descriptive statistics were examined for all variables, and model diagnostics (i.e., variance inflation factor and tolerance) were assessed to determine good model fit. A Spearman's Rho Correlation matrix was run to examine the relationship between all variables in the models.

The Institutional Review Board of Partners HealthCare, the Partners Human Research Committee, determined that this research does not meet the definition of human subjects research since investigators performed secondary analyses of an anonymized and publicly available data set, and did not obtain data through an intervention or interaction with individual subjects or identifiable private information about living individuals.

RESULTS

The original publicly available dataset included 1,219 participants, 891 participants of whom had a primary diagnosis of ischemic stroke (vs. hemorrhagic). Of those with ischemic stroke, 699 lived in a community setting at 3 months post discharge. There were 442 participants who had complete participation data and 422 of those participants also had complete social support data. There were no statistically significant differences on key variables (i.e., age, years of education, number of comorbidities, number of stroke symptoms, FIM Motor, FIM cognitive, sex, race, or depression) between the included 422 and the excluded 277 who had ischemic stroke and were living in the community 3 months post discharge but did not have complete data. **Table 1** summarizes the demographics and characteristics of the study sample ($n = 422$). Included participants were admitted to inpatient rehab between December 2005 and October 2006. The relationship between all predictor and outcome variables is depicted in a correlation matrix in **Table 2**.

The base model (Model 1), which included race, sex, age, years of education, number of comorbidities, number of stroke symptoms, depression, FIM Motor, and FIM Cognitive explained 18.0% of the variance in participation at 3 months [$F_{(9,406)} = 9.903$, $p < 0.001$]. After social support was added to the model

TABLE 1 | Demographics and characteristics.

N (%) or mean (*SD*)	*N* = 422
Age	68.35 (13.173)
Years of education	12.15 (3.143)
Sex (female)	206 (48.8)
Race (white)	302 (71.6)
Depression status (depressed)	112 (26.5)
Number of comorbidities	2.89 (1.309)
Number of stroke symptoms	1.37 (1.023)
FIM cognitive at discharge	25.94 (6.767)
FIM motor at discharge	60.79 (15.860)
DUKE-UNC FSSQ at discharge	50.33 (7.251)
PAR-PRO at 3 months post discharge	10.443 (4.314)

SD, Standard deviation.

(Model 2), all predictors together accounted for 30.2% of the variance in participation at 3 months [$F_{(10,405)} = 17.546$, $p < 0.001$]. Social support alone accounted for 12.2% of the variance in participation [$F_{(1,405)}\ \Delta = 70.977$, $p < 0.001$, $R^2\Delta = 0.122$]. In Model 1, number of comorbidities, depression, and FIM Motor had a significant relationship with participation holding all other variables constant. After social support was added in model 2, number of comorbidities was no longer a statistically significant independent predictor of participation. Based on the standardized betas in Model 2, social support ($\beta = 0.396$) was the strongest predictor of participation at 3 months relative to the other predictors in the model. Detailed results are in **Table 3**. Model fit diagnostics indicated an overall good fit for the model. Residuals were fairly normal and homoscedastic in conformance with significance test assumptions, and the variance inflation factor ranged from 1.01 to 1.56, and the tolerance ranged from 0.64 to 0.99, indicating no collinearity among predictors.

DISCUSSION

The purpose of this study was to determine the unique contribution of perceived social support at discharge from inpatient rehabilitation for first time ischemic stroke to the participation among community dwelling adults 3 months later. As hypothesized, social support was a highly significant independent predictor of community participation. These findings mirror the evidence for social support and community participation among healthy adults (40) and extend the limited existing literature on social support and community participation post stroke (28).

For first time stroke survivors living in the United States, social support was the strongest predictor of participation among all significant predictors in the model, which included physical function (i.e., FIM Motor) and depression. Social support may impact one's ability to overcome the environmental challenges outside of the home in the setting of a physical impairment and may also act as a protective factor against post stroke depression. This link between social support and community participation highlights the importance of including an individual's social support network in discharge planning from inpatient rehabilitation for ischemic stroke. Although rehabilitation providers include caregiver training in intervention plans, this training typically focuses on activities of daily living, transfers, and medical management without attention to community reintegration and participation (3, 41). Sources of social support, especially perceived social support, can be broad and highly individualized.

While these findings suggest that rehabilitation professionals should train caregivers in strategies to improve social support, it is important to acknowledge the extensive literature on caregiver burden post stroke (42). Caregivers of individuals post stroke who are living at home are charged with new responsibilities that impact their own roles, routines, and ability to resume participation in meaningful activities. Additional training on strategies to optimize perceived social support and community participation may inadvertently increase the burden on caregivers. However, given that social support is an even stronger predictor of community participation than physical function, rehabilitation professionals must develop new approaches for optimizing this outcome without adding further burden to caregivers. Since caregivers are not the only source of perceived social support, rehabilitation professionals should consider working with individuals with stroke to explore other people in their lives who may also provide social support and include them in interventions.

In addition to caregiver burden, access to specialized neurorehabilitation, cost, time, transportation, and post stroke fatigue are a few of the obstacles to delivering time intensive, prolonged in-person interventions that address stroke outcomes across all ICF domains. The growing field of telehealth mitigates many of these challenges by broadening access and maximizing therapy time within the individual's natural environment (43). Telehealth is the provision of healthcare services via telecommunication technology (44). The American Heart Association/American Stroke Association supports the use of telehealth within stroke systems of care for the delivery of occupational therapy, physical therapy, or speech disability assessment and intervention via videoconferencing systems (45). Despite research demonstrating that telerehabilitation post stroke has equal effects compared with conventional rehabilitation and that it may even prevent or minimize the well-documented decline in function that occurs post usual rehabilitation (43, 46), telerehabilitation is not widely implemented. Further, similar to in-person practice, community participation has been overlooked in telerehabilitation with studies primarily examining motor recovery, depression, caregiver burden, and higher cortical dysfunction (46). Telehealth post stroke should include interventions that: (1) provide social support to the individual with stroke, (2) promote interactions with social support networks beyond the caregiver, and (3) address caregiver well-ness. Targeting these areas may improve community participation without additional burden to caregivers or creating challenges for other members of one's social support network.

Strengths of this study include a large sample size of persons with first time stroke from multiple sites across the United States

TABLE 2 | Correlation matrix of all variables.

	1	2	3	4	5	6	7	8	9	10	11
1. PAR-PRO	–										
2. DUKE-UNC FSSQ	0.511*	–									
3. Race	0.081	0.004	–								
4. Sex	−0.033	0.021	−0.075	–							
5. Depression	−0.301*	−0.441*	0.070	−0.026	–						
6. Age	−0.062	0.092	0.199*	0.067	−0.082	–					
7. Years of education	0.068	−0.055	0.108*	−0.038	0.017	−0.076	–				
8. # of comorbidities	−0.111*	−0.118*	−0.030	−0.030	0.064	0.038	−0.095	–			
9. # of Stroke Symptoms	−0.133*	−0.107*	−0.123*	0.019	0.020	−0.091	−0.057	−0.010	–		
10. FIM Motor	0.226*	−0.037	−0.016	−0.029	0.076	−0.200*	0.047	−0.030	−0.215*	–	
11. FIM Cognitive	0.118*	−0.029	−0.161*	0.023	−0.111*	−0.159*	0.100*	0.005	−0.181*	0.492*	–

Spearman's correlation is significant at the 0.05 level (two-tailed).

TABLE 3 | Hierarchical regression results.

Model 1			Model 2		
	Standardized beta (95% CI lower, upper)	***P*-value**		**Standardized beta (95% CI lower, upper)**	***P*-value**
Race	0.084 (−0.086, 1.695)	0.077	Race	0.060 (−0.248, 1.40)	0.170
Sex	−0.017 (−0.916, 0.626)	0.711	Sex	−0.016 (−0.848, 0.577)	0.708
Age	−0.047 (−0.046, 0.015)	0.318	Age	−0.073 (−0.053, 0.004)	0.097
Years of education	0.064 (−0.036, 0.213)	0.162	Years of education	0.078 (−0.007, 0.223)	0.066
# of comorbidities	−0.104 (−0.647, −0.046)	0.024	# of comorbidities	−0.052 (−0.453, 0.108)	0.227
# of stroke symptoms	−0.076 (−0.713, 0.068)	0.105	# of stroke symptoms	−0.050 (−0.573, 0.150)	0.251
Depression	−0.292 (−3.753, −1.979)	<0.001	Depression	−0.127 (−2.15, −0.347)	0.007
FIM motor	0.203 (0.025, 0.085)	<0.001	FIM motor	0.243 (0.038, 0.094)	<0.001
FIM cognitive	−0.20 (−0.083, 0.058)	0.728	FIM cognitive	−0.010 (−0.071, 0.059)	0.850
			Social support	0.396 (0.181,0.290)	<0.001
	$R^2 = 0.180$	<0.001		$R^2 = 0.302$	<0.001
	$R^2_{\text{Adj}} = 0.162$			$R^2_{\text{Adj}} = 0.285$	
				$R^2\Delta = 0.122$	<0.001

R^2, R Square; R^2_{Adj}, Adjusted R Square; $R^2\Delta$, R Square Change; $R^2{}_{Adj}\Delta$, Adjusted R Square Change, CI, Confidence Interval.

and the use of established outcome measures. Limitations that may affect generalization of these findings to the broader clinical stroke population include the administration of the PAR-PRO via telephone without evidence to support the validity of the scores, the lack of a baseline measure of pre-stroke participation and the lack of measure of satisfaction with participation. It is unknown whether a person had poor participation prior to the stroke or if a person is satisfied with lower levels of participation. Further, this study included participants who were admitted to inpatient rehabilitation for stroke from 2005 to 2006 which may not be a contemporary representation of stroke survivors. Over the last decade, many measures of participation have been developed and studied in the stroke population that may provide a more sophisticated perspective of participation than the PAR-PRO (8). In addition, the dataset did not include time post stroke, so we are unable to make implications beyond the assumption that the individuals were likely admitted to rehab within the first 2 weeks post stroke. There were other potential biases such as non-blinding of the assessors in the original study, and our analysis of a sample only included participants with complete participation and social support data. Lastly, despite the inclusion of demographic and clinical covariates, a large amount of the variance of community participation remains unexplained.

In conclusion, perceived social support at discharge from inpatient rehabilitation for first time ischemic stroke survivors in the United States is the strongest independent predictor of community participation at 3 months post discharge. Although further examination of the unexplained variance is required, it is clear that interventions targeting the outcome of participation should include a social support component without creating additional caregiver burden.

DATA AVAILABILITY STATEMENT

The Stroke Recovery in Underserved Populations 2005–2006 dataset analyzed for this study can be found in the Archive of Data on Disability to Enable Policy and Research (https://doi.org/10.3886/ICPSR36422.v1).

ETHICS STATEMENT

The Institutional Review Board of Partners HealthCare, the Partners Human Research Committee, determined that this research does not meet the definition of human subjects research since investigators performed secondary analyses of an anonymized and publicly available data set, and did not obtain data through an intervention or interaction with individual subjects or identifiable private information about living individuals.

AUTHOR CONTRIBUTIONS

KE, VS, SM, and RI contributed to study concept, drafted the manuscript, and design. KE performed data, statistical analysis, and drafted the tables and figure.

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A Paradigm Shift: Rehabilitation Robotics, Cognitive Skills Training, and Function After Stroke

Susan E. Fasoli[1]* *and Catherine P. Adans-Dester*[2]

[1] Department of Occupational Therapy, School of Health and Rehabilitation Sciences, Massachusetts General Hospital Institute of Health Professions, Boston, MA, United States, [2] Department of Physical Medicine and Rehabilitation, Harvard Medical School, Spaulding Rehabilitation Hospital, Boston, MA, United States

Introduction: Robot-assisted therapy for upper extremity (UE) impairments post-stroke has yielded modest gains in motor capacity and little evidence of improved UE performance during activities of daily living. A paradigm shift that embodies principles of motor learning and exercise dependent neuroplasticity may improve robot therapy outcomes by incorporating active problem solving, salience of trained tasks, and strategies to facilitate the transfer of acquired motor skills to use of the paretic arm and hand during everyday activities.

Objective: To pilot and test the feasibility of a novel therapy protocol, the Active Learning Program for Stroke (ALPS), designed to complement repetitive, robot-assisted therapy for the paretic UE. Key ALPS ingredients included training in the use of cognitive strategies (e.g., STOP, THINK, DO, CHECK) and a goal-directed home action plan (HAP) to facilitate UE self-management and skill transfer.

Methods: Ten participants with moderate impairments in UE function >6 months after stroke received eighteen 1-h treatment sessions 2–3/x week over 6–8 weeks. In addition to ALPS training, individuals were randomly assigned to either robot-assisted therapy (RT) or robot therapy and task-oriented training (RT-TOT) to trial whether the inclusion of TOT reinforced participants' understanding and implementation of ALPS strategies.

Results: Statistically significant group differences were found for the upper limb subtest of the Fugl-Meyer Assessment (FMA-UE) at discharge and one-month follow-up favoring the RT group. Analyses to examine overall effects of the ALPS protocol in addition to RT and RT-TOT showed significant and moderate to large effects on the FMA-UE, Motor Activity Log, Wolf Motor Function Test, and hand portion of the Stroke Impact Scale.

Conclusion: The ALPS protocol was the first to extend cognitive strategy training to robot-assisted therapy. The intervention in this development of concept pilot trial was feasible and well-tolerated, with good potential to optimize paretic UE performance following robot-assisted therapy.

Keywords: stroke, robot-assisted therapy (RAT), upper extremity (UE), cognitive strategy training, activity performance, transfer of training strategies, motor learning

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Naomi Josman,
University of Haifa, Israel

Reviewed by:
Elisabetta Farina,
Fondazione Don Carlo Gnocchi Onlus (Istituto di Ricovero e Cura a Carattere Scientifico), Italy
Antonino Naro,
Centro Neurolesi Bonino Pulejo (Istituto di Ricovero e Cura a Carattere Scientifico), Italy

****Correspondence:***
Susan E. Fasoli
sfasoli@mghihp.edu

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INTRODUCTION

Rehabilitation efforts to optimize motor function, activity performance and participation after stroke require an understanding of factors that contribute to stroke recovery and an intervention approach focused on the individual's goals and desire to re-engage in valued life roles. Despite recent advances in acute medical interventions to reduce the impact of stroke, residual upper extremity (UE) motor deficits persist long term in up to 65% of stroke survivors, contributing to a loss of independence in activities of daily living and negatively impacting quality of life (1). To advance rehabilitative practice and facilitate satisfaction and participation after stroke, improved methods are needed to optimize the recovery of motor function for home and community activities.

Evidence of neural recovery following highly intensive therapy and the high cost of health care have driven the development of rehabilitation robots to treat motor impairments after stroke. Rehabilitation robots have provided researchers and clinicians with new treatment options to improve UE motor capacity and performance after stroke. The number of robot-assisted therapy trials to address UE function has grown significantly over the past 20 years. Previous studies have shown robot-assisted therapy to be as effective as repetitive task-specific training at increasing motor capacity, as measured by standard assessments in clinical settings (2, 3). While systematic reviews of robot-assisted therapies confirm gains in motor capacity after stroke, they provide little evidence for the transfer of trained motor skills to paretic UE performance during activities of daily living (4, 5). This disparity between improved UE motor capacity (i.e., what a person can do in a standardized, controlled setting) and daily use of the paretic arm and hand is a significant clinical issue (6) and critical barrier to the integration of robotic technology into clinical practice. These findings may be attributed to the limited development of rehabilitation robots that specifically train voluntary control of finger flexion and extension of the paretic hand, and a primary focus on intensity of practice with little regard for other *principles of motor learning and experience-dependent neuroplasticity* (7, 8). These principles, including the salience of training tasks, transfer of acquired skills to similar activities, and active engagement and problem solving, are key to task-oriented training paradigms in stroke but have not been well-integrated into robot-assisted therapy protocols. Recent studies on the use of active problem solving and guided discovery to facilitate skill acquisition during task-oriented training have demonstrated transfer to untrained tasks (9) and significant improvements on measures of UE motor capacity and performance after stroke (10). While these treatment components are instrumental to the transfer of motor skills acquired during task-oriented training, they previously have been absent in robot-assisted therapy trials.

TABLE 1 | ALPS motor learning principles.

Motor learning principles	Example
Use it or lose it (7, 13)	Identify interfering and changeable impairments
	Provide targeted UE training based on individual's motor capacity
Salience of training tasks (7)	Establish clear patient-centered goals
Transference (7, 8, 12)	Facilitate UE self-management through active problem identification and problem solving
Feedback (9, 10, 15)	Provide knowledge of performance
	Encourage self-assessment and discovery
Motivation (7, 8)	Assure challenging and meaningful practice
	Address self-efficacy and confidence

Objectives

The primary aim of this pilot study was to develop and refine a theory-based stroke therapy protocol, the Active Learning Program for Stroke (ALPS), to facilitate the transfer of robot-trained UE motor skills to functional use of the paretic arm and hand during every day activities. The secondary aim was to examine effects of ALPS training combined with either robot-assisted therapy or robot therapy + task-oriented training. We hypothesized that the intervention would be feasible and well-tolerated by participants and would yield positive outcomes on standard measures of paretic UE motor capacity and performance across domains of the International Classification of Functioning, Disability and Health (ICF) (11). This study has potential for improving the effectiveness of robot-assisted therapy by facilitating UE self-management and specifically addressing the transfer of acquired skills (e.g., UE motor capacity) to the performance of UE tasks during activities of daily living. The ALPS protocol is relevant to clinical practice because it provides clinicians with a structured, client-centered motor learning approach to optimize use of the paretic arm and hand.

Active Learning Program for Stroke (ALPS): Conceptual Framework and Application

The ALPS protocol is based upon principles of experience dependent neuroplasticity as described by Kleim and Jones (7); empirical evidence from UE motor learning and task-oriented training programs for individuals with stroke (8, 12); and a conceptual framework for integrating skill, capacity and motivation as described in multiple publications by Winstein et al. (12–14). While principles of repetition, intensity, and specificity of training are active ingredients of robot-assisted therapy protocols to improve motor capacity, other motor learning principles, such as salience and transference, have not been well-infused into prior robot training programs. The ALPS protocol incorporates these principles during robot-assisted therapy sessions, and they are an integral component of each participant's home action plan (HAP) aimed to facilitate UE performance in the home and community. Examples of learning principles are highlighted in **Table 1**.

The ALPS protocol involves instructions to engage in active problem solving, activity analysis and use of general cognitive

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Abbreviations: ALPS, Active Learning Program for Stroke; CO-OP, Cognitive Orientation to daily Occupational Performance; CAHM, Confidence in Arm & Hand Movement; FMA-UE, Fugl-Meyer Assessment—upper limb subtests; HAP, Home Action Plan; MAS, Modified Ashworth Scale; MAL, Motor Activity Log; RT, Robot-assisted Therapy; SIS, Stroke Impact Scale; TOT, Task-Oriented Training; WMFT, Wolf Motor Function Test.

strategies (e.g., STOP, THINK, DO, CHECK), modeled after the Cognitive Orientation for daily Occupational Performance (CO-OP) (15), during paretic UE tasks. We purposely altered our strategy approach from that used in CO-OP because we found that individuals typically don't explicitly establish goals for performance prior to activity engagement. Rather, when they run into challenges while attempting to use their paretic UE functionally they benefit from cues to stop and identify factors impeding performance. Examples of general and domain specific movement strategies are shown in **Appendix A**.

In conjunction with cognitive strategy training, individuals are provided with a HAP to encourage the application of ALPS principles and use of the paretic UE when engaged in everyday activities in the home and community. Participants identify specific, achievable tasks for their HAP based on personal interests. The clinician may use scores from the upper limb subtest of the Fugl-Meyer Assessment (FMA-UE) (16, 17) when providing input to select appropriate tasks based on the participant's current level of function. Due to this participant-centered approach, there are no core tasks included in every HAP, however, similarities do occur across individuals. Participants identify 3–5 UE tasks to be completed daily at home and are taught general and specific ALPS strategies that may facilitate performance. Participants are encouraged to engage in HAP tasks for at least 30 min each day.

MATERIALS AND METHODS

Study Design

While the primary aim was to develop and refine the ALPS protocol for use with robot-assisted therapy, we were also interested in learning whether the inclusion the both robot-assisted therapy and task-oriented training during treatment sessions reinforced participants' understanding and implementation of ALPS strategies. This single-blind randomized control pilot study examined effects of the ALPS protocol combined with robot-assisted therapy alone, or robot-assisted therapy plus task-oriented training, as described below. The clinical evaluator was blinded to group assignment and research hypotheses (**Figure 1**).

Recruitment

Individuals between the ages of 18–82 years and diagnosed with stroke more than 6 months prior to study enrollment were recruited for this study. Informational flyers were provided to attending physicians, outpatient therapists and stroke survivors who previously had given permission to be contacted about research opportunities at Spaulding Rehabilitation Hospital, Boston MA. Inclusion criteria were: moderate UE hemiparesis with initial score on the upper limb subtest of the Fugl-Meyer Assessment (FMA-UE) between 21 and 50/66) (18); and intact cognitive function to understand and actively engage in the ALPS protocol as measured by a Montreal Cognitive Assessment Score of $\geq$26/30 (19) during the initial evaluation visit. Exclusion criteria were: no more than moderate impairments in paretic UE sensation, passive range of motion, and pain as assessed with the Fugl-Meyer Assessment (18); increased muscle tone as indicated by score of $\geq$3 on the Modified Ashworth Scale (20); hemispatial neglect or visual field loss measured by the symbol cancellation subtest on the Cognitive Linguistic Quick Test (21); and aphasia sufficient to limit comprehension and completion of the treatment protocol. Participants could not be enrolled in other UE therapy or research during the study period or present with contraindications for robot-assisted therapy, including recent fracture or skin lesion of paretic UE.

The study protocol was reviewed and approved by the Partners Human Research Committee, the Institutional Review Board for Partners HealthCare, and registered at https://clinicaltrials.gov (NCT02747433). All participants provided written informed consent in accordance with the Declaration of Helsinki.

Intervention

All enrolled participants were administered the ALPS protocol and were randomly assigned to one of two treatment groups: (1) Robot-Assisted Therapy (ALPS + RT) or (2) Robot-Assisted Therapy + Task-Oriented Training (ALPS + RT-TOT).

Robot-Assisted Therapy (RT)

Participants received robot-assisted UE therapy using two commercially-available rehabilitation devices: the Armeo®Spring (Hocoma AG, Switzerland) and Amadeo™ (Tyromotion, Graz, AT) (**Figure 2**).

The Armeo®Spring is a passive exoskeletal spring suspension system that provides repetitive practice of virtual goal-directed reaching tasks for the paretic UE. A distal sensor that detects grip pressure allows the grasp and release of virtual objects during computer-generated games. The amount of gravity assistance and virtual task demands are selected by the clinician to provide challenging yet achievable movement therapy.

During the first treatment session, the Armeo®Spring was adjusted for the participant's arm size and required angle of suspension (~45° shoulder flexion, 25° elbow flexion) and the workspace was measured via standard device operation procedures. The versatility of the Armeo®Spring system allowed repetitive practice of single degree-of-freedom motions (e.g., elbow flexion/extension, supination/pronation) as well as multiple degree-of-freedom training for the paretic shoulder, elbow, forearm, wrist, and hand.

The Amadeo™ robotic system provides position-controlled exercises during computerized games that emphasize grasp and release of the paretic hand. Participants were seated comfortably with the paretic forearm and wrist strapped to an adjustable support attached to the robot device with the wrist in approximately neutral position. A small magnetic disc was secured to the distal phalanx of each digit for connection to the robotically controlled slide that guides movement. Each 1-h session included visually evoked games that provided active-assistive training of collective and individual flexion and extension of the digits, isometric flexion/extension contractions, and continuous passive motion with visual feedback to rest and relax digits when fatigue or increased muscle tone began to impact motor performance.

All participants received 1-h sessions, 2–3×/week for 6–8 weeks (total 18 sessions), divided into two 9 session treatment

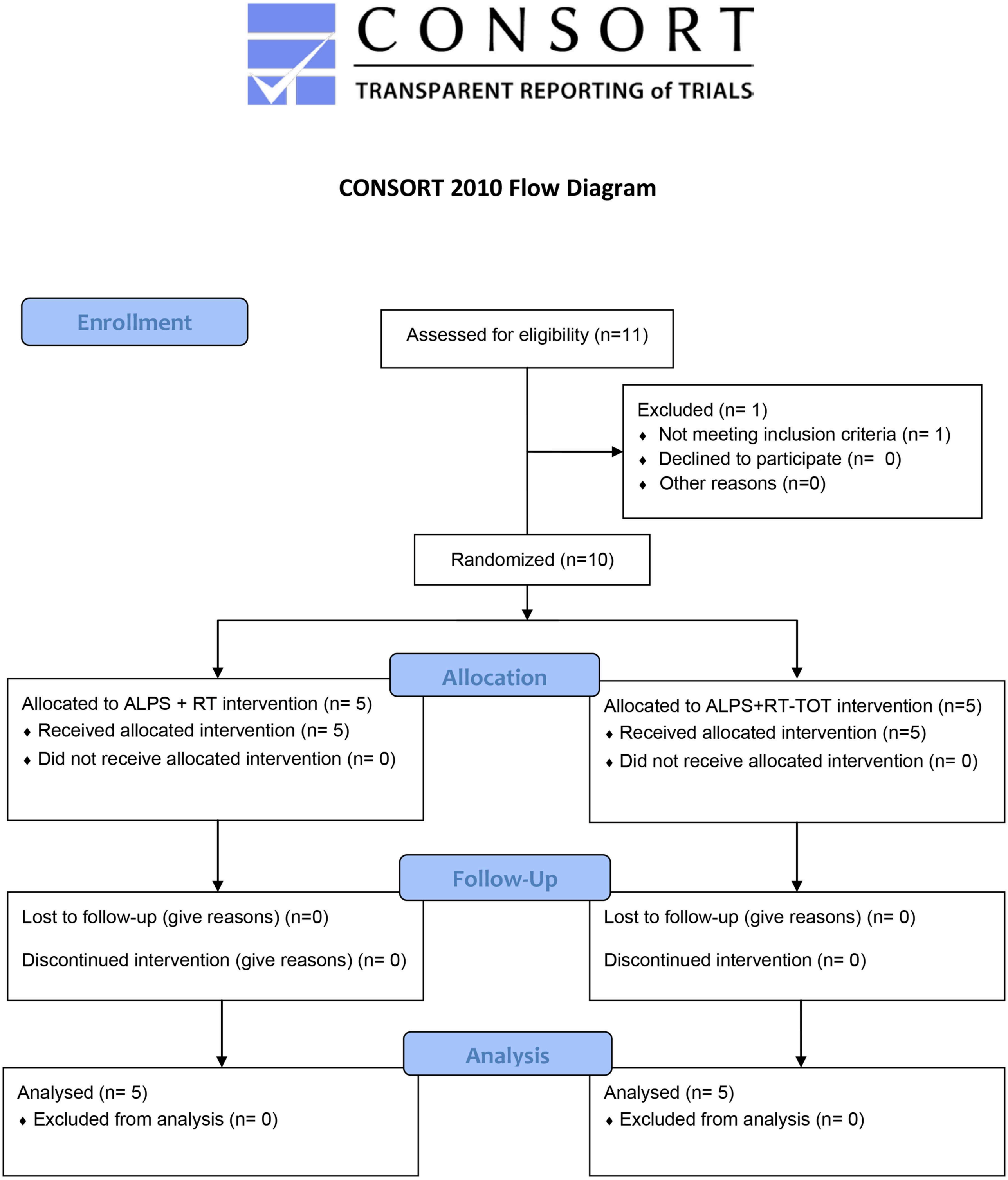

FIGURE 1 | CONSORT flow diagram.

blocks. The two treatment blocks were given in order, with all participants receiving proximal training via Armeo®Spring during the first block followed by Amadeo™ distal training during the second block. All training sessions for one treatment block were completed before proceeding to the next. The robot training sessions provided highly repetitive movement training,

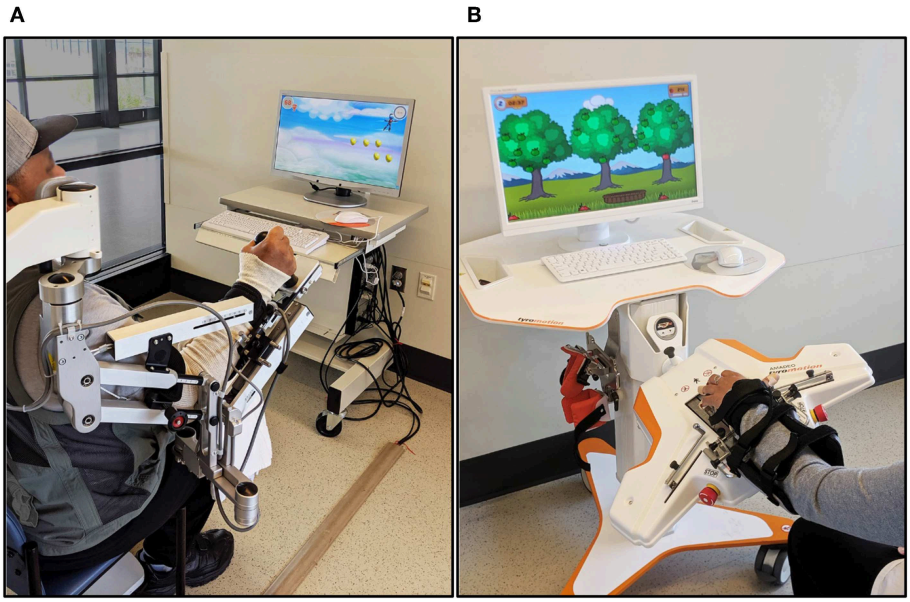

FIGURE 2 | Rehabilitation robots. **(A)** Armeo®Spring **(B)** Amadeo™.

and the robot training time completed during each session was recorded. Rest periods were offered between computer-generated games, as needed. Task challenge for each training device was incrementally increased or decreased based on participant performance.

Task-Oriented Training (TOT)

Participants randomized to the robot and task-oriented training (RT-TOT) group received therapist-guided task-oriented training in addition to RT during 20–30 min of each 1-h treatment session. The participant's baseline performance on the FMA was reviewed, and the FMA keyform and patient-targeted treatment activities outlined by Woodbury et al. (17) aided the selection of UE tasks with greatest potential for improvement during TOT. While we tracked the number of repetitions performed and/or time that participants engaged in continuous motions (e.g., wiping table) the actual dose of TOT differed among participants, based on their activity tolerance and level of function. We attempted to control for this difference by assuring that the overall treatment dose (duration and frequency of therapy sessions) was comparable across RT and RT-TOT groups.

ALPS Protocol

Participants randomly assigned to both intervention groups (RT and RT-TOT) received ALPS cognitive strategy training (e.g., STOP, THINK, DO, CHECK), as described above, during each treatment session. The UE training during RT and RT-TOT reinforced the importance of repetitive practice to optimize motor capacity and performance. Guided discovery during RT facilitated participant understanding of how robot-trained motor skills could generalize to everyday tasks. Individuals randomized to the RT-TOT group also engaged in dynamic performance analysis to identify breakdowns in task completion and attempt solutions during "real-life" activities, such as retrieving objects from the fridge (15). Clinician feedback encouraged self-assessment and knowledge of performance, and participants were motivated to explore ways to use their paretic UE better for HAP tasks. Level of engagement, strategy use, achievements, and concerns regarding the completion of the HAP were reviewed at each session. Participants engaged in active problem solving to identify specific strategies to facilitate success by modifying motor actions (e.g., changing body position, assisting with the less affected UE) or activity demands. The HAP was updated weekly to include new everyday activities and strategies to optimize performance and transfer of motor skills trained during robot therapy.

Outcomes

Clinical assessments were administered at baseline, discharge (<1 week after intervention), and at a 1-month follow-up visit. Evaluation sessions lasted ∼1 ½ to 2 h, and the standardized measures listed in **Table 2** were administered. All are reliable and valid measures of UE motor function, activity performance and participation for individuals post-stroke.

Statistical Analysis

We first performed non-parametric Mann Whitney *U* tests to examine effects of ALPS training combined with RT vs. RT-TOT from admission to discharge, and from admission to the 1-month follow-up assessment. To determine whether the addition of ALPS training to RT and RT-TOT resulted in significant gains on measures across ICF domains, raw scores from both groups were combined and Friedman tests examined whether changes in performance at these three time points were significant. *Post-hoc* analyses with Wilcoxon signed-rank

TABLE 2 | Outcome measures.

ICF DOMAIN/ASSESSMENTS
Body Functions
Fugl-Meyer Assessment—UE (FMA-UE), pain, sensation subtests (18)
Modified Ashworth Scale (MAS) (20)
Activities and Participation
Wolf Motor Function Test (WMFT) (22)
Motor Activity Log (MAL) (23)
Stroke Impact Scale (SIS) (24)
Confidence in Arm & Hand Movement (CAHM) (Lewthwaite et al., unpublished)

TABLE 3 | Participant baseline characteristics.

	RT ($n = 5$)	RT-TOT ($n = 5$)	Total ($n = 10$)	p
Age				
Years, mean ± SD	59.86 ± 19.81	46.51 ± 19.52	53.19 ± 19.83	0.31
Gender				
Female/male, n (%)	1 (20)/4 (80)	3 (60)/2 (40)	4 (40)/6 (60)	0.19
Time since stroke				
Months, mean ± SD	19.91 ± 22.28	97.60 ± 84.06	58.75 ± 70.98	0.11
Hemiparesis				
Left/right, n (%)	3 (60)/2 (40)	2 (40)/3 (60)	5 (50)/5 (50)	0.52
Affected side				
Dominant/non-dominant, n (%)	2 (40)/3 (60)	4 (80)/1 (20)	6 (60)/4 (40)	0.47
Fugl-Meyer assessment upper extremity				
Score (/66), mean ± SD	34.40 ± 6.73	34.00 ± 12.41	32.20 ± 9.60	0.59

tests were conducted. In addition, Cohen's d effect sizes for dependent samples were calculated in Microsoft Excel for Office 365. Analyses were completed with the IBM SPSS, Version 25.0 Statistical Package.

RESULTS

Ten individuals (53.19 ± 19.83 years of age) more than 6 months post-stroke onset participated in this study between July 2016 and November 2018. Participant characteristics for each group are reported in **Table 3**. Group differences in baseline demographics and FMA-UE scores were non-significant.

The ALPS protocol was feasible and well-tolerated, as participants ($n = 10$) completed all assessment and intervention sessions, described use of ALPS cognitive strategies during their HAPs, and reported high satisfaction with the therapy process.

Mann Whitney U tests revealed statistically significant gains on the FMA-UE from admission to discharge ($Z = -2.32$, $p = 0.02$) and admission to the 1-month follow-up assessment ($Z = -2.64$, $p = 0.008$), with the RT group outperforming those who received RT-TOT. No between-group differences were found for the remaining clinical outcome measures following intervention. Friedman tests and *post-hoc* Wilcoxon analyses to evaluate effects of the ALPS protocol in addition to RT and RT-TOT ($n = 10$) revealed statistically significant improvements at discharge and follow-up for the FMA-UE, WMFT, MAL (AOU and HW scales), and the hand portion of the SIS (see **Table 4**).

Wilcoxon *post-hoc* tests of participant ratings on the Confidence in Arm and Hand Movement (CAHM) scale indicated that confidence in use of the paretic UE for a variety of functional activities (e.g., cutting food with a knife and fork or performing tasks in public) trended upward at the one-month follow-up visit, with admission to follow-up results reaching statistical significance ($p = 0.037$). Moderate to large Cohen's d effect sizes for these measures are reported in **Table 5**.

DISCUSSION

The clinical acceptance and widespread use of rehabilitation robots for UE therapy post-stroke has been limited, in part, by the lack of empirical evidence for its impact on UE performance and engagement in meaningful activities of daily living (4, 5). This development of concept pilot trial (25) is the first to test an ALPS that shifts robot-assisted therapy away from an impairment focused intervention to one aimed to facilitate the transfer of robot-trained motor skills to functional use of the paretic arm and hand after stroke. This new paradigm is based upon principles of experience-dependent neuroplasticity (7) and cognitive strategy training (15), and embraces the distinct strengths of robot-assisted technology and clinician-driven interventions. The rehabilitation robots deliver a higher dose of repetitive task-specific training than is possible in conventional rehabilitation settings, while the clinician empowers participants with a step-by-step problem-solving approach to facilitate use of trained motor skills during meaningful everyday activities, thereby adding salience and transference to the rehabilitation process.

The Mann Whitney U group analyses revealed statistically and clinically significant improvements in motor capacity, as measured by the FMA-UE, with the ALPS + RT group improving more than those who received a combination of ALPS + RT-TOT. Participants in the ALPS + RT group received on average a total of 524.0 min of Armeo®Spring and Amadeo™ training during the study protocol, as compared to 303.0 min in the ALPS + RT-TOT group. Although individuals randomized to the RT-TOT group also received repetitive task-oriented training during 20–30 min of each treatment session, it was not possible to achieve as many movement repetitions during this time due to the nature of the training, which was focused on guided discovery and problem solving during challenging, yet achievable UE tasks. The number of repetitions, choice of discrete vs. continuous tasks (e.g., reaching vs. stirring), and practice of unilateral and bilateral tasks during task-oriented training was individualized, based on the participant's UE motor capacity and target of intervention. Therefore, it is likely that individuals in the ALPS + RT group completed more movement repetitions than those in the RT-TOT group, which may have contributed to greater improvement in UE motor capacity, as measured by the FMA-UE.

TABLE 4 | Friedman analyses ($n = 10$).

Outcome measure	Baseline	Post-intervention	1-month follow-up	Significance
FMA-UE (0-66)				χ^2 (2) = 13.26***
Mean	32.20	39.50	39.50	$p = 0.001$
Median	32	41.50	44.50	
SD	9.60	10.01	11.48	
Range	20-45	23-51	19-51	
MAS (0–4)				χ^2 (2) = 0.87
Mean	0.58	0.63	0.65	$p = 0.649$
Median	0.56	0.64	0.61	
SD	0.28	0.35	0.43	
Range	0.22–0.94	0–1.11	0–1.28	
WMFT (task rate)[a]				χ^2 (2) = 6.20*
Mean	13.50	17.26	19.22	$p = 0.045$
Median	13.42	17.47	18.07	
SD	6.26	7.39	8.04	
Range	6.08–21.87	5.29–26.40	5.65–32.64	
MAL-AOU (0–5)				χ^2 (2) = 15.20***
Mean	1.17	2.01	1.90	$p = 0.001$
Median	1.00	1.98	2.10	
SD	0.72	0.86	0.91	
Range	0.52–2.45	0.79–3.59	0.71–3.21	
MAL-HW (0–5)				χ^2 (2) = 15.00***
Mean	1.20	2.05	1.98	$p = 0.001$
Median	0.98	1.99	2.20	
SD	0.62	0.78	0.80	
Range	0.53–1.93	0.79–3.22	0.71–2.89	
CAHM (0–100)				χ^2 (2) = 5.40
Mean	45.83	62.01	58.39	$p = 0.067$
Median	44.50	58.38	53.25	
SD	16.92	21.26	18.70	
Range	26–80.75	28.50–98.55	30–86.50	
SIS-Hand (0–100)[b]				χ^2 (2) = 11.74**
Mean	24	36.40	33.20	$p = 0.003$
Median	24	32	36	
SD	15.89	18.13	18.09	
Range	4–48	12–72	8–56	
SIS-recovery (0–100)				χ^2 (2) = 4.67
Mean	62.80	69.50	71.30	$p = 0.097$
Median	60	70	72.50	
SD	12.07	14.42	12.61	
Range	50–87	40–85	50–88	

[a] *Task Rate indicates average # of times each test item could be completed within 1 min. Higher scores indicate improved task completion.*

[b] *SIS-Hand, Transformed scores reported [0–100].*

$^*p<0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$.

TABLE 5 | Cohen's *d* effect sizes ($n = 10$).

Outcome	Admission to discharge	Admission to follow-up
Fugl-Meyer ASSESSMENT (FMA-UE)	$d = 0.74$	$d = 0.69$
WMFT (task rate)	$d = 1.06$	$d = 0.89$
Motor Activity Log (MAL-AOU)	$d = 1.21$	$d = 1.09$
Motor Activity Log (MAL-HW)	$d = 0.85$	$d = 0.71$
Confidence in Arm & Hand Movement (CAHM)	$d = 0.56$	$d = 0.81$
Stroke Impact Scale, Hand (SIS-Hand)	$d = 0.73$	$d = 0.54$

Whyte et al. (26, 27) have developed the Rehabilitation Treatment Specification System to specify and study the effects of rehabilitation treatments and uncover the "black box" of rehabilitation. This framework is useful for describing the treatment outcomes or *targets* as well as the many treatment *ingredients* that comprise a given intervention and their potential *mechanisms of action*. The primary *target* for most robot-assisted therapy studies has been a reduction in motor impairment, with less attention to measuring gains in functional use of the paretic arm and hand during everyday activities. A missing element in much of this research is the examination of what treatment *ingredients* other than the number of repetitions delivered (e.g., type of human machine interface, instructions, motor skills practiced by robot therapy games) are integral to the intervention protocol, and how they contribute to changes in performance. An intervention study that compared effects of Amadeo$^{\text{TM}}$ robot-assisted therapy to conventional hand training by an occupational therapist revealed significantly greater improvements on neurophysiological measures of cortical plasticity and interhemispheric inhibition in the Amadeo$^{\text{TM}}$ group that paralleled gains in clinical outcome scores (28). Controlled studies such as this are essential to our understanding of the relationship between treatment ingredients delivered by these different forms of hand training and potential mechanisms of action that contribute to observed changes on standardized clinical assessments and in functional use of the paretic arm and hand after stroke.

The recently published RATULS randomized control study of more than 700 stroke participants who received robot-assisted therapy, enhanced upper limb training (EULT) by a rehabilitation clinician, or usual care reported that the intensive training interventions (robot- therapy and EULT) did not significantly improve its targeted outcome, UE function as measured by Action Research Arm Test (ARAT) (29). In addition, the small gains that were observed in UE function did not transfer to activities of daily living. These findings, and similar reports from systematic reviews of robot-assisted therapy (4, 5), indicate that greater attention is warranted to treatment ingredients other than repetition. While rehabilitation robots are highly capable of repetitive movement training, it is apparent that robot-assisted therapy alone is not sufficient for optimizing UE activity engagement and participation in persons with UE motor impairments after stroke. In the current ALPS protocol, treatment ingredients to specifically enhance the transfer of robot-trained motor skills included instruction in cognitive strategies to enhance problem solving during UE activities and a HAP to encourage carry-over of robot-trained motor skills to daily activities in the home and community. While the ALPS pilot was not designed to differentiate the effects of these treatment ingredients, the statistically significant gains and medium to large effect sizes for outcomes across ICF domains, coupled with clinically significant improvements in FMA-UE scores at follow up (n = 10, mean = 7.3/66 points) are promising. They far exceed gains reported in the 36 session RATULS study (adjusted mean FMA-UE difference of 2.79/66 points between robot and usual care groups at 3 months) and in systematic reviews of robot-therapy outcomes (5, 29). The present findings align with assertions by Valero-Cuevas et al. (30) that changes in performance are multidimensional and cannot be measured by a single primary outcome, such as the Fugl-Meyer Assessment or ARAT.

A systematic review of UE rehabilitation methods after stroke (31) emphasized the importance of tailoring evidence-based treatments to the needs of the individual. Each component of the ALPS protocol (robot therapy, cognitive strategies, and HAP) was individualized, based on the participant's level of UE functioning and identified task goals. The HAPs provided to ALPS participants were tailored to their individual interests and contexts, and were based upon prior research on the effectiveness of cognitive strategy training for individuals post-stroke (10, 32). While adherence to daily HAP completion varied among participants, semi-structured interviews administered more than 6 months post-ALPS training revealed that the HAPs were a separate, yet valued ingredient of the intervention. Participants applied ALPS strategies (e.g., STOP, THINK, DO, CHECK) to problem-solve challenges encountered during everyday tasks. Those with greater distal function at baseline were more likely to follow through with HAP activities for the paretic arm and hand and reported greater ability to independently apply problem solving strategies during HAP activities. Participants who did not consistently complete HAP activities suggested ways to improve adherence, including discussions to better manage fatigue, time management, and potential benefits of a computer or mobile application to improve ease of reporting. Thematic analysis of post-intervention interviews has begun, and the initial results have contributed to our understanding of the treatment ingredients most beneficial to past participants. Many reported continued use of the ALPS strategies more than 1-year post-intervention and viewed each treatment component as essential to improving use of their paretic arm and hand during daily activities. Participant input has been used to refine the intervention manual prepared for our next ALPS trial.

Limitations of this research, including its small sample size and variable daily adherence to the HAP across participants, suggest caution when interpreting study outcomes. The inclusion criteria limited our participant sample to individuals with moderate upper extremity impairments as measured by the Fugl-Meyer Assessment (inclusion range 21–50/66 points), therefore generalization of findings to individuals with milder or more severe impairments is limited. Also, our participants were individuals more than 6 months post-stroke onset, and many had developed learned non-use of the paretic arm and hand during this time. Earlier training and implementation of ALPS strategies during acute and subacute phases of recovery may facilitate greater ease of transfer and adherence to HAP activities.

CONCLUSIONS

The novel Active Learning Protocol for Stroke (ALPS) has the potential to shift current research paradigms for intensive robot-assisted therapy by training stroke participants to engage in self-analysis and active problem solving to better utilize recovered UE motor skills during daily living tasks. This innovative project is the first to extend this cognitive strategy and motor learning approach to robot-assisted therapy for persons with moderate UE impairments after stroke: individuals who may not qualify for task-oriented training protocols. The ALPS protocol and client-centered HAP are derived from principles of experience-dependent neuroplasticity (7), motor learning strategies applied to task-oriented training (8, 12) and the Cognitive Orientation to daily Occupational Performance (15). Although this initial pilot study to develop and test the ALPS protocol was well-tolerated and produced significant gains in paretic UE capacity and performance, we are in the process of refining and formalizing the intervention protocol in preparation for a larger confirmatory trial.

DATA AVAILABILITY STATEMENT

The datasets generated for this study are available on request to the corresponding author.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Partners Human Research Committee (PHRC), the IRB for Partners Healthcare in Boston, MA. The patients/participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

AUTHOR CONTRIBUTIONS

SF developed the Active Learning Program for Stroke research protocol, obtained IRB approval, administered the intervention, and was primarily responsible for data analysis, interpretation, and writing of the manuscript. CA-D was a blinded evaluator, assisted with data analysis, interpretation of results, and editing of the manuscript.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2019.01088/full#supplementary-material

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The remaining author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Participation in Younger and Older Adults Post-stroke: Frequency, Importance, and Desirability of Engagement in Activities

Joan Toglia[1,2]*, *Gulce Askin*[3], *Linda M. Gerber*[3], *Abhishek Jaywant*[2,4,5] *and Michael W. O'Dell*[2]

[1] Mercy College, Dobbs Ferry, NY, United States, [2] Rehabilitation Medicine Department, Weill Cornell Medicine, New York, NY, United States, [3] Department of Healthcare Policy and Research, Weill Cornell Medicine, New York, NY, United States, [4] NewYork-Presbyterian Hospital, New York, NY, United States, [5] Department of Psychiatry, Weill Cornell Medicine, New York, NY, United States

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David Jing-Piao Lin,
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United States
Galina Gheihman,
Brigham and Women's Hospital,
United States

***Correspondence:**
Joan Toglia
jtoglia@mercy.edu

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Purpose: To characterize and compare frequency and subjective dimensions of post-stroke participation in younger (<65) and older adults (>age 65), in social, productivity and leisure activities, 6 months post-inpatient rehabilitation. Secondary aims included exploration of demographic and clinical factors influencing desire for increased participation and comparison of two measures of participation.

Methods: A prospective cohort study of people with stroke ($n = 99$) who were identified during their inpatient rehabilitation stay and followed-up 6 months post-discharge with telephone interviews using two self-report participation measures. The Stroke Impact Participation subscale (SIS-P) measured the frequency of perceived limitations in social, leisure, productive activities and extent of stroke recovery. The Community Participation Indicators (CPI) examined activity frequency, importance, and desire for increased activity engagement. Descriptive statistics were used to summarize demographic variables and characterize SIS-P and CPI items. Differences between age groups on individual items were examined. Associations between measures and demographic variables were explored.

Results: Both groups reported a wide variation in participation restrictions that was not associated with stroke severity and weakly associated with discharge functional status (rho = 0.20–0.35). There were no significant differences between age groups in CPI frequency (for 18/19 items), or the SIS-P. However, there was a trend toward more participation restrictions on the SIS-P among those <65 ($p = 0.07$). Younger adults ($n = 46$; median age = 53) were significantly more likely to indicate that they were not doing selected activities enough on the CPI, compared with older adults ($n = 56$; median age = 76). While age and ethnicity were independently associated with some activities, it was not associated with other activities. The CPI and SIS-P were moderately related at a correlation of rho = 0.54, $p < 0.001$.

Conclusion: The CPI demonstrated value and utility in examining subjective perspectives of activity importance and desire for change for people who are 6 months post-stroke. Although the CPI and SIS-P are moderately related, subjective appraisal of participation in selected individual activities (CPI) better distinguished between age groups and provided unique and distinct information from the SIS-P.

Keywords: outcome assessment, social participation, stroke, rehabilitation, subjective appraisal, community participation indicators, Stroke Impact Scale

INTRODUCTION

Stroke is a leading cause of long-term disability. Annually, ∼795,000 people experience a stroke each year in the United States (US) (1). Despite declining incidence and mortality rates, the number of people living with a disability as a result of ischemic stroke has increased by 55% between 1990 and 2016 in the US (2). Improved medical management, higher survival rates, and longer lifespans have resulted in people living longer after a stroke.

Although decreased incidence of stroke in the general population has been reported, a trend toward rising stroke occurrences among younger age groups over the past decade has been reported globally in numerous studies (3–5). For example, the number of Americans hospitalized for a stroke below age 65 increased by 49% in the last decade (6). The underlying cause of stroke incidence in younger age groups is multifactorial but increases in risk factors such as cocaine use and cannabis use appear to be associated with this trend (7).

In general, both younger and older adults report significant long-term participation restrictions following a stroke. *Participation* is widely regarded as the ultimate goal of rehabilitation following a stroke. The International Classification of Functioning, Disability and Health defines participation broadly as involvement in life situations, including roles and activities (8). The aim of rehabilitation is to help people return to their lives and fulfill roles and engage in meaningful life activities. There is little information however, comparing activity engagement in younger and older adults post-stroke, particularly among those who have completed a course of short term intensive inpatient rehabilitation (defined by a minimum of 3 h of therapy per day).

The impact of stroke disability on the lives of people who are 65 years and younger may be very different than those who are older. For example, stroke during working age years has a large socioeconomic impact due to loss of productivity, and results in people living with a long-term disability over a longer time (3, 9). Further, the relative value and meaning placed on various functional activities and social roles likely differs by age (9). Overall, the rise in the number of people living with a chronic stroke-related disability indicates a pressing need to fully understand the unique participation restrictions experienced by both younger and older people who are living with the effects of stroke.

The measurement of a complex construct such as participation presents challenges because there is a lack of consensus regarding its conceptualization and operationalization (10). It is not always clear if different participation assessments will yield consistent results. Most participation instruments examine self-reported frequency such as the amount of time one experiences limitations, or spends in social, leisure, productive activities and roles. This has been described as the objective aspect of participation, because it can be observed, easily quantified or reported, and ratings can be compared across different people or groups (10). In addition to frequency, another dimension of participation involves the subjective aspect or the person's experiences, feelings and self-perceptions. The subjective aspect of participation includes autonomy, importance of activities to the person, satisfaction, and desire for changes in participation (10, 11). Activities that are important or meaningful to a person or that the person would like to do more often, are individualized and depend on the person's preferences, interests, life roles or the context of that person's life (12). Although there are a few exceptions, the majority of participation instruments only focus on the objective (i.e., frequency) dimension of participation (10).

Comparisons of both subjective and objective dimensions of participation in people with stroke are limited in the literature. Studies that have included measures of subjective participation have focused on perceived satisfaction (11), however desire for increased participation in valued activities has not been explored. Additionally, the subjective and objective aspects of participation have not been compared in younger and older adults.

Therefore, this study aims to describe and compare self-reported participation restrictions including frequency, importance and desire for change in younger and older stroke survivors above or at and below age 65. Specifically, our aims are to (1) Compare the frequency of participation and perceived stroke recovery between age groups, (2) Describe and compare the subjective aspects of participation (activity importance, desire for change) between age groups, (3) Determine the association of participation domains with demographic and clinical variables, (4) Assess the relationship between objective and subjective aspects of participation as measured by the Stroke Impact Scale-Participation subscale (SIS-P) and the Community Participation Indicators (CPI), respectively.

MATERIALS AND METHODS

Participants

We prospectively identified participants with a diagnosis of stroke, who were consecutively admitted to an inpatient rehabilitation unit (IRU) within a large academic medical center

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Abbreviations: CPI, Community Participation Indicators; NIHSS, National Institute of Health Stroke Scale; SIS-P, Stroke Impact Scale, Participation domain; IRU, Inpatient rehabilitation unit; FIM, Functional Independence Measure.

between July 25, 2012 and July 6, 2016. All included participants provided written informed consent to have demographic and routine clinical information obtained during their inpatient stay, entered into a stroke rehabilitation database. At the same time, they also provided consent to be contacted for a follow-up telephone interview 6 months after discharge. The study was approved by the facility's Institutional Review Board for Human Subjects Research. Inclusion criteria were the same as those for admission to the IRU and included individuals who were 18 years of age or older, who were medically able to participate in inpatient rehabilitation therapies for 3 h daily, and who had a reasonable chance of making functional gains. Those who fully completed targeted follow-up telephone measures with no more than 4% of responses missing, between 6 and 7 months following discharge from inpatient rehabilitation ($n = 99$), and were living in the community were included in this analysis.

Participation Assessment Measures

The Community Participation Indicators (CPI), Part 1

The Community Participation Indicators (CPI) is a newer participation measure that was developed by Heinemann et al. using multiple stakeholder focus groups to explore what the concept of participation meant to people with disabilities (13). In addition to examining activity frequency, part 1 of the CPI accounts for individual preferences for activity engagement by examining importance and the person's desire to engage in each activity more often.

The CPI (part 1) includes 20 items related to productive roles activities, social activities and relationships, recreations and leisure (13). For 19 items, respondents rate each item on (1) frequency of engagement on a scale of either 1 (none) to 5 or 6 (high frequency) in terms of number of hours, days or times or times per week depending on the activity type; (2) whether it was important (yes/no), and (3) to what extent they were doing the activity too much, enough, or not enough. The ratings of "enough" and "too much" were collapsed to create a dichotomous variable. One item (#7), was not rated by frequency. There is no total score for the CPI but a CPI ratio, calculated the number of important activities engaged in often enough or too much (numerator) to the number of important activities (denominator), across participants as well as for each item. Scores range between 0 and 1 with higher scores indicating increased participation in activities that are meaningful to the individual (14). The CPI was validated through Rasch analysis in a sample of 1,163 individuals with a variety of diagnoses (13, 14), however results focused solely on a stroke population have not been previously reported for Part 1 of the CPI.

Stroke Impact Scale 3.0 Participation Subscale (SIS-P) and Visual Analog Stroke Recovery Scale

The SIS-P is the most frequently used scale to measure participation following stroke (15). The SIS-P is a self-report questionnaire containing 8 questions that ask the participant to rate how much of the time he or she has been limited in the past 4 weeks in work, social, productive activities and control over one's life (16). The responses to each question are scored on a scale of 1 (all of the time) to 5 (none of the time). Domain scores range from 0 to 100, with higher scores indicating that fewer problems (less impact) are perceived. Scores of <50 indicate limited participation (17, 18). The SIS also includes 1 item, presented in the form of a vertical visual analog scale (VAS), that assesses perceptions of overall stroke recovery, ranging from 0 = "no recovery" to 100 = "full recovery." The SIS domains have high reliability, with Cronbach's alphas ranging from 0.83 to 0.90 and intraclass correlation coefficients (ICCs) ranging from 0.70 to 0.92 (19). Validity of the domains have been established through Rasch analysis (16). Concurrent validity (19) and construct validity have also been established (20). The SIS has been demonstrated to have good agreement between persons with stroke and proxies (21).

Procedures

Participants were contacted by their preferred method (e-mail, phone, mail) 2 weeks before their 6-month post-discharge date to set up a time for a phone interview to complete the SIS-P, Stroke recovery scale and CPI. Questions were sent to the participant prior to the phone interview, so that they had them during the phone interview. All participants were living in the community. If the person was unable to participate in a phone interview, the interview was completed by proxy. Data were entered into a stroke research database using REDCap (Research Electronic Data Capture), a secure, web-based data management application (22). Participants with missing or incomplete assessment data were excluded from the analysis. The National Institutes Stroke Scale score (NIHSS) documented from the emergency department or upon admission to neurology, along with demographic, background, and stroke-related characteristics from rehabilitation admission or discharge including the Functional Independence Measure (FIM), were extracted from the electronic medical record into the stroke database and subsequently analyzed along with the 6-month measures.

Statistical Analysis

Descriptive statistics including median, interquartile range, frequency, and percent, were used to summarize demographic variables, and the CPI and SIS-P questionnaire items. Visual inspection of histograms as well as the Shapiro-Wilk test were used to assess normality of continuous variables. Participant age was categorized into 66 years and older or 65 and younger. It should be noted that the age cut-off for defining young strokes is unclear. The World Health Organization (WHO) defines young stroke as under age 65, while other studies include age 65 and below (Sweden study). Since the official retirement age in the United States is 66, we chose to divide younger and older adults by those above, or at and below age 65.

Individual CPI and SIS-P items, the total SIS-P score, stroke recovery rating and CPI ratio score were all compared across the two age groups. The Wilcoxon rank-sum test was used to assess the association between age group and continuous variables while the chi-square or Fisher's Exact test, as appropriate, was used to assess the association between age group and discrete variables. CPI items that were significantly associated with age group at $p < 0.05$ were used as outcomes in multivariable logistic regression models to assess the independent effect of age on the participation item, controlling for ethnicity and discharge FIM total score. These items were collapsed into binary variables. The CPI items relating to doing an activity "enough" were collapsed into "enough or too much" vs. "not enough" while the item relating to frequency was collapsed into "with some frequency (1 to > 35 h)" vs. "none." Co-variates and potential confounders were selected based on literature review and clinical knowledge. The correlation between the CPI ratio score and the total SIS score was assessed with Spearman's rank correlation coefficient. All *p*-values are two-sided with statistical significance evaluated at the 0.05 alpha level. All analyses were performed by a biostatistician in *R* Version 3.5.3 (Vienna, Austria) (23).

TABLE 1 | Demographic and clinical characteristics of the participants ($N = 99$).

Characteristic	Entire sample, $n = 99$	Younger ≤ 65, $n = 43$	Older ≥ 66, $n = 56$	*P*
Age	69 (55, 77.5)	53 (49.5, 61)	76 (71.8, 83.2)	<0.001*
Sex *n* (%)				1.000
Male	50 (50.5)	22 (51.2)	28 (50)	
Female	49 (49.5)	21 (48.8)	28 (50)	
Ethnicity *n* (%)				<0.001*
Caucasian	58 (58.6)	14 (32.6)	44 (78.6)	
Black	18 (18.2)	14 (32.6)	4 (7.1)	
Hispanic	10 (10.1)	9 (20.9)	1 (1.8)	
Asian/Pacific Islander	10 (10.1)	3 (7)	7 (12.5)	
Other	3 (3)	3 (7)	0 (0)	
Education				0.347
Less than high school	8 (8.1)	2 (4.65)	6 (10.7)	
Completed high school	26 (26.3)	14 (32.6)	12 (21.4)	
Some college	14 (14.1)	8 (18.6)	6 (10.7)	
College degree or higher	51 (51.5)	19 (44.2)	32 (57.1)	
Length of Stay	12 (8, 17)	13 (9, 19)	12 (8, 15.2)	0.214
Side of Lesion *n* (%)				0.199
Left hemisphere	42 (42.4)	18 (41.9)	24 (42.9)	
Right hemisphere	47 (47.5)	18 (41.9)	29 (51.8)	
Bilateral	10 (10.1)	7 (16.3)	3 (5.4)	
Type of Stroke *n* (%)				0.063
Ischemic	82 (82.8)	32 (74.4)	50 (89.2)	
Hemorrhagic	17 (17.1)	11 (25.6)	6 (10.7)	
Prior TIA/CVA *n* (%)	20 (20.2)	9 (20.9)	11 (19.6)	1.000
Days post-CVA	6 (4, 11)	7 (5, 13)	5 (3, 11)	0.037*
NIHSS score	4 (3, 8.5)	5 (3, 10.5)	4 (2, 6)	0.039*
Discharge-home *n* (%)	73 (74.5)	30 (71.4)	43 (76.8)	0.919
Work prior to stroke *n* (%)	36 (36.3)	25 (58)	11 (19.6)	<0.001*
Work after stroke *n* (%)	16 (16.2)	9 (20.9)	7 (12.5)	<0.001*
Discharge FIM				
Motor FIM	57 (49.5, 65.5)	59 (51.5, 65.5)	55.5 (47, 64)	−0.586
Cognitive FIM	31 (24, 34)	32 (24, 34)	31(24.8, 34)	−0.192
Total FIM score	88 (76.5, 99.5)	89 (80.5, 102)	87 (72.8, 97.2)	−0.787
SIS total score	65.6 (42.2, 90.6)	56.2 (31.2, 82.8)	70.3 (46.9, 90.6)	0.075
SIS <50 *n* (%)	33 (33.3)	18 (41.9)	15 (26.8)	0.12
SIS stroke recovery	75.0 (50.0, 85.0)	75.0 (50.0, 85.0)	72.5 (50.0, 86.2)	0.879
CPI ratio score	0.53 (0.22, 0.75)	0.45 (0.21, 0.69)	0.57 (0.24, 0.79)	0.132

*$P < 0.05$.

RESULTS

Of 273 inpatients who provided consent to be contacted on 6-month follow-up, ∼36% ($n = 99$), responded and fully completed participation outcome measures. This resulted in a final sample that demonstrated relatively mild and some moderate neurological and cognitive/ language deficits. **Table 1** summarizes demographic and clinical characteristics of the final sample.

Compared with the final sample, those not included had greater language and cognitive disability as reflected by median [IQR] FIM discharge cognitive score (median = 28, [IQR = 21.0; 33.0] compared to 31 [IQR = 24.0; 34.0] and higher median [IQR] NIHSS scores 6 [3.00; 12.00] vs. 4 [3.00; 8.50]; $p = 0.02$. No significant differences were observed for the discharge motor FIM score, or other demographic variables such as age, sex, ethnicity, length of stay, or side of lesion.

Participants included in the final analysis (**Table 1**) had a median age of 69, equal representation of gender, 80% first time stroke, median NIHSS score of 4, a total discharge FIM score of 88 and were mostly Caucasian (59%). Twenty-seven percent of respondents were by proxy. Those with proxy respondents had significantly lower discharge FIM cognitive (median = 25 vs. 32), $p < 0.001$) and motor scores (50 vs. 59) $p = 0.003$.

The final sample was divided by age groups. The <65 age group demonstrated significantly more ethnic diversity than the older group, were admitted to inpatient rehabilitation after a longer number of days post-stroke and had a higher median NIHSS score. There were no significant differences between groups in sex, educational level, length of stay, side of lesion, proxy respondents, prior stroke, discharge home, or admission and discharge FIM scores.

Comparison of Frequency of Participation Between Age Groups

CPI Frequency (Objective Participation)

Overall, both groups reported high frequency of participation with getting out and about, spending time with family, keeping in touch with family or friends, and engaging in hobbies or leisure activities. Least frequently engaged activities were participating in civic activities, self-help groups, clubs, and volunteer work. There were no significant differences between age groups in reported frequencies of activities with the exception of looking after children or providing care for a loved one, with older adults reporting less frequency compared to younger adults ($p = 0.033$). **Table 2** summarizes the frequency of engagement in CPI activities (dichotomized into none vs. level of frequency combined).

TABLE 2 | Community Participation Indicators (CPI): Descriptive Statistics of activities in younger and older adults post-stroke.

	Younger < 65				**Older >65**			
Activity	**Frequency % > none**	**Important %**	**% Doing activity enough**	**CPI Ratio**	**Frequency % > none**	**Important %**	**% Doing activity enough**	**CPI Ratio**
1. Get out and about	97.7	95.3	53.5	51	89.3	92.9	50.9	48
2. Spend time with family	86	90.7	76.7	74	85.7	90.9	74.5	72
3. Keep in touch with family by phone or internet	93	93	79.1	78	94.6	94.6	74.5	72
4. Spend time with friends	65.1	86	52.4	46	78.6	87.5	56.4	49
5. Keep in touch with friends by phone or internet	88.4	83.7	76.7	72	89.3	85.7	80.4	77
6. Go to parties, out to dinner, or other social activities	55.8	81.4	53.5	43	55.4	78.6	51.8	43
7. Spend time with a significant other or intimate partner	–	85.7	58.5	50	–	59.3	79.6	69
8. Work for money	23.3	86	37.2	27	16.1	35.7	71.4	20
9. Cook, clean, and look after your home	72.1	88.4	55.8	50	55.4	67.9	60.7	45
10. Manage household bills and expenses	67.4	85.7	71.4	67	67.9	80.4	75	71
11. Look after children or provide care for a loved one	30.2	62.8	58.1	33	14.3	32.1	80	39
12. Go to classes or participate in learning activities	20.9	65.1	51.2	25	28.6	45.5	73.2	40
13. Volunteer	11.6	55.8	53.5	21	14.3	37.5	76.8	38
14. Participate in religious or spiritual activities	55.8	74.4	51.2	38	40	48.2	66.1	30
15. Go to support groups or self-help meetings	7	41.9	65.1	17	3.6	25	76.8	7
16. Engage in hobbies or leisure activities	79.1	100	38.1	37	82.1	91.1	58.9	55
17. Go to movies, sporting events or entertainment events	48.8	86	44.2	35	48.2	60.7	67.9	47
18. Participate in sports or active recreation	76.7	90.7	39.5	36	73.2	82.1	55.4	46
19. Participate in community clubs or organizations	9.3	48.8	60.5	19	17.9	35.7	76.8	40
20. Participate in civic or political activities	7	20.9	79.1	0	8.9	28.6	78.6	25

CPI ratio- Scores closer to 1.00 indicates greater participation in meaningful activities (both important and enough) (14).

Stroke Impact Scale (SIS-P) (Objective Participation and Perceived Stroke Recovery)

We observed no statistical evidence that older and younger subjects in this cohort differed between SIS-P individual item responses, total SIS-P scale or the SIS stroke recovery scale at 6 months. However, a large variation in both groups and a trend toward lower participation scores on the SIS-P for younger adults ($p = 0.075$) was observed. Overall, the scores on the SIS-P ranged from 6 to 100 in the younger group and 3 to 100 in the older group. A greater proportion of younger adults (42%) had a total SIS-P score below 50, while only 27% of older adults scored below 50. At the same time, ¼ of younger participants (26%) and 1/3 of older participants (36%) reported high levels of participation with scores >80. Similarly, there was a wide range of perceptions on the stroke recovery scale, ranging from 0 to 100. The distribution of scores however, was nearly equivalent across groups with 28–29% reporting a recovery of 80 or above. The relationship between perceived recovery and the SIS-P was stronger in the older group rho $= 0.69$, $p = 0.001$ than the younger group, rho $= 0.45$, $p = 0.002$). There was a moderate, positive correlation between the CPI ratio and SIS Total scores (rho $= 0.54$, $p < 0.001$).

CPI Activity Importance and Engagement in Meaningful Activities (Subjective Participation)

Table 2 summarizes the proportion of participants in each age group who viewed an activity as important, and who reported an activity was being done enough. Overall, 13 items on the CPI were identified by at least 40% or more of the younger group as activities that were not done enough. In contrast, 5 items were identified by at least 40% of the older group as not being done enough. **Table 2** also includes the average CPI ratio or the extent that items reflected engagement in meaningful activities (both important and enough) by each group.

Activities that were most important to people, generally included those that had high frequent engagement, however there were significant differences in some activities that were more important to younger adults. For example, compared to older adults, younger people more frequently identified important activities as spending time with a significant other or intimate partner ($p = 0.009$) working ($p < 0.001$), cooking ($p < 0.031$), looking after a loved one ($p = 0.005$), spiritual activities ($p = 0.02$), and entertainment ($p = 0.01$).

Participation in activities that are meaningful to the person in both groups as reflected by higher CPI ratio scores (important and doing enough) included spending time with family, keeping in touch with family or friends by phone or internet and managing household bills and expenses. In contrast, activities identified as important but not being done enough by both groups included a desire to get out and about more (46–49%), participate in social activities (46–48%) engage in hobbies and leisure (41–62%), participate in sports or recreation (45–60%). Younger adults were significantly more likely to indicate that they were not doing the following activities enough compared with older adults: Spend time with a significant other or intimate partner ($p = 0.045$), work for money ($p = 0.001$), look after children or provide care for a loved one ($p = 0.033$), go to classes or participate in learning activities ($p = 0.040$), volunteer, and go to movies, sporting events or entertainment events ($p = 0.031$). Although differences were observed at an individual item level, the average CPI ratio was not significantly different between age groups, although there was a slight trend toward younger participants reporting less participation in meaningful activities (median = 0.45) compared to older adults (median = 0.57).

Association Between Participation Domains and Demographic and Clinical Variables

We did not find an association between acute stroke severity as measured by the NIHSS and participation restrictions (SIS-P or CPI). There was a weak positive association between the SIS-P and FIM total score (rho = 0.36, $p = 0.0003$) that was slightly stronger in the older group (0.43, $p < 0.001$) compared to the younger group (0.35, $p < 0.05$). The relationship between the CPI ratio score and FIM total score was also weak (rho = 0.20, $p = 0.05$). Upon closer analysis, this relationship only existed in the older group (rho = 0.43, $p < 0.001$) and not in the younger group.

CPI: Demographic Factors Influencing Desire for Participation

In multivariate logistic regression models, controlling for ethnicity, sex and FIM Total Score at 6 months following discharge, the independent effect of age group on desire for participation was maintained for the following items: "work for money" enough (OR = 3.83 (95% CI: 1.45, 10.09), $p = 0.007$) and "go to movies, sporting events or entertainment events" (OR = 3.03 (95% CI: 1.15, 7.97), $p = 0.024$). Subjects that were 66 or older had *higher odds* of saying they did the activity "work for money" and "Go to movies, sporting events or entertainment events" *enough* compared to those 65 and younger, controlling for ethnicity, gender and discharge FIM total score. We did not find an independent association of age for the other outcomes. This may have been due to the different distribution of ethnicity in the two age groups. **Supplementary Figure 1** illustrates these differences graphically.

On the CPI frequency outcome of interest, subjects that were 66 or older had lower odds of saying they did the activity "look after children or provide care for a loved one" with some frequency compared to those 65 and younger, controlling for ethnicity, gender, and discharge FIM total (OR = 0.23 (95% CI: 0.07, 0.75), $p = 0.015$). See **Supplementary Figure 2**.

Relationship Between SIS-P (Frequency) and CPI (Engagement in Meaningful Activities)

There was a moderate, positive correlation between the CPI ratio score (engagement in meaningful activities) and the SIS-P (frequency of participation) (rho = 0.54, $p < 0.001$). This relationship was slightly stronger in the older group (rho = 0.55, $p = 0.000$) as compared to the younger group (rho = 0.44, $p < 0.001$).

DISCUSSION

We compared both objective (frequency) and subjective dimensions (importance, doing activities enough) of participation in younger and older adults, 6 months after discharge from intensive inpatient stroke rehabilitation. Associations between participation, demographics, stroke severity and functional discharge status were explored and the relationship between objective and subjective participation measures (SIS-P and CPI) was examined. We discuss our findings for each these areas.

Frequency of Participation Across Age Groups

Both age groups reported decreased frequency of participation particularly in social activities and entertainment events. There were however, no significant differences in perceived frequency of participation restrictions (SIS-P), activity participation (CPI), or perceived stroke recovery for those <65 compared with those >65. An exception was 1 item on the CPI; look after children or caring for a loved one, that was less frequent for older adults. The similarities observed between age groups in frequency of participation might be confounded by the effects of aging in older adults. Increases in perceived participation restrictions have been reported for healthy adults after the age of 80 years old (24). Studies have found that older adults do not score at the maximum level on participation instruments (25, 26). For example, Lai et al.

(26) found that healthy older adults had an average score of 86/100 on the SIS-P. Similar to Lai et al. (26) we found that the average SIS-P for people with stroke was lower than that reported for healthy adults. This however, raises questions about whether the lower frequency for some items on the CPI or SIS-P may be partially related to normal aging rather than to the effects of stroke. If some older adults have a lower participation baseline prior to the stroke, comparison to younger adults after stroke may not necessarily reflect true differences.

Younger adults demonstrated a trend toward reporting more participation restrictions than the older group (42 vs. 27%) on the SIS-P, despite similar perceived stroke recovery ratings. This suggests that the younger group may have had higher expectations for performance or engagement in life activities. Therefore, greater participation restrictions were perceived despite relatively good stroke recovery.

The lack of an association in perceived frequency of participation and age in this sample is in contrast to other studies that have found that older age is associated with more participation restrictions compared to those who are younger (27, 28). For example, researchers in the Netherlands found that stroke survivors age 70 and above reported greater participation restrictions after 1 year than those below age 70. It is difficult to compare studies due to differences in participation outcome measures, time points and variations in age groups, however, differences in our findings may be at least in part to variations in sample characteristics. Our sample only included those who participated in intensive short-term rehabilitation. The cognitive and motor functional level of both age groups was similar on rehabilitation admission and discharge, whereas in other studies, there were significant differences in cognitive and functional skills between younger and older age groups shortly following stroke (9).

Subjective Aspect of Participation

Despite similarities between age groups for frequency of participation, important differences were observed in the value and desire for activity engagement across selected items on the CPI. Given the increased incidence of young stroke discussed earlier, this finding implies that stroke rehabilitation may need to tailor programs to meet the different priorities of younger and older adults. For example, 43% of younger adults identified *caring for a child or loved one* as an activity that is not done enough, 6 months post-stroke. Childcare is particularly relevant to participation immediately after discharge from inpatient rehabilitation, however there is very little attention or research in this area after a stroke (29). Greater attention to the priorities of younger people with stroke may be needed earlier in the rehabilitation process.

The differences observed between age groups also implies that some modifications in item content of participation measures for younger stroke survivors should be considered. Items that were significantly more meaningful for younger adults could be expanded. For example, a single item related to employment or childcare is likely insufficient in measuring the impact of stroke on participation in younger adults. Follow-up qualitative interviews related to these areas could provide further insights into the experiences and perspectives of young stroke survivors that could further shape development of participation assessment tools and intervention programs.

The differences in the subjective aspects of participation observed across several CPI activities highlight the need to assess both dimensions of participation, particularly at an individual activity level. This is consistent with the observations and findings of others (11).

Subjective appraisal of activity importance and desire for change (not doing an activity enough) provides key insights into priorities and valued activities for the individual that can help interpret the significance of reported activity frequency. Questions that ask if activities are carried out often enough is a unique aspect of the CPI and as Plow et al. (14) observed, is different than asking about activity satisfaction. For example, a person may be dissatisfied with their level of participation in household activities but at the same time, may not be interested in increasing engagement because other activities are more important to them. Measures of satisfaction have been used to assess the subjective aspect of participation, however inclusion of importance and desire for doing an activity more often, provides additional information on the subjective dimension of participation that may differ across ages and individuals. Since engagement in personally meaningful activities is associated with improvement in emotional well-being post-stroke and quality of life (30), information on valued and desired activities is essential for client centered treatment planning and goal setting in rehabilitation.

Association Between Participation, Demographic, and Clinical Variables

The variations we observed in participation 6 months post-stroke was not associated with acute stroke severity. This is similar to that reported by other studies with mild-moderate stroke populations and age groups below an average of 65 years (17, 31). Additionally, frequency of participation restrictions (SIS-P) was weakly associated with functional discharge level (FIM). No relationship, however, was observed between participation in meaningful activities (CPI ratio) and functional discharge level (FIM) for younger adults. This is likely because perceptions of participation restrictions may be influenced more by the context of a person's life including community and home environment, individual preferences, lifestyle and expectations rather than level of impairment or ability to perform specific activities (12). This is particularly true for younger adults. Although a person may have a mild stroke or has achieved a high functional level following intensive rehabilitation, our results suggest that participation should still be monitored.

We further demonstrated that the desire to participate in some activities such as work or entertainment events was independently associated with age and was not explained by functional dependency level, sex, or ethnicity whereas desire for participation in other activities may have been possibly confounded by the relationship between ethnicity and age group. Different factors may therefore contribute to participation in different types of activities. Our younger group had greater ethnic diversity, mirroring the demographic profile of people with younger adults reported in the literature (4). The significant differences in minority representation in the younger group suggests that there might be other factors such as cultural preferences influencing participation. It also raises issues of possible health disparities that could restrict participation. Future studies examining differences in participation among age groups should further investigate ethnicity or cultural differences that may influence activity importance and desire for participation in select activities.

Relationship Between SIS-P (Frequency) and CPI (Engagement in Meaningful Activities)

The relationship between frequency of participation restrictions (SIS-P) and subjective participation in valued and meaningful activities (CPI ratio) was moderate. This is consistent with other studies that have reported a moderate association between the subjective and objective aspects of participation (11). The correlation between the CPI ratio score to the established SIS-P score also supports the concurrent validity of the CPI as a participation measure. Although ∼29% of both participation scales overlap, this finding indicates that each scale taps information that is unique or not captured by the other. This further supports the need to use multiple measures to provide a comprehensive assessment of different aspects of participation. This is consistent with recommendations by others (11, 32).

LIMITATIONS

We acknowledge several limitations. Our sample consisted primarily of people with a mild-moderate stroke from a single inpatient rehabilitation unit within an academic medical center. A wider range of people with stroke and a larger sample size across different locations or facilities would allow for greater generalizability of results.

The small percentage of people (36%) who completed all follow-up measures is also a limitation. It was observed that the included sample was similar to the excluded sample, with the exception of cognitive/language deficits, however, this attrition indicates that results cannot be generalized to those with more significant cognitive or language deficits. Similarly, when necessary, a proxy completed follow up phone interviews. Those who had a proxy complete the interview also had lower language/cognitive abilities, and this could have led to bias in responses. Research on the SIS has found that observed biases between the individual and proxy were small and not clinically meaningful (21), however proxy agreement for the CPI has not been investigated for people with stroke.

Finally, it should also be noted that although both groups had a median NIHSS score in the mild range, the younger group had significantly greater stroke severity than the older group, more ethnic diversity and a higher percentage of hemorrhagic stroke (although not significantly different from the older group). Although we found no association between stroke severity and participation, these differences should be noted. Investigation of the effect of different types of stroke or specific cognitive and motor impairments on participation might provide further insights into factors impacting participation.

It should also be noted that while the CPI-part 1, was used to assess the subjective aspect of participation, it focused on importance and desire to increase engagement in participation. Other areas of subjective participation such as perceived autonomy (CPI-part 2) were not included in this study. While the CPI is quick and feasible to use, it is a survey instrument. Qualitative interviews could provide greater insights and a deeper understanding of the client's subjective perspective and experiences regarding participation after a stroke. Although cognitive interviewing has been reported with the CPI, to clarify the wording of questions and response format (33), interviews of people with stroke regarding their thoughts about the content of CPI items could further validate it as a tool.

CONCLUSIONS

This is the first study to describe use of the CPI in people post-stroke 6 months following intensive rehabilitation. It highlights the unique aspects of the CPI and the merit of combining both frequency ratings and subjective appraisal of activity engagement for a deeper understanding of perceived participation restrictions. The value of examining the subjective dimension of participation at an individual activity level was demonstrated by comparing activity importance and desire for increased participation in those < 65 and > 65. Despite similar perceived impact of stroke, stroke recovery and frequency rating, differences in age groups were most apparent for the subjective dimension of participation in selected items or activities. These differences suggest that stroke rehabilitation may need to tailor assessment and treatment programs to meet the different priorities of younger and older adults. Total frequency scores tended to mask individual differences in activity engagement. This suggests that clinicians should therefore focus on identifying individual activities or combinations of activities that are valued and that the person is motivated to change.

The desire to engage in some types of activities was independently associated with age, while other activities were not associated with age. Since there tends to be a greater minority representation in people with younger stroke, the influence of ethnicity and culture on participation needs further exploration. Additional research examining differences in participation among people in different age groups, including healthy older adults is needed. In addition to age, other groups differences such as those with low and high motor or cognitive impairments could be compared. Pre-stroke employment status could also be examined to explore how perceived participation restrictions after a stroke are related to pre-stroke participation.

Short term intensive rehabilitation focuses on discharge planning and increased independence in activities of daily living. Broader participation goals including the ability to fulfill family and life roles, integrate into the community, and engage in meaningful life activities require continued support. Participation outcomes may be optimized by monitoring and assessing participation post-stroke with follow up questionnaires after 6 months, such as the CPI. The CPI provides a strong foundation for implementation of individually tailored, client centered rehabilitation interventions, aimed at increasing engagement in meaningful activities when participation needs are identified.

DATA AVAILABILITY STATEMENT

The datasets used for this manuscript are not publicly available because it is still part of an active IRB research protocol. Requests to access the datasets should be directed to the corresponding author.

ETHICS STATEMENT

This study was carried out in accordance with the ethical standards and approval of the Institutional Review Board of the participating institution with written informed consent from all subjects. All subjects gave written informed consent in accordance with the Declaration of Helsinki.

AUTHOR CONTRIBUTIONS

JT was involved the study concept and design, interpretation, manuscript development, and writing. GA and LG were involved in data analysis and interpretation and writing. AJ and MO'D were involved in conceptualization of results and manuscript editing. All authors reviewed final draft for intellectual content and revisions.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2019.01108/full#supplementary-material

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Physical Activity, Sedentary Behavior, and Barriers to Exercise in People Living With Dystonia

*Alana McCambridge[1], Rebecca M. Meiring[2] and Lynley V. Bradnam[2,3]**

[1] Graduate School of Health, Discipline of Physiotherapy, University of Technology Sydney, Sydney, NSW, Australia, [2] Department of Exercise Sciences, Faculty of Science, University of Auckland, Auckland, New Zealand, [3] Faculty of Health and Medical Science, Centre for Brain Research, University of Auckland, Auckland, New Zealand

Background: Dystonia is a neurological movement disorder that presents as sustained or intermittent involuntary muscle contractions causing abnormal postures and movements. Knowledge of dystonia is mostly at the impairment level with minimal understanding of activity and participation limitations. Physical activity (PA) is an important aspect of neurological disease management, with wide-ranging benefits for overall health and quality of life. No studies have quantified PA and sedentary behavior (SB), nor explored barriers to being physically active in people with dystonia.

Methods: Participants diagnosed with any form of dystonia completed a mixed-methods anonymous online survey on activity behaviors. The International Physical Activity Questionnaire (IPAQ) and Adult Sedentary Behavior Questionnaire (SBQ) assessed self-reported PA and SB. Barriers to exercise engagement were investigated according to the five-factor social-ecological framework and dystonia-specific questions regarding the impact of exercise on symptoms were included.

Results: Two-hundred and sixty-three participants consented to the study (mean (SD) age = 55 (13) years, 76% Female). A large proportion of respondents (40%) reported living with cervical dystonia (CD). Overall, the median (IQR) time spent in walking, moderate, and vigorous activity was 60 (0–120), 120 (15–300), and 0 (0–13) min/day, respectively. SB time during weekdays was 285.0 (157.5–465.0) min/day and 345.0 (195.0–502.5) min/day on weekends. Fifty-five percent of participants were dissatisfied with their current level of PA and 75% reported dystonia had decreased their level of PA. Fifty-seven percent found their symptoms were worsened during exercise though the after-effects on symptoms varied. Fatigue, motor symptoms, pain, and poor balance were commonly cited limiting factors. Qualitative and quantitative data indicated difficulties with more vigorous intensity activity. The common barriers to engagement were personal and governmental factors, such as physical impairments, lack of funding and lack of trained exercise professionals.

Conclusion: While more than half of respondents indicated they were not satisfied with their current level of PA, and exercise primarily worsened their dystonia symptoms, most

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Lisa Tabor Connor,
Washington University in St. Louis,
United States

Reviewed by:
Ota Gál,
Charles University, Czechia
Giovanni Fabbrini,
Sapienza University of Rome, Italy

Correspondence:
Lynley V. Bradnam
lynley.bradnam@auckland.ac.nz

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participants were meeting the minimum guidelines. Future studies should incorporate robust objective methods of PA and SB measurement and explore the causal mechanisms underpinning exercise-induced aggravation of dystonic symptoms to further enhance life participation of people living with dystonia.

Keywords: dystonia, physical activity, exercise, sedentary behavior, barriers

INTRODUCTION

Engaging in physical activity (PA) is vital for ongoing health, reducing risk of cardiovascular and comorbid diseases, and maintaining a high quality of life (1). Exercise (or structured PA) is rapidly becoming a core component for rehabilitation of people living with neurological disorders, with positive impacts on various areas of health, and also disease progression (2–4). Global public health recommendations suggest a person should be physically active and limit their sedentary behavior time. Being sufficiently physically active is defined as achieving a minimum of 150 min of moderate to vigorous intensity activity per week (1), while there are currently no definitive guidelines for sedentary behavior (SB) (5). Lower levels of SB are associated with better health outcomes (6). Despite strong evidence in support of the beneficial effects of PA, most people living with neurological disorders do not meet recommended guidelines and are sedentary (2, 4, 7, 8).

Dystonia is a neurological movement disorder, characterized by involuntary muscle contractions causing abnormal and painful postures, repetitive movements, and sometimes tremor of the affected regions (9). Knowledge of PA and SB in dystonia is limited (2–4, 7, 8). Some studies in people with dystonia report that exercise worsens many motor symptoms, amplifying involuntary contractions, postures and tremor (3, 7). However, there has been little systematic investigation into the amount of PA being achieved by people with dystonia, the impact of dystonia on the ability to exercise, nor conversely of the impact of exercise on dystonic symptoms. Understanding participation in activity behaviors is an important step in discerning areas that health practitioners can intervene to ensure people with dystonia are participating in meaningful life activities, engaging in sufficient PA, and limiting their time spent in SB.

Furthermore, an important component to understanding activity behaviors and encouraging PA in neurological populations is to investigate the impacts of, and barriers to, participation in PA or exercise. Only one study to date has investigated impacts on self-reported PA in people living with dystonia affecting the neck (termed cervical dystonia, CD) using a cross-sectional online survey (10). The study found being employed and having high levels of self-efficacy were major contributors to greater amounts of PA in people with CD (10). However, the study did not determine actual PA levels undertaken by people with CD, nor did the authors address SB. A synthesis of literature further investigated factors affecting PA participation in people living with physical disabilities, to enhance the development of strategies to increase PA (11). The authors identified barriers based on a five-factor social ecological framework; intra- and inter-personal, institutional, community, and policy (11). This framework was used in the current study to generate questions regarding barriers to exercise to enhance the translation of findings about barriers into future intervention strategies.

Investigating activity behavior levels, barriers to PA or exercise, and the impact of PA or exercise on dystonic symptoms will be useful for the development of suitable interventions that promote activity in this population. Therefore, the primary aim of this study was to understand the level of self-reported PA and SB in people with dystonia. The secondary aim was to investigate barriers to exercise and explore the impact of exercise on dystonic motor and non-motor symptoms during and after exercise. The hypotheses were that people living with dystonia would not meet recommended levels of PA, and that exercise would aggravate dystonic symptoms providing a barrier to participation.

MATERIALS AND METHODS

Participants diagnosed with any form of dystonia completed a mixed methods anonymous online survey of qualitative and quantitative data on activity behaviors. Ethical approval was provided by the University Ethics Committee (UTS HREC ETH18-3048) prior to survey distribution. Qualtrics online survey software (version XM) was used to deliver the survey to an international audience. Self-reported PA was measured using the International Physical Activity Questionnaire (IPAQ) and time spent in SB was assessed using the sedentary behavior questionnaire (SBQ). The IPAQ asks participants to recall the time spent performing either walking, moderate or vigorous intensity activities in four domains (work/occupational, household, travel, leisure time) for the previous week (12). The SBQ assesses the amount of time spent doing nine sedentary behaviors (watching television, playing computer/video games, sitting while listening to music, sitting and talking on the phone, doing paperwork or office work, sitting and reading, playing a musical instrument, doing arts and crafts, sitting and driving/riding in a car, bus, or train) per day on a typical weekday and weekend (13). Participants were also asked to state whether the activity they reported was usual of their current activity and whether they were satisfied with their current level of PA. Participants completed a series of questions regarding the impact of exercise on their dystonic motor symptoms using closed and open-ended questions, developed in collaboration with a person living with CD (see **Supplementary Material 1**). Finally, barriers to exercise were investigated using closed-ended questions informed by the social ecological barriers framework

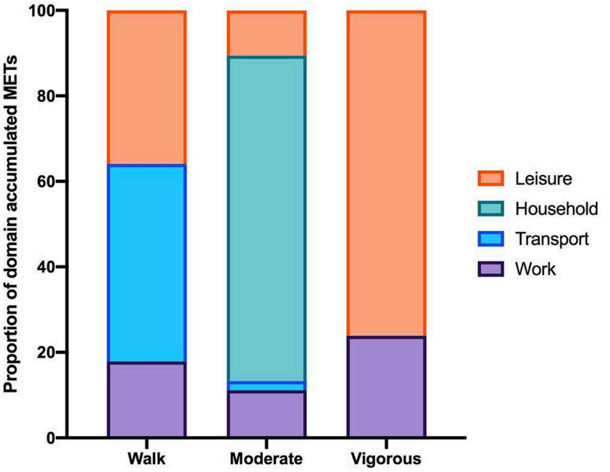

FIGURE 1 | The proportion of the total MET-min/wk in each activity category accumulated per IPAQ domain. Data excludes participants who did not report accumulating activity in any of the activity categories therefore the number of participants in each activity category is 190, 203, and 69. Note that in the household domain activities are all assigned MET values within the moderate-intensity range.

(11) and open-ended questions about barriers and enablers. The survey was advertised globally, appearing on Dystonia Support Group webpages in Australia and Sweden, and distributed via email lists, newsletters, and social media in New Zealand, South Africa, the United Kingdom and United States of America. The online survey was available to participants for 4 weeks in 2019.

Data Analysis

Data were exported into Excel spreadsheets for analysis. Demographic data were analyzed descriptively. The IPAQ and SBQ were scored and analyzed according to established methods (12, 13). StataI/C (version 15.1, StatCorpLLC, TX USA) was used to analyse data. The data from the IPAQ were scored within each activity domain (occupational, household, travel, leisure time related activity) and overall. IPAQ scores were calculated by first summing the time spent in each activity category (walking, moderate or vigorous) within each domain, then multiplying the number of minutes by the number of days of the week the activity was performed during the week. The final step was to multiply by a metabolic equivalent (MET) value (3.3. for walking, between 3.0 and 6.0 for moderate intensity activities and 8.0 for vigorous intensity activities). Therefore, IPAQ scores are reported in MET minutes/week (MET-min/wk). Classifications into activity categories based on recommendations by the WHO were those participants who achieved a minimum of 600 MET-min/wk (considered moderate) and those who achieved 3,000 MET-min/wk (considered high) (14). In addition, for each participant the total amount of time per day spent in walking, moderate, and vigorous activity was summed over all domains and reported as minutes per day (min/day). Data are reported as median values and inter-quartile ranges. The total daily reported time spent in sedentary behavior from the SBQ was calculated separately for weekdays and weekends. Data are represented median values and inter-quartile ranges. Questions regarding the impact of exercise on dystonia symptoms and barriers to exercise were analyzed descriptively for each question by calculating the proportion of responses for each answer in relation to the total number of responses. Inductive analysis determined themes from the open-ended questions and applied where relevant to the social-ecological barrier framework (11).

RESULTS

Demographics

Two-hundred and sixty-three participants completed the demographic section. The mean age was 56 years (range 19–83) and 199 identified as female. There were 353 responses to the question regarding dystonia type (participants could select multiple dystonia types). The types of dystonia were broadly grouped, related to the area affected. Focal dystonia on the neck (i.e., CD) was the most common type of dystonia reported with 142 (40%), followed by focal or segmental dystonia involving the hand or foot ($n = 55$, 16%), focal or segmental dystoia involving the face (e.g., craniofacial or oromandibular dystonia; $n = 44$, 12%), blepharospasm ($n = 39$, 11%), generalized dystonia ($n = 36$, 10%), spasmodic dysphonia ($n = 19$, 5%), and “other” ($n = 18$, 5%). As the CD sub-group was relatively large, we have displayed CD data where possible. At the time of the survey, 49% of all respondents had been living with dystonia for more than 10 years. Fifty-three percent were currently undergoing botulinum toxin (BTX) injections for their dystonia, 20% reported they had been treated in the past with BTX but have now discontinued treatment, and 27% had never had BTX injections. One hundred and 63 respondents (62%) were currently taking oral medication to manage dystonic symptoms and of these 149 participants were taking at least one psychoactive drug.

IPAQ and SBQ

Of the total number of respondents, 45 did not report on any PA in the IPAQ and 46 did not report on any SB and were excluded from each analysis. The number of respondents analyzed for the IPAQ and SBQ were 220 and 219, respectively. Of the 220 people who reported activity on the IPAQ, 190 reported accumulating activity by walking, 203 reported accumulating activities of moderate intensity and only 69 reported accumulating activities of vigorous intensity. The participants excluded were those who reported zero activity in any of the walking, moderate or vigorous intensity categories. **Figure 1** shows the proportion of accumulated METs of the total METs within each activity category (walking, moderate and vigorous) for each domain (where applicable). To note, 76.2% of the METs accumulated in the vigorous intensity category was done in the leisure time domain though there were only 69 participants that reported any vigorous activity. A large proportion of accumulated METs of moderate intensity (76.1% from 203 respondents) occurred in the household domain, which included garden work and inside housework. The largest proportion of walking METs (46.2% of 190 respondents) were accumulated in the transport domain. For

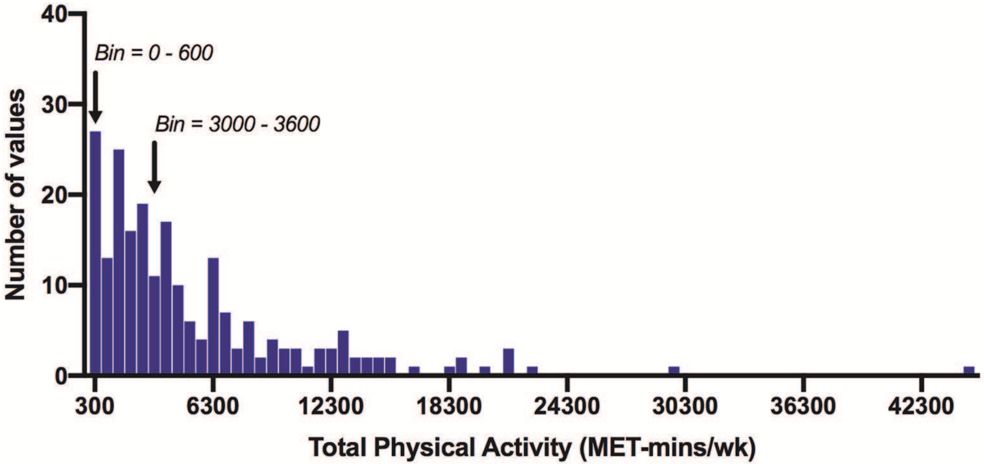

FIGURE 2 | Frequency distribution of total physical activity time measured with the IPAQ (MET-min/wk). Arrows indicate the 600 MET-min/wk and 3000 MET-min/wk thresholds. Of all participants, 12% did not achieve 600 MET-min/wk, and 45% did not achieve 3000 MET-min/wk. Bin width = 600.

the total physical activity (**Figure 2**) and per activity category (walking, moderate, vigorous) the data was left-skewed.

Table 1 shows the median (IQR) IPAQ activity scores for all respondents ($n = 220$) within each domain as well as for the total IPAQ score. Overall, the median (IQR) physical activity score was 3,586 (1,617–6,989) (**Table 2**). Eighty-eight percent of all participants achieved at least 600 MET-min/wk, and 55% achieved 3,000 MET-min/wk.

Table 2 shows PA time in minutes per day spent in each activity category as reported on the IPAQ and SB time as measured by the SBQ. Time spent in SB was 4.75 h/day on weekdays and 5.75–6 h/day on weekends. The distribution of SB time on the weekdays and weekends is shown in **Figure 3**. The proportion of participants satisfied with their current PA level was 52% and not satisfied 48%. Thirty percent reported that the recalled PA was not typical of their usual activity.

Dystonia-Specific Questions

Seventy-five percent of respondents indicated dystonia had decreased their amount of PA each week. Participants identified the reasons their dystonia prevented engagement in PA from a provided list of symptoms, of which they could choose multiple reasons (**Table 3**). The most common symptoms that prevented PA were fatigue, motor impairment, pain and poor balance. During exercise, 57% reported dystonia symptoms were worse and 13% reported symptoms were better (**Table 4**). After exercise, 34–41% indicated symptoms were worsened and 19–25% reported their symptoms were better (**Table 4**). Forty-nine percent of respondents reported that their symptoms are affected by exercise immediately or within 5 min of the onset of exercise and 60% of respondents indicated dystonia was aggravated after a single session of exercise (**Table 5**). Sixty percent of respondents said they could never exercise without symptoms worsening. When asked to elaborate on this, participants said the ability to exercise varied depending on factors such as the type, intensity and amount of exercise, effect of botulinum toxin injections, and how well or unwell they were feeling on a particular day (**Table 5**).

Table 6 displays the number of responses for various modes of exercise and the impact on participant symptoms. Most of the exercises were considered to worsen symptoms, however, yoga/pilates and general stretching reduced symptoms for several respondents (**Table 6**). Vigorous activities like jogging, running, fast cycling and heavy gardening and playing sport negatively affected dystonia symptoms for most respondents. Participants could comment further on this question. Representative participant comments were "*usually anything fast paced or high intensity causes the spasms to be worse,*" "*generally anything that raises the heart rate raises the Dystonia symptoms*" and "*any exercise which results in increased breathing rate causes my spasmodic dysphonia to worsen.*" Participants recommended exercising using a recumbent bike, exercise classes such as yoga. Pilates or tai chi (although some commented that holding poses in yoga caused the tremor and muscle spasms to worsen), classes held in heated room or pool, and gentle stretching and walking were suggested as activities less likely to cause symptom aggravation. Ninety-one respondents reported they had been prescribed exercises for dystonia by a health professional, consisting of gentle stretching and strengthening, posture, balance and mobility exercises and walking. Finally, participants described what happened to their dystonia symptoms during and after exercise. The most common responses included increased muscle spasms, pain, tremor, stiffness and weakness, greater fatigue and reduced balance and coordination and ability to control affected muscles, although many said the response depended on the type of exercise. An example participant comment was "*Increased twisting of head, left shoulder rises, increased spasms, increases strain and tension on muscles on left side of neck and upper back, pain in neck, shoulde r and head,*" "*the frequency, intensity and strength of the spasms, tremors and involuntary movements all increase,*" "*my eyes slam shut as soon as I start an exercise class or try to ride my bike.*"

TABLE 1 | IPAQ activity scores for each domain and the total across all domains.

	Respondents ($n = 220$)	CD ($n = 126$)
Work		
Walking	0 (0–17)	0 (0–0)
Moderate	0 (0–0)	0 (0–0)
Vigorous	0 (0–0)	0 (0–0)
Total	0 (0–495)	0 (0–330)
Transport		
Walking	256 (0–845)	297 (0–792)
Bicycling	0 (0–0)	0 (0–0)
Total	297 (0–990)	314 (0–792)
Domestic		
Inside work	360 (90–1,080)	360 (90–1,080)
Moderate garden/yardwork	240 (0–960)	240 (0–960)
Vigorous garden/yardwork	0 (0–330)	0 (0–165)
Total	1,140 (290–2,940)	1,200 (325–2,940)
Leisure activities		
Walking	198 (0–396)	198 (0–396)
Moderate	0 (0–198)	0 (0–88)
Vigorous	0 (0–160)	0 (0–0)
Total	396 (0–1,386)	396 (0–1,320)
Totals		
Walking activity	792 (198–2,178)	891 (297–2,376)
Moderate activity	1,680 (479–3,969)	1,647 (478–3,984)
Vigorous activity	0 (0–480)	0 (0–240)
Total physical activity	3,586 (1,617–6,989)	3,281 (1,680–7,110)

Data are the median (interquartile range) MET-min/wk. Note bicycling and all domestic work are assigned a MET value within the moderate intensity range. CD, cervical dystonia.

Symptom behavior during and after exercise responses fell into three categories. First, exercise worsened dystonia during and after exercise, for example "*My neck muscles contract and pull against my head causing significant pain, restricted head movement and often leading to tension headaches that can sometimes last days.*" Second, exercise worsened dystonia during exercise but improved afterwards, for example "*During exercise my tremors, shakes and jerks are much worse. After exercise, they come back to normal levels. Exercise helps keep my fatigue under control.*" Third, dystonia was better during exercise but worse afterwards, for example *"During exercise my spasms 'feel' less intrusive. But once I stop, the symptoms and pain can be significantly increased."* The other main message arising from participant responses to this question was that type and intensity of exercise was a factor in symptom aggravation and it was easy to "over do" it and suffer the consequences. Representative participant comments were "*I have to be careful not to overdo it as then the tremors and spasms and pain can become pretty intense,*" and *"This varies greatly, usually they subside but sometimes worsen during exercise. After exercise they are generally better but are much worse if I over-exercise."* There were a few participants reporting benefits of exercise for their dystonia, such as "*I feel more relaxed and do not feel I am fighting against my neck as much as normal," "Exercise gives me more energy throughout the day and I feel better for it and proud of my accomplishments,"* and *"My muscles feel really stiff before exercise. As I get warmer the muscles begin to relax and the pain and tremor reduces a lot."*

TABLE 2 | Total self-reported daily time spent in walking, moderate and vigorous activities and in sedentary behavior across all domains.

IPAQ	Respondents ($n = 220$)	CD respondents ($n = 139$)
Walking activity	68 (30–140)	75 (30–150)
Moderate activity	180 (60–325)	180 (60–340)
Vigorous activity	0 (0–30)	0 (0–20)
SBQ	**Respondents ($n = 219$)**	**CD respondents ($n = 139$)**
Weekday sedentary behavior	375 (225–510)	308 (210–465)
Weekend sedentary behavior	390 (270–525)	360 (240–525)

Data are median (IQR) minutes/day. IPAQ, International Physical Activity Questionnaire; SBQ, Sedentary Behavior Questionnaire; CD, Cervical Dystonia.

Barriers

The most common barrier to PA was the personal factor "physical and bodily impairments" (41%). The next common personal factor was "negative emotions make it hard to engage in physical activity" (16%). Neither relationship or community level factors were identified as significant barriers to exercise (**Supplementary Material 2**). The main governmental barriers to exercise were that exercise professionals were not trained in a way that met their needs (18%), the lack of funding for exercise programs (23%), and cost to the individual (18%). The open-ended questions yielded similar results; the most common barriers were intrapersonal, institutional and policy level factors. Participants expressed the desire to return to a wide variety of moderate to vigorous activities, including team sports as well as activities around the house such as gardening and family activities. Participants felt access to appropriate exercise classes or gyms was a barrier due to cost and transportation issues. To further identify barriers to PA, participants were asked "what they thought would help them to become more physically active?" Answers were analyzed according to the five-factor model. The most common answers were intrapersonal; less worsening of symptoms with activity, less fatigue, pain and tremor, better range of motion, more consistent results from botulinum toxin treatment, and increased confidence and motivation. The main interpersonal factor cited was the lack of opportunity to exercise with others. The institutional factor was the lack of exercise professionals who understand dystonia prescribing appropriate exercises and the policy factor was to reduce the cost of participating in exercise programs.

> "*Dystonia is an orphan disease. This affects not only research into cause(s) and treatment(s) but also medical and community awareness, knowledge and support. In my experience as a very long term dystonia sufferer there are no meaningful support structures to encourage/assist sufferers to engage in regular exercise, no programs specifically designed to facilitate the process nor medical/exercise professionals trained to provide such support or assistance.*"

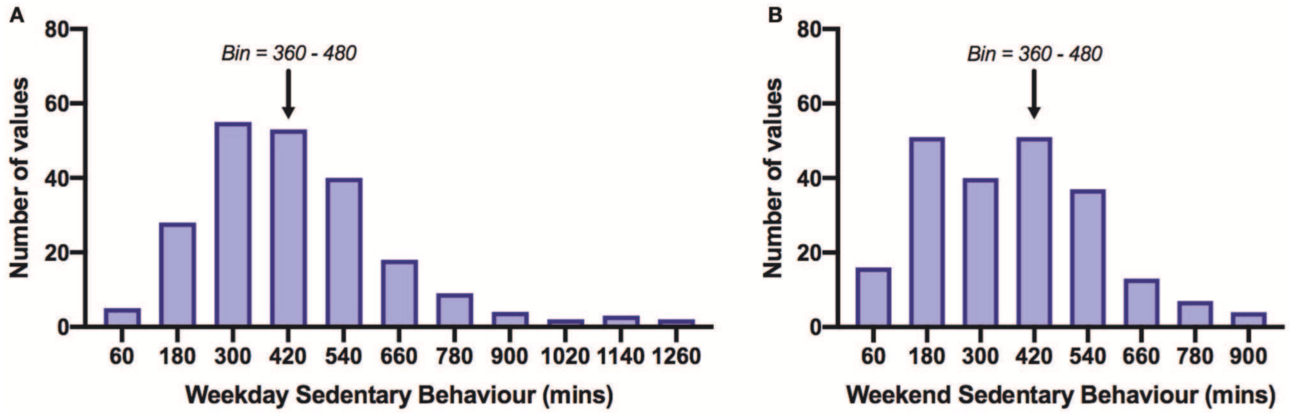

FIGURE 3 | Frequency distribution of daily sedentary behavior time on weekdays **(A)** and weekends **(B)**. All bins above the arrows are those acquiring more than 8 h/day (480 min/day) of sedentary behavior. Of all participants, 27% exceeded 480 min/day on weekdays and 32% on weekends. The overall mean SB time across weekdays and weekends was 401.8 min/day. Bin width = 120.

TABLE 3 | Reasons that prevent people with dystonia from engaging in physical activity and exercise.

Factors	Number of responses	Percentage (%)
Fatigue	136	17
Motor symptoms	132	16
Pain	118	15
Balance	95	12
Social embarrassment	68	8
Weak muscles	64	8
Mood	46	6
Vision/Risk of collision with objects/people	45	6
Fear of falling	39	5
Nothing	31	4
Other	27	3
Previous injury	15	2

TABLE 4 | Dystonia symptom behavior during and after exercise in the short and long term.

Factor	% Better	% Unchanged	% Worse
During exercise	13	30	57
After exercise – same day	25	34	41
After exercise – next day and onwards	19	47	34

TABLE 5 | Impact of exercise on dystonia symptoms.

When symptom change begins	Percentage (%)
Immediately at the onset of physical activity or exercise	25
Soon (5 min) after the onset of physical activity or exercise	24
Symptoms do not change	20
After 30 min of starting physical activity or exercise	14
Unsure	10
More than 1 h after the start of physical activity or exercise	7
How much exercise is needed to impact on dystonia symptoms	
A single bout of exercise	60
A period of exercise training (e.g., more than a month of regular exercise)	5
Both	35
Number of days one could exercise without symptom aggravation	
Never	61
Every day	16
Three or more times per week	13
Twice a week	6
Once a week	4

DISCUSSION

The current study was a mixed-methods exploratory investigation of PA and SB in people living with dystonia, their perceived barriers to PA, and impact of exercise on dystonic symptoms. The main findings were that a large proportion of people self-reported engaging in walking and moderate levels of activity, especially in the transport and household domains, respectively. Total physical activity met the minimum recommended guidelines set by the WHO, yet over half of all respondents were dissatisfied with their current level of PA and three-quarters reported dystonia interfered with their ability to be physically active. The most common barrier to PA was the personal factor "physical and bodily impairments," followed by governmental factors regarding the lack of funding for exercise programs and few trained exercise professionals able to meet their needs. Questions about the effects of exercise on dystonia symptoms revealed a tendency for exercise to worsen symptoms, although some people experience no change or even beneficial effects following exercise. Interestingly, a common theme was

TABLE 6 | Different modes of exercise and the impact on dystonia symptoms.

Factor	Number of responses	% Better	% Unchanged	% Worse
Strengthening/resistance	134	14	30	56
Strengthening without weights	130	21	35	44
Yoga or Pilates	116	39	34	27
General stretching	155	38	37	25
Light walking	176	27	35	38
Brisk walking	153	22	25	53
Jogging	99	11	24	65
Running at a pace that makes it hard to breathe	89	9	20	70
Light cycling	103	12	34	54
Heavy/fast cycling	95	5	26	68
Dancing	95	35	23	42
Aerobics	86	14	30	56
Light gardening	149	12	39	49
Heavy gardening (e.g., digging, cutting trees)	120	7	21	72
Household chores	173	9	36	55
Playing sport (e.g., football, tennis, golf)	84	5	30	65

that the mode and intensity of exercise was an important factor in symptom aggravation, and that it was easy to "over do" it and suffer the consequences.

The WHO guidelines recommend a minimum of 600 MET-min/wk for health benefits, approximately equivalent to 140–150 min of brisk walking (1). Contrary to our expectations, 88% of all dystonia respondents scored above 600 MET-min/wk suggesting most people with dystonia that were included in our sample are meeting the minimum recommended level of PA for adults. However, findings must be considered with regards to the inherent risks of bias in self-report survey research, such recall bias and over-reporting. In our study walking and moderate intensity activities were the largest contributor to PA time, with minimal contribution from vigorous intensity activities. Walking or low intensity activity was performed during transport related activities, and moderate intensity activity during domestic duties both inside the home and outside garden work. Time spent physically active was not often accumulated during work, although the number of respondents in full-time and/or paid work was not captured in our survey. Leisure time was the greatest contributor to vigorous intensity activity, but the actual time spent at a vigorous level of activity was markedly low, as was the number of participants that performed any vigorous activity. The lack of vigorous intensity exercise may relate to several factors identified in the qualitative analysis. For example, respondents who felt that exercise aggravated their symptoms may be cautious about vigorous intensity exercise as they wished to avoid prolonged exacerbation of symptoms. Some participants also did not feel supported by trained exercise professionals therefore engagement in more vigorous types of activities may have been avoided as they do not feel sufficiently supported or safe to exercise at higher intensities.

Self-reported SB time was considerably lower than that reported in a large-scale study of healthy adults in the US [National Health and Nutrition Examination Survey (NHANES) 2003/4 and 2005/6 (15)]. In the current study, respondents reported spending an overall average of 401.8 min/day (standard deviation in SB while men and women from NHANES spent an average of 490.8 and 484.5 min/day in SB, respectively). To date, there are no widely accepted recommended guidelines for SB however some studies suggest risk of mortality is increased when SB time is more than 8 h/day (16–18). The NHANES study measured PA and SB objectively using accelerometery, whereas the present study used self-reported SB time with the IPAQ. In a study that examined both self-reported and accelerometery-based SB time in people with multiple sclerosis, self-reported SB time was 505.6 min/day while the accelerometer detected SB time was 548.5 min/day (19). No studies to date have reported on self-reported or objectively measured SB in people living with dystonia. As self-reported SB time has been suggested to underestimate accelerometery-based estimates (16), further studies are needed to objectively measure activity behavior in people with dystonia to accurately categorize the amount of SB time and potentially identify areas for improvement.

Our analysis of self-reported PA and SB is the first study to show that a high proportion of people with dystonia are currently meeting public health recommended guidelines. However, there is a growing body of evidence suggesting the current recommendations may be too conservative. In a dose-response meta-analysis of PA, a higher level of PA was strongly associated with a lower risk of five chronic diseases (breast cancer, colon cancer, diabetes, ischemic heart disease, ischemic stroke) (20). For a significant reduction in risk of disease, total PA was shown to be between 3,000 and 4,000 MET-min/wk, several times higher than the minimum 600 MET-min/wk recommendation by the WHO (20). In our data, only 55% of respondents were achieving 3,000 MET-min/wk, indicating that although majority of participants with dystonia are accumulating some time spent physically active, only half are accumulating a dosage that will have meaningful effects on their risk of developing chronic disease. About half of participants were dissatisfied with their current level of PA, a similar proportion to those achieving 3,000 MET-min/wk. Supporting people with dystonia achieve their desired dosage of PA and promoting a dosage that will significantly reduce the risk of cardiovascular disease should be a component in the long-term care of people with dystonia or any chronic neurological movement disorder.

Achieving a higher dosage of PA is possible by increasing the volume and/or intensity of exercise (i.e., structured PA) or incidental PA performed each week. However, for most people in our study exercise exacerbated the symptoms of dystonia, particularly with high intensity activities, and symptoms became aggravated immediately or very soon after the onset of a single bout of exercise. Because of the known relationship between voluntary movement and the presentation of dystonic contractions (9) exercise in this population is inherently difficult, but nonetheless important for overall health and quality of life. A common theme in the qualitative data was that people with dystonia felt concerned about pushing themselves too hard and exacerbating their symptoms further. This may suggest that people with dystonia could be supported to perform low-to-moderate intensity activity for longer or more frequent periods of exercise to achieve a sufficiently high dosage of PA. The modes of exercise identified in our study that either improved or did not change dystonia symptoms for majority (>50%) of respondents were also the types of exercise that were low-to-moderate intensity. These were general stretching, yoga/pilates/tai chi, light walking, dancing, strengthening without weights, and light gardening. In contrast to the modes of exercise that were more likely to worsen symptoms required a more vigorous intensity (see **Table 6**; heavy gardening, running, fast cycling, etc.). Encouragingly, despite most people with dystonia reporting their symptoms are worsened during exercise, the after-effects of exercise were slightly more positive. For example, a greater proportion of respondents identified that their symptoms were either improved or unchanged following a bout of exercise compared to those that reported their symptoms were worsened after exercise. The qualitative responses confirmed that symptom behavior during and after exercise is considerably varied, with some experiencing relief but most experiencing symptom aggravation. To support the results of our survey, an empirical investigation into exercise intensity and modality should be conducted to better determine how the intensity and mode of activity impacts on dystonia symptoms. As the presentation of dystonia is considerably varied, it will likely be important to do this for each type of dystonia separately. Then it will become important to understand how people with dystonia can exercise without overly exacerbating their symptoms. Future investigations could explore which modes of exercise are less likely to aggravate symptoms, which mode of exercise is best suited to which type of dystonia, and how to maximize the dosage of PA whilst keeping in mind the difficulty experienced with vigorous intensity activities.

The major barriers that inhibited people with dystonia from being physically active were physical impairments, lack of funding, and lack of trained exercise professionals. Fatigue, motor symptoms, and pain were the most common symptoms that prevented people engaging in PA. Without a curative treatment for the physical impairments of dystonia, exercise professionals need to identify methods to help support people with dystonia stay physically active for their general health and well-being. Interestingly, only 91 respondents had previously received an exercise program from a health professional, supporting their assertions that a major barrier to their engagement was a lack of trained professionals able to meet their needs. As clearly indicated by a study participant, there are limited if not nil support structures specifically dedicated for people with dystonia to encourage or assist them to meet their physical activity needs. Education of exercise professionals about dystonia, the various presentations of dystonia, and what is currently known about the beneficial effects of exercise for people with neurological movement disorders would be the first step toward addressing the governmental barriers to PA engagement. Participants suggested they could be more physically active if their symptoms were less aggravated by exercise, they were less fatigued or in pain, had better range of motion, and/or increased confidence or motivation to exercise. Further development of how to appropriately manage non-motor symptoms of dystonia (e.g., pain, fatigue) and negative emotions (e.g., anxiety, depression) within a multi-disciplinary support structure would likely people with dystonia to perform regular exercise, and being supported by trained evidence-based professionals would likely increase confidence and motivation to exercise as well.

In addition, more consistent effects of BTX injections were also suggested by participants as an area of improvement. Participants may be enabled to perform more exercise and/or incidental physically activity if the consistency and effectiveness of BTX injections were improved. Given that BTX is currently the first-line treatment option for focal and segmental dystonia's (e.g., cranial, cervical, hand) (21), understanding the potential role of exercise in conjunction with BTX treatment is also important to ensure people with dystonia are achieving the best outcomes possible. Although the evidence of exercise/physical therapy for dystonia is scarce, a few small randomized controlled trials (RCT) have been performed. In one RCT ($n = 40$ CD), a combined program of exercise, stretching, massage, and BTX treatment was compared to BTX treatment alone (22). The authors found that the effects of BTX were prolonged in the combined program group, and patient reported outcome measures of activities of daily living and pain scored better in the combined program group vs. BTX treatment alone (22). High-quality RCTs are needed to support this preliminary evidence suggesting exercise could be used to augment BTX treatment, and potentially improve the cost-effectiveness of treatment. Reducing the number of BTX treatment sessions needed per year, the volume of BTX needed per treatment, and enhancing the effects on patient outcomes with the addition of a simple, low-cost exercise/physical therapy program could add significant value to the quality of life for many people with dystonia (22). The effects of an exercise program using aerobic and motor control exercises in conjunction with BTX treatment for people with dystonia is not known. Though it would be interesting to determine if exercise could alleviate some of the unwanted side-effects of BTX treatment and decrease the number of people dissatisfied with, and therefore discontinuing, their BTX treatment (23). Furthermore, public dissemination of high-quality evidence is important to ensure people with dystonia are informed about relevant evidence-based treatment options. Dystonia is usually a life-long movement disorder, and evidence-based self-management strategies may be the most viable option in the long-term management of this condition.

STUDY LIMITATIONS

There are several limitations to consider when interpreting the results. Firstly, although the IPAQ is a widely used instrument to assess PA at a population-level it does require participants to self-report and recall their PA time from the past week which can bias the results. Some studies have suggested the IPAQ overestimates total PA time (24, 25) and public health recommendations may be too easily achieved when assessed using the IPAQ due to the recording of many incidental activities (26). In comparison to the gold-standard doubly-labeled water method the IPAQ was found to underestimate higher intensity activity (27). The IPAQ is yet to be psychometrically assessed in chronic neurological populations such as dystonia, and administration of an online version of the IPAQ needs to be validated also. The administration of the IPAQ online without supervision could have contributed to the number of participants that scored the IPAQ inappropriately in our study. Forty-five participants reported a total PA time of 0 min/wk which is not possible if the IPAQ is answered correctly and the cases were excluded from analysis. Quantifying PA and SB time in people with dystonia using objective methods of assessment, such as accelerometery or doubly labeled water are needed. In addition, as the survey was only available online people without access to the internet could not participate. Furthermore, the online survey was available to people from all countries so cross-cultural differences may have also influenced the results. In relation to the qualitative results and barriers to exercise, some closed-ended questions may have limited the ability of participants to accurately record their lived experience. Future qualitative studies could utilize focus groups or interviews to obtain more in-depth data about the perspectives of people living with dystonia and the barriers they experience. Follow-up studies to support the current findings are recommended.

CONCLUSIONS

Knowledge of activity and participation limitations in people living with dystonia is limited. Understanding the factors that impact PA engagement is fundamental to supporting people with dystonia maintain their activities of daily living and meaningful participation in life after diagnosis. Overall, from this self-reported activity data it appears people living with dystonia are achieving the minimum requirements of PA time according to their self-reported activity levels, by means of incidental activity during transport and domestic duties. Future studies should incorporate objective methods of PA and SB measurement such as accelerometery to confirm the results of this study. The immediate and short-term effects of exercise seem to aggravate dystonia symptoms, however the longer-term impact of an appropriately prescribed exercise program with consideration given to the mode and intensity of exercise is not known. Addressing the barriers to PA in this population could lead to meaningful improvements to the well-being and overall quality of life of people living with dystonia.

DATA AVAILABILITY STATEMENT

The datasets generated for this study are available on request to the corresponding author.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by University of Technology Sydney (UTS) HREC ETH18-3048. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

LB: conception of the initial idea. AM, RM, and LB: survey development, survey dissemination, and manuscript preparation. AM: ethical approval and set up online survey. RM and LB: data analysis.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2019.01121/full#supplementary-material

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Money Management in Multiple Sclerosis: The Role of Cognitive, Motor, and Affective Factors

Goverover Yael [1,2]****, Chiaravalloti Nancy*** [2,3] ***and DeLuca John*** [2,3]

[1] Department of Occupational Therapy, New York University, New York, NY, United States, [2] Kessler Foundation, West Orange, NJ, United States, [3] Department of Physical Medicine and Rehabilitation, New Jersey Medical School, Rutgers University, Newark, NJ, United States

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Harvard Medical School,
United States

****Correspondence:***
Goverover Yael
yg243@nyu.edu

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Introduction: Few studies have examined the motor, cognitive, and emotional factors involved in effective money management in persons with multiple sclerosis (MS). The aim of this study was to assess money management in persons MS and examine whether cognitive, motor, and emotional processes can predict money management.

Methods: This study included 72 persons with MS and 26 healthy controls (HC). Using an *a priori* definition of efficient vs. inefficient money management skills, based on the money management questionnaire (self and others), and performance on Actual Reality^{TM} (AR) money management items, MS participants were divided into two groups: efficient or inefficient money management (MS Efficient- MM, $n = 34$ vs. MS Inefficient-MM, $n = 38$). These groups were compared on cognitive, motor, and emotional variables.

Results: Participants in the MS efficient MM group performed significantly better on executive function and processing speed measures, as well as performance on the 25WT. The MS Efficient -MM group also showed significantly less affective symptomatology (depressive and state anxiety). Importantly, HC performed similarly to the Efficient MM group on these tests. Good executive functioning and low depressive symptomatology predicted efficient money management.

Conclusions: This study characterizes some of the major problems and underlying impairments persons with MS are encountering in money management. Practitioners working with persons with MS should be aware that executive function impairments together with depressive symptomatology could signal possible money management dysfunction. The early identification of at-risk persons for money management difficulties could have a profound impact on the quality of life for this subsample of the MS population.

Keywords: activities of daily life (ADL), multiple scleorsis (MS), money management, cognition, executive functions, quality of life

INTRODUCTION

Multiple sclerosis (MS) is a common neurodegenerative disease affecting adults between the ages of 20 to 50, and is two to three times more common in women than men (1). The disease is characterized by inflammation, demyelination, and axonal loss, while chronic axonal degeneration succeeds later. The disease presents with a variety of symptoms including pain, fatigue, poor muscle control, balance and postural difficulties, cognitive impairments, and optic neuritis (2, 3). MS has a considerable impact on a patient's everyday functioning, quality of life, and the costs of disease management are substantial (4, 5).

Money management is a critical skill for everyday functional independence. The ability to perform tasks, such as managing cash, banking, paying bills, and budgeting, are all necessary for successful participation within the community (6). Although it had been already established that cognitive impairments are predictive of everyday functioning limitations [e.g., (7, 8)], an effort has been made on identifying cognitive abilities that are linked directly with specific real-world tasks, such as managing finances, to target intervention strategies (9, 10). Two studies (11, 12) were conducted specifically targeting money management with persons with MS. Both studies have shown that (1) participants with MS have more problems managing finances compared with healthy controls (HC) and (2) financial management tasks require several underlying cognitive abilities, such as working memory and, executive function (11, 12). This current study extends these prior studies (11, 12), by directly focusing on the financial management outcome of patients with MS as the primary objective, involving a larger sample of patients with MS than used in previous studies, and using collateral reports provided by participants' informants (e.g., caregiver, spouses, or siblings).

The primary aim of the present study was to first describe the main obstacles in money management of persons with MS with inefficient money management compared to persons with MS with efficient money management and HC. Second, we sought to examine the role of cognition, motor performance, and depressive symptomatology in predicting the functional outcome of money management in persons with MS. Our hypotheses were that (1) participants with MS with efficient money management will perform similarly to HC on cognitive tests, and report similar levels of affective symptomatology. Furthermore, HC and persons with MS with efficient money management will have better cognitive functioning and affective symptomatology than participants with MS with inefficient money management. (2) Impairment in executive functions, would predict group membership of efficient vs. inefficient money management in persons with MS after controlling for motor skills and affective symptomatology.

METHODS

Participants

Participants consisted of 26 HC and 72 individuals with clinically definite MS [based on (13)] between the ages of 18 and 65 years. This study was designed with 0.80 probability of finding a significant difference between the groups. Based on comparison's effect size observed in the present study ($d = 0.35$), power analysis indicated that an n of ∼90 would be needed to obtain statistical power at the recommended 0.80 level (14).

Participants with MS were recruited from support groups, advertisements, and from the Kessler Foundation. HC were recruited from advertisements and by word of mouth. All recruitment and study procedures were approved by the Institutional Review Board, consistent with the Health Insurance Portability and Accountability Act (HIPAA). Participants were excluded if they had any neurological or medical condition other than MS, had an exacerbation of symptoms and/or steroid treatment within the past month, had insufficient visual acuity to see the test materials, and did not speak English. Participants similarly could not participate in any cognitive rehabilitation program at the time of the study. Demographic characteristics are described in **Table 1**. Additionally, participants in the present study self-identified informants, who also consented to participate in this study. Ninety-eight Informants (26 of the HC and 72 of the persons with MS) were either a friend, relative, or a care taker and were identified by the study participants as someone who knows them very well and sees them regularly.

Measures

Money Management

Overall money management status was assessed using two assessment methods: the performance based Actual Reality^{TM} (AR), and self- and informant ratings of the Money management questionnaire (described below).

Actual reality

Actual Reality^{TM} (AR) (8, 11) is a performance-based functional assessment that uses the internet to accomplish the actual real world task of purchasing a cookie bouquet from a business website. This task required participants to choose an appropriate cookie bouquet within a specified price range while taking into account the cost of shipping and handling. To score money management within AR, five behaviors within AR that are related to money management were targeted: staying within the indicated price range, using the credit card correctly, choosing an appropriate cookie bouquet, performing the task at an efficient pace and correctly responding to unforeseen occurrences [similar procedure described elsewhere (11)]. A score of a 0 (no error), 1 (minor error), or a 2 (major error) was given for performance of each of these behaviors indicated above. The scores depended on the significance and frequency of the errors made during performance. The score could range from 10 (severe deficit) to 0 (competent performance). AR has moderate to large Interrater Reliability, ranging from 0.79 to 0.89 and moderate test-retest reliabilities with intraclass correlations ranging from 0.5 to 0.83. AR also has good discriminant and concurrent validity for use with person with MS (15).

Self and informant-report money management

Money management was also assessed by a self-report and an informant report questionnaire (16) that was designed

TABLE 1 | Demographic characteristics of MS and HC.

	MS inefficient ($n = 38$)	MS efficient ($n = 34$)	HC ($n = 26$)	Test	p	Tukey
Age	50.1 ± 7.9	51.6 ± 9.3	44.4 ± 10.5	$F = 4.8$	0.01	c>b,a
Education	15.5 1.9	15.8 ± 1.9	17.2 ± 1.8	$F = 6.1$	<0.01	c>b,a
Gender						
Male	21.1% ($n = 8$)	11.8% ($n = 4$)	34.6% ($n = 9$)	$\chi^2_{(2)} = 3.8$	0.14	
Female	78.9% ($n = 30$)	88.2% ($n = 30$)	65.4% ($n = 17$)			
Disease type						
Relapsing remitting	80%	95.7%	NA	$\chi^2_{(2)} = 4.5$	0.10	
Primary progressive	17.5%	0	NA			
Secondary progressive	2.5%	4.3%	NA			
Disease duration (month)	198.3 ± 121.9	198.4 ± 104.8	NA	$F = 0.00$	0.99	
MSFC-*z* score	−0.36 ± 0.68	−0.05 ± 0.56	0.17 ± 0.43	$F = 6.5$	<0.01	c>a; c>b
Employment (%)						
Disability/unemployed	63.2	47	11.5	$\chi^2 = 48.1$	<0.001	
Part-time work	18.4	20.6	15.4			
Student	0	0	11.5			
Volunteer	2.6	2.9	0			
Full-time work	15.8	20.6	61.5			

MS, Multiple sclerosis; HC, healthy controls; MSFC, Multiple sclerosis functional composite.

for patients with acquired brain injury and their informant. The questionnaire includes 11 short, concrete questions. On the patient form, the questions focus on whether the patient did or did not perform money management skills such as paying bills, using the ATM, budgeting, and borrowing money. Note that the patient is not asked to rate the quality or indicate any reasons for his/her performance. For example, one question asks, "Do you pay the rent late?" *Never (score of 0)*, *Sometimes (score of 1)*, or *Often (score of 2)*. For the informant version, the form consists on the same questions as in the patients form. The scores for each form can range from 0 to 22, with a lower score indicating fewer problems managing money.

MS participants were divided into two groups based on money management abilities, as assessed with the AR money management portion (11) and the money management questionnaires (self and informant report). Scores of the both money management questionnaires and AR were summed and averaged for the participants with MS. Based on a median split of the summary and average scores, a score of 3 (observed range: 0.33–9) was *set* as cut-off to distinguish patients with efficient (score of 3 and lower; MS Efficient-MM) and inefficient (MS Inefficient -MM) (higher score than 3) money management. Note that all HC money management scores were lower than 3 except for one and thus was excluded from the analyses.

Affect Symptomatology

Depression and Anxiety were assessed using the Chicago Multi-scale Depression Inventory (CMDI) (17, 18) and the State and Trait Anxiety Inventory (STAI) (19), respectively. These questionnaires are based on self-report where participants are asked to rate their mood (i.e., depression and anxiety) on a 4 or 5-point Likert scale.

Cognitive Skills

Learning and memory: Verbal memory and learning were assessed by the Selective Reminding Test (SRT) (20). *Z*-score of the SRT was used in this study as dependent variables. Visual learning and memory were assessed by the Brief Visuospatial Memory Test-Revised (BVMT-R) (21). Total Recall across the three learning trials and the Delayed Recall t-scores served as the dependent variables.

Executive functions were assessed using the Delis-Kaplan Executive Function System (DKEFS) (22) letter-number sequencing trails subtest. The DKEFS scaled score (SS) was used in the analyses.

Processing speed and working memory were assessed using the (1) Symbol Digit Modalities Test SDMT; oral version (23); higher z-scores indicate faster processing speed and served as the dependent variable; and (2) Paced Auditory Serial Addition Test (PASAT) (24); There are two trials of 60 numbers each. The first consists on a 3-second inter-stimulus interval and the second on a 2-second inter-stimulus interval. Total number correct responses across the two trials served as the dependent variable.

Physical Functioning

Two subtests of the MS Functional Composite measure (25) were used: the Timed 25-Foot Walk Test (TWT) to assess lower limb function, and the 9-Hole Peg Test (9-HPT) to assess upper limb function. Z scores of these measures were calculated based on published norms (26, 27).

Procedure

Potential participants were screened according to the inclusion/exclusion criteria described above during an initial phone conversation. All participants had to sign an informed consent form approved by the Institutional Review Board before study enrollment and then were scheduled for testing. During the testing, participants performed the AR task and the neuropsychological tests, and completed questionnaires to assess money management skills, and affective symptomology (order was randomized across subjects).

Data Analysis

Group differences for demographics, cognitive performance, affect symptomatology, and physical performance were each analyzed by one-way analysis of variance with age and education as covariates (ANCOVA) with Tukey *post-hoc* analyses. For each item/question on the money management survey, responses were divided into two, with responses of 0 indicating "no problems" and responses of 1 and 2 indicating there were "problems" [based on (16)]. Multiple planned comparisons were analyzed using likelihood ratios to examine the individual items related to money management where individuals with MS (Efficient vs. Inefficient MM) were more likely to have problems compared to HC. These comparisons were also used to examine the AR task items. Lastly, a backward stepwise logistic regression with group membership (Efficient vs. Inefficient MM) as the criterion variable was used to investigate which of the independent variables could best predict efficient vs. inefficient MM functioning.

RESULTS

As shown in **Table 1**, there were significant differences between HC and MS in years of education [$F_{(2,94)} = 6.1$, $p < 0.01$], disability score (MSFC) and employment status. The three groups (MS Efficient-MM, MS inefficient-MM functioning and HC) did not differ with respect to gender and age, but they differed on years of education, MSFC score and employment status. The two MS groups were more likely to be unemployed, and have less years of education and lower disability score compared with HC.

Characteristics of the Difficulties With Money Management Across the Groups

Table 2 reports the problems with money management reported across the three groups based on the money management questionnaire. The MS inefficient-MM group reported problems with money management included using an ATM, paying the rent or bills late, owing money, spending all their money within the first few days of receiving it, going without essentials such as food because they had run out of money, impulse buying, and spending money on things they do not really need and needing to borrow money because they ran out of money. Similar patterns were reported by the informants of the participants, with the MS inefficient MM functioning group informants reporting similar frequencies of MM problems as the participants themselves.

In terms of money management on the AR task, the main difficulties presented by the MS inefficient MM group were that they committed more credit card errors, performed the task at a slower pace, did not choose the best option in terms of price, and did not respond efficiently to unexpected issues in comparison to the efficient MM group and HC groups (see **Table 3**).

Cognition, Motor Performance, and Depressive Symptomatology and Money Management

Comparisons between the three groups on cognitive and motor skills and affective symptomatology while controlling for age and education are presented in **Table 4**. On all cognitive measures except the PASAT, participants in the inefficient MM group performed significantly worse than participants in the efficient MM group, while HC performed similarly to the efficient MM group. On the BVMT delayed recall however, there were no significant differences between the inefficient MM group and the efficient MM group. The HC group performed significantly better than both MS groups.

With regard to affective symptomatology, the inefficient MM group reported significantly higher depressive and state anxiety symptomatology compared to efficient MM and HC. HC and MS-efficient MM reported similar symptomatology. A slightly different pattern was noted with regard to motor skills performance. On both the 25 FW and the 9HP MS-efficient MM performed similarly to the MS-inefficient group and the HC group. However, HC performed significantly better than inefficient MM, MS.

Which Is the Best Predictor of Inefficient vs. Efficient Money Management in Patients With MS Only: Cognitive, Motor, or Affect?

A backward logistic regression analysis was performed to examine the relative contribution of cognitive, motor skills, and affect symptomatology in predicting efficient MM vs. inefficient MM functioning. Four predictors were included in this regression model, based on their significance in determining money management skills. These predictors were, executive functions score (DKEFS trails SS), processing speed score (SDMT *z* score), motor performance (9 HP *z* score) and depressive symptomatology (CMDI total t score). A test of the full model with backward stepwise method with the 4 predictors against a constant only model was statistically reliable [$X^2{}_{(2, N = 70)} = 19.7$, $p < 0.001$], indicating that the predictors (CMDI: Odds ratio = 1.1; 95% CI = 1.03–1.2; $p = 0.04$; DKEFS: Odds ratio = 0.81; 95% CI = 0.68–0.97; $p = 0.02$) reliably distinguished between participants who had efficient MM vs. those who had inefficient MM (as described in **Table 5**). Overall, prediction success of the

TABLE 2 | Percentage of participants in the MS inefficient and efficient MM functioning groups and HC group reporting problems in money management on the money management survey.

	% MS inefficient (*n* = 38)	% MS efficient (*n* = 34)	% HC (*n* = 26)	Likelihood ratio	*p*
Problems with ATM	21.2	9.1	0	9	0.01
Don't often check change	36.4	31.8	42.3	0.57	0.75
Pay bills or rent late	33.3	0	0	22.3	0.00
Thrown out of accommodation	9.1	0	0	5.5	0.06
Owe money for debts	42.4	0	0	29.6	0.00
Spend all money within first few days	39.4	4.5	3.8	16.7	0.00
Go without essentials	24.2	0	0	15.6	0.00
Problematic impulse buying	30.3	4.5	0	15.7	0.00
Spend all money on things they like	30.3	4.5	0	15.7	0.00
Need to borrow money	57.6	0	0	43.2	0.00

ATM, automatic teller machine; MM, money management.

TABLE 3 | Percentage of participants in the MS inefficient and efficient MM and HC groups who performed more errors on the AR money management skills.

	% MS inefficient (*n* = 38)	% MS efficient (*n* = 34)	% HC (*n* = 26)	Likelihood ratio	*p*
Going over the price range	73.6	58.8	46.1	7.6	0.11
Credit card errors	42.2	35.3	15.4	9.4	0.05
Pace	76.3	50	26.9	24.1	<0.001
Choosing the best option	97.4	85.3	73	16.5	0.002
Noticing and responding to unexpected issues	90.5	55.8	34.6	33.0	<0.001

model was 67.1% and only executive functions and depressive symptomatology reliably predicted persons with MS with efficient vs. inefficient MM.

DISCUSSION

The results of the current study show that persons with MS may struggle to perform fundamental money management tasks, which may have significant negative effects on their day to-day life. The main problems that were reported by persons with MS who have inefficient MM are owing money to others, the need to borrow money, and also spending money they have within a few days from the time they received it. During money management performance, problems in making appropriate choices related to price, choosing the most appropriate items and reviewing prices were observed. Thus, participants with MS in the inefficient-MS MM group clearly present with several money management errors/problems that can be extremely problematic to managing independent daily life. These problems can also lead to significant economic and safety consequences for patients and significant stress and burden for caregivers (28). It is important however, to note that the present study also showed that not all participants with MS have money managment issues; some individuals with MS have comparable abilities in money managment functioning to HC. It is thus important to determine who is at risk for the development of MM difficulties to avoid negative consequences.

A second goal of the study was to examine the underlying characteristics in persons with MS with money management difficulties, and examine the role of cognition, motor performance, and depressive symptomatology in predicting the functional outcome of money management in persons with MS. Results showed that the HC and efficient MS MM groups differed from the MS-inefficient MM group with respect to each of these aspects of functioning.

With regard to cognition, the MS-inefficient MM group performed worse on verbal memory, executive function and processing speed measures as compared with HC and the MS-efficient MM. Those with efficient MM skills performed similarly to HC on these tests. More specifically, participants in the inefficient MM group performed poorer on new learning and recall (SRT) than the comparison groups. This finding suggest that those patients with inefficient MM also have difficulties in learning and memory of verbal information. Consistent with this finding, impairment in verbal memory has been suggested to be a predictor of work impairment in persons with MS (29) and other clinical populations (30). In addition to differences in verbal memory, there were also significant differences noted between the groups with regard to executive functioning, as documented by the DKEFS letter-number sequencing subtest. MS participants with inefficient MM functioning scored significantly below HC.

TABLE 4 | Difference between groups in cognitive, physical, and affective functioning while controlling for age and education as covariates.

	MS inefficient	b. MS efficient	c. HC	*F*	*p*	Tukey
COGNITIVE						
Memory						
BVMT-imm *t*-score	40 ± 14.3	45.4 ± 14.7	53.9 ± 7.5	5.8	<0.01	c>a
BVMT delayed	42.9 ± 14.4	47.9 ± 13.6	57.1 ± 4.7	7.6	<0.01	c>a c>b
SRT-*z* score	−2.1 ± 1.3	−1.2 ± 1.2	−0.85 ± 1.1	7.9	<0.01	c>a b>a
Processing speed						
SDMT *z* score	−1.02 ± 1.5	−0.19 ± 1.1	0.33 ±.72	7.5	<0.01	c>a b>a
PASAT 2 & 3	73.7 ± 22.7	80.5 ± 20.7	82.4 ± 21.9	0.93	0.39	None
Executive functions						
DKEFS Trails SS	8.6 ± 3.7	10.9 ± 3.3	11.2 ± 2.9	5.8	0.004	c>a b>a
AFFECT SYMPTOMATOLOGY						
CMDI-mood	50.3 ± 9.6	45.9 ± 7.9	45.6 ± 5.8	3.4	0.03	None
CMDI-evaluative	53.3 ± 13.7	45.9 ± 5.8	44.6 ± 1.4	7.8	<0.01	c>a b>a
CMDI-vegetative (Fatigue)	63.4 ± 13.2	53.3 ± 11.7	48.7 ± 7	11.7	<0.01	c>a b>a
STATE Anxiety	53.9 ± 10.6	44.6 ± 8.5	46.1 ± 9.5	8.9	<0.01	c>a b>a
TRAIT Anxiety	58 ± 12.4	47.8 ± 9.2	50.7 ± 11.3	7.5	<0.01	c>a b>a
PHYSICAL						
9-HPT *z* score	−0.53 ± 0.86	0.01 ± 0.76	0.57 ± 0.50	11.6	<0.01	c> a b>a
25 foot walk *z* score	0.13 ± 0.37	0.29 ± 0.13	0.40 ± 0.07	5.5	<0.01	c>a

In considering the relationship between task and financial management, one must consider the task demands of effective financial management. That is, when managing finances, it is important to adjust to changes in income and expenses as well as to control spending. Indeed, these constructs are necessary for effective completion of the letter number sequencing task as well. That is, to successfully complete the task one must exhibit impulse/inhibitory control, similar to that which is necessary to curb unnecessary spending. In addition, the task requires mental flexibility/set shifting, such as that which may be needed when one must generate solutions to financial challenges and not perseverate on the manner in which one always managed income and expenditures. The final cognitive construct determined to be important to MM ability was *processing speed*. As can be seen in the literature, numerous studies have demonstrated the importance of processing speed in everyday functions [e.g., (5, 31)].

In terms of affective symptomatology, HC and participants with MS with efficient MM skills were less anxious and less depressed than those in the inefficient MM group. Those with efficient MM skills performed similarly to HC on these tests. We should note that all MS participants, across groups, showed mild symptoms of depression, and anxiety. Affective symptomatology may have a complex relationship with self-appraisal of personal abilities in MS (32). The absence of depression may be related to overestimation of abilities, while mild depression may be related to accurate self-assessment (33). It is also relevant to consider the role of coping in this relationship. That is, Arnett and Randolph (34) showed that patients with MS whose depressive symotomatology had worsened showed decreased active coping strategies. Although the nature of our design cannot determine causality, it may be possible that increases in depressed mood, may lead to decreased use of strategies which may affect every day functioning, including money management.

It is similarly important to note that individuals with inefficient money management skills also had worse motor performance on the 25-foot walk test compared to efficient MM and HC. This confluence of decline across measures of cognition, physical functioning, and money management skills may reflect an overall functional decline consistent with increased general disability.

Lastly, we hypothesized that executive functions would predict MM quality above and beyond affective symptomatology and motor skills. This hypothesis was partially confirmed because both executive function and depressive symptomatology were significant predictors of MM functional level. The results related to executive functions accord well with prior investigations in MS (11, 12). Prior research however, did not find that depressive

TABLE 5 | Logistic Regression Analysis with cognitive, physical, and affective Measures as Predictors of Group Membership (efficient MM vs. inefficient MM).

Measures	B	SE	Wald	df	sig
Step 1					
CMDI	0.10	0.03	8.2	1	0.004
9HP	−0.30	0.49	0.38	1	0.53
SDMT	−0.06	0.34	0.02	1	0.87
DKEFS	−0.16	0.11	2.1	1	0.14
Constant	−3.5	2	3.1	1	0.07
Step 2					
CMDI	0.10	0.03	8.2	1	0.004
9HP	−0.29	0.45	0.40	1	0.52
DKEFS	−0.16	0.10	2.3	1	0.12
Constant	−3.6	1.9	3.3	1	0.07
Step 3					
CMDI	0.10	0.03	8.5	1	0.004
DKEFS	−0.20	0.09	5.3	1	0.02
Constant	−3.2	1.9	2.9	1	0.09

CMDI, Chicago Multi-scale Depression Inventory; DKEFS, Delis-Kaplan Executive Function System; 9HP, 9-Hole Peg Test.

symptomology is associated with MM. As such, depressive symptomatology may serve as a key vulnerability for MM among patients with MS. We concur with the Tracy et al. (12) recommendation that future research should examine whether more specific aspects of executive function and depressive symptomatology contribute to inefficient MM in MS.

The current research has a number of weaknesses. Participants were recruited through community-based lists and support groups. As a result, many participants in the study were independent in their daily life. Before generalizing the findings to all individuals with MS, further studies using participants with MS with a wider variety of disability could assist in determining the relationship between competence to manage personal finances and cognitive status. There are a limited number of performance-based measures to assess MM in clinical populations. In this study, we used the Money management questionnaire (self and informant reports) and few items from AR related to money management. Psychometric properties of both must be established before it can confidently be used by future studies. Lastly, it would be interesting to assess MM in an objective context. This will help clinicians assess it empirically without evoking subjective biases and errors.

CONCLUSION

For individuals with MS and their families, MM may be a crucial activity of daily living. Impairment in MM can have clinical, psychological, economic, and legal implications (35). Therefore, practitioners working with persons with MS should be aware that cognitive impairment generally, and impairments in executive functions specifically, could signal possible MM limitations, and prompt the clinician to urge patients and families to engage in advance financial and legal planning. Furthermore, timely documentation and assessment of MM limitations can often prompt beneficial financial planning that could improve the economic, psychological, and legal implication of financial dysfunction in people with MS. Further research is needed to establish standardization and guideline for such issue.

DATA AVAILABILITY STATEMENT

The datasets generated for this study are available on request to the corresponding author.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Kessler Research Foundation New York University. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

GY conceptualized the study idea, drafted the paper, and did all the analyses and interpretation of data. DJ and CN revised it and added important intellectual content.

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The Initiation of Swallowing Can Indicate the Prognosis of Disorders of Consciousness: A Self-Controlled Study

Jianan Wang[1†], Jing Wang[1†], Xiaohua Hu[2], Lingqi Xu[1], Jinna Tian[1], Jiayin Li[1], Danruo Fang[1], Wangshan Huang[1], Yuxiao Sun[1], Minhui He[1], Steven Laureys[3] and Haibo Di[1*]

[1] International Unresponsive Wakefulness Syndrome and Consciousness Science Institute, Hangzhou Normal University, Hangzhou, China, [2] Rehabilitation Center for Brain Damage, Wujing Hospital of Hangzhou City, Hangzhou, China, [3] GIGA, GIGA-Consciousness, Coma Science Group, Neurology Department, University Hospital of Liege, University of Liège, Liège, Belgium

Objective: To detect the initiation of swallowing in patients with disorders of consciousness (DOC) as well as the relationship between the initiation of swallowing and the prognosis of DOC patients.

Methods: Nineteen DOC patients were included in this study, and a self-controlled trial compared five different stimuli. The five different stimuli were as follows: (1) one command, as recommended by the Coma Recovery Scale-Revised (CRS-R), which was "open your mouth"; (2) placing a spoon in front of the patient's mouth without a command; (3) placing a spoon filled with water in front of the patient's mouth without a command; (4) one command—"there is a spoon; open your mouth"—with a spoon in front of the patient's mouth; (5) one command, "there is a spoon with water; open your mouth," with a spoon filled with water in front of the patient's mouth. All 19 patients were given these five stimuli randomly, and any one of the commands was presented four times to a patient, one at a time, at 15-s intervals. The sensitivity and specificity of the initiation of swallowing in detecting conscious awareness were determined.

Results: None of the patients responded to the first four stimuli. However, six patients showed initiated swallowing toward the fifth stimulus. Among those six, five patients showed improvement in their consciousness state 6 months later. The sensitivity and specificity of the initiation of swallowing for DOC patients was 83.33% [95% CIs (36%, 100%)] and 92.31% [95% CIs (64%, 100%)], respectively.

Conclusions: The initiation of swallowing can be an early indication of conscious behavior and can likely provide evidence of conscious awareness.

Clinical Trial Registration: www.ClinicalTrials.gov, identifier: NCT03508336; Date of registration: 2018/4/16.

Keywords: disorders of consciousness, swallowing, consciousness, minimally conscious state, prognosis

Edited by:
Lisa Tabor Connor,
Washington University in St. Louis,
United States

Reviewed by:
Rocco Salvatore Calabrò,
Centro Neurolesi Bonino Pulejo
(IRCCS), Italy
Antonino Naro,
Centro Neurolesi Bonino Pulejo
(IRCCS), Italy

***Correspondence:**
Haibo Di
dihaibo19@aliyun.com

† These authors have contributed equally to this work

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INTRODUCTION

Disorders of consciousness (DOC) include several states, ranging from coma and unresponsive wakefulness syndrome/vegetative state (UWS/VS) to a minimally conscious state (MCS) (1). Per definition, UWS/VS patients show no sign of consciousness of either themselves or the environment (2). However, MCS patients differ from UWS/VS patients according to the presence of inconsistent but reproducible signs of awareness (3). The clinically heterogeneous MCS patients were subcategorized into two distinct entities: "MCS minus" (MCS−) and "MCS plus" (MCS+) (4, 5). MCS− patients showed low-level purposeful behaviors without command following (e.g., visual pursuit, localization to noxious stimulation, object localization [reaching], automatic motor response, and appropriate smiling or crying related to an external stimuli). MCS plus (MCS+) patients were those who presented higher-level behavioral interactions (e.g., a movement in response to a command, non-functioning communication, and intelligible verbalization). For DOC patients, the differential diagnosis of consciousness state is of great importance, especially for decisions on treatment, care, and end-of-life actions (2, 6).

The assessment of awareness has increasingly been gaining attention and is still an urgent unmet need. At present, the gold standard for diagnosing DOC patients is the standardized behavioral assessment tool (7–9). A misdiagnosis rate of about 40% has been reported by some studies, scilicet some patients with a higher ability were misdiagnosed as being in UWS (10–12). At present, the Coma Recovery Scale-Revised (CRS-R) is strongly recommended and considered for assessing DOC patients (13, 14), with a higher percentage of MCS subjects correctly diagnosed and better overall classification accuracy than the current clinical criteria (12). However, some patient-related factors, such as aphasia, agnosia, cortical deafness, and motor impairment, often lead to a false negative result on a standard CRS-R (7, 15). As has been reported, 19 DOC patients participated in CRS-R and brain–computer interfaces in this study, of which three patients exhibited no responses in the CRS-R assessment but were responsive to auditory startle in the brain–computer interfaces assessment. The results revealed that a proportion of DOC patients who have no behavioral responses in the CRS-R assessment can generate neural responses (16), and a CRS-R total score of 10 or higher yielded a sensitivity of 0.78 for the correct identification of patients in either MCS or EMCS (14). There is an urgent need in behavioral assessment to find effective stimuli to improve diagnostic accuracy; recent studies have shown different stimuli indeed have different effects on the behavioral response of patients (17).

From a recent study, some DOC patients who recovered their swallowing ability at an early stage had a good prognosis (18), and a previous study showed that 64% of DOC patients could recover to unrestricted dieting within 126 days (19). Per another previous report, the initiation of swallowing of the pharyngeal phase is controlled by active cortical control for spontaneous as well as volitional swallowing in awake people (20). The cortex exerts volitional control over the onset and magnitude of neural activity for swallowing. Sensory feedback from the oral cavity, pharynx, and larynx is crucial for initiating the brainstem swallowing response and for modulating cortical activity. Deprivation of sensory input can be detrimental to swallowing safety because it can alter airway protection during swallowing. When peripheral and cortical inputs exceed an activation threshold, the brainstem swallow response is triggered. Additionally, some functional neuroimaging studies have indicated that the left hemisphere has greater activation in certain sensory and motor-related swallowing regions in patients with cerebral vascular accidents (20, 21). Considering that some patients may also have either aphasia or agnosia, some reports have shown that different stimuli have different sensitivity regarding eliciting a behavioral response from DOC patients (22). Hence, the choices of objects and stimuli seem to be important for appropriate clinical behavioral assessment. In this study, we hypothesized that an informative and familiar stimulus might better elicit a response from patients. In addition, we aimed to detect the relationship between the initiation of swallowing and the prognosis of DOC patients using a well-controlled test for the initiation of swallowing for DOC patients.

MATERIALS AND METHODS

Patients

This study protocol was approved by the Ethics Committee of Hangzhou Normal University, which complies with the Code of Ethics of the World Medical Association (Declaration of Helsinki). Written informed consent was obtained from the guardians/next of kin of the patients who participated in the study.

According to the Aspen workgroup criteria for disorders of consciousness (3) and based on the repeated CRS-R assessments, ≥five assessments within 1 week (23) were performed by two trained and experienced neuropsychologists. Meanwhile, each patient's swallowing ability was confirmed by a water drinking test, the protocol of which was as follows: with the patient in a seated position, an injector was used to absorb 30 ml of warm water and fed to the patient. Recorded information was included and recorded the time of drinking water, whether he/she choked or coughed in the process, and whether he/she drank up all the water. We then recruited patients who could drink the water within 5 s in one or two attempts without choking or coughing during the process. In total, 24 patients with the desired swallowing ability who had been diagnosed as either UWS or MCS− were prospectively recruited. Of those 24 patients, 19 (79%) had follow-up information available during the following 6 months (**Figure 1**). Inclusion criteria included (1) age ≥18 years; (2) no administration of central nervous system stimulants, neuro-muscular blocking agents, or sedatives within the prior 24 h; (3) a diagnosis of UWS or MCS−, based on the behavioral assessment of the standardized CRS-R; (4) periods of eye opening. Exclusion criteria included (1) a documented history of a prior brain injury; (2) a premorbid illness resulting in documented functional disabilities up to the time of injury; (3) acute illness (e.g., pyrexia, pneumonia, or diarrhea); (4) receiving hyperbaric oxygen treatments within 2 h; (5) a fracture of the

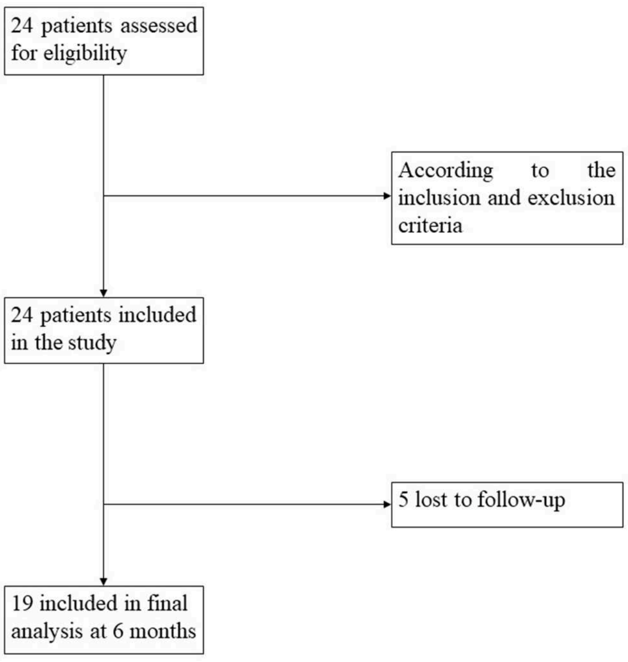

FIGURE 1 | Flow chart of patient selection in the study.

TABLE 1 | Demographic characteristics of patients.

Characteristic	Median	Range
Age	57	27–77
Month post-injury	4	1–12
	n	
Gender		
Males	14	
Females	5	
Etiology		
TBI	10	
NTBI	9	

TBI, traumatic brain injury; NTBI, non-traumatic brain injury.

mandible. The process for recruitment of patients was showed in **Figure 1**.

Study Design

Five stimuli were established: (1) one command, as recommended by the Coma Recovery Scale-Revised (CRS-R), which was "open your mouth"; (2) placing a spoon in front of the patient's mouth without a command; (3) placing a spoon filled with water in front of the patient's mouth without a command; (4) one command—"there is a spoon; open your mouth"—with a spoon in front of the patient's mouth; (5) one command, "there is a spoon with water; open your mouth," with a spoon filled with water in front of the patient's mouth. The patients were placed in a seated position, and we presented the five stimuli in front of each patient's mouth in a random order (i.e., numbers one to five were written (once each) on one of five pieces of paper. We placed the papers into a box, mixed them, drew one, and did not return it to the box, repeating this a total of four times. Therefore, any of the stimuli could be presented each time, one at a time, at 15-s intervals. If the patient opened his/her mouth and attempted to stick out his/her tongue, we considered that the initiation of swallowing had been elicited in that patient.

During this study, the spoon could not touch any part of the patient's body (e.g., mouth, face). Special care was taken not to present stimuli when spontaneous oral movements were occurring. The initiation of swallowing was evaluated through a standardized methodology, as described in the CRS-R (23). Here, we considered that a patient had initiated swallowing if he/she had displayed at least one response to one of the four trials during the presentation of the stimuli. Movements that occurred between stimuli (i.e., after the response interval had elapsed) could not be scored. A complete CRS-R assessment was then performed to diagnose the current state of the patient.

During the assessment, the patients were subject to a standardized arousal facilitation protocol [i.e., we presented deep pressure stimulation unilaterally to the shoulder, arm, and hand until the muscle was firmly grasped at its base between the thumb and forefinger. While squeezing the muscle firmly, it was "rolled" back and forth through the finger tips three to four times (8, 23)].

To obtain a good prognostic value, 6-month follow-up evaluations and further research of the patient's outcomes were conducted via the CRS-R.

Statistical Analysis

Descriptive data were expressed as median and interquartile ranges (Q) $[M\ (P_{25}\sim P_{75})]$ for the variables. Differences between the appearances of the initiation of swallowing (positive response), as assessed by five different stimuli, were measured using the Exact Cochran's Q test. The outcome of whether the consciousness state of 19 patients, as assessed by the CRS-R, had improved after 6 months was analyzed by a McNemar's test. We computed the frequency of improvement between the positive and negative reactions during the 6-month follow-up evaluation.

RESULTS

Demographic and clinical data of the DOC patients who were enrolled in this study are shown in **Tables 1**, **2**. Of the 19 patients (5 females/14 males; age: 57 (49.4∼65.6) years; time since injury: 4 (2.36∼7.25) months), 11 were diagnosed as MCS−, and 8 were diagnosed as UWS. The etiology was traumatic in 10 patients (e.g., DOC was caused by a car accident, a fall from a high place, etc.) and non-traumatic in 9 patients (e.g., DOC was caused by stroke, anoxia, etc.).

The frequency of the initiation of swallowing that was assessed by different stimuli and the diagnoses at the 6-month follow-up evaluation are listed in **Table 3**. It shows that none of the MCS− and UWS patients responded to the first four stimuli; however, six DOC patients (five MCS− and one UWS) initiated swallowing toward the fifth stimulus (i.e., a spoon filled with

TABLE 2 | Demographic and clinical data of DOC patients.

Patient	Etiology	Time since injury (months)	CRS-R (total scores)	Sub-scale scores
MCS-1	TBI	5	10	1-3-2-1-0-3
MCS-2	NTBI	4	10	2-1-3-1-0-3
MCS-3	TBI	1	10	2-3-2-1-0-2
MCS-4	TBI	12	10	1-3-2-2-0-2
MCS-5	TBI	6	10	2-3-2-1-0-2
MCS-6	TBI	8	11	1-3-3-1-0-3
MCS-7	NTBI	4	10	1-3-2-1-0-3
MCS-8	NTBI	3	7	1-2-2-0-0-2
MCS-9	TBI	2	8	1-2-2-1-0-2
MCS-10	NTBI	1	9	1-3-2-0-0-3
MCS-11	NTBI	3	9	0-3-2-1-0-3
UWS1	TBI	6	2	0-0-0-1-0-1
UWS2	NTBI	2	7	2-1-2-0-0-2
UWS3	NTBI	12	7	1-1-2-1-0-2
UWS4	TBI	2	3	0-1-0-0-0-2
UWS5	TBI	10	4	0-0-2-0-0-2
UWS6	NTBI	2	2	0-0-0-0-0-2
UWS7	NTBI	8	4	0-0-2-0-0-2
UWS8	TBI	1	6	1-1-2-0-0-2

DOC, disorders of consciousness; MCS, minimally conscious state; UWS, unresponsive wakefulness syndrome; CRS-R, Coma Recovery Scale-Revised; TBI, traumatic brain injury; NTBI, non-traumatic brain injury.

water in front of the patient's mouth and the command "there is a spoon with water; open your mouth"). Two of the five MCS− patients displayed four clearly discernible responses over the four trials, two MCS− patients displayed three clearly discernible responses over the four trials, one MCS− patient displayed two clearly discernible responses over the four trials, and one UWS patient displayed only one clearly discernible response over the four trials. Thirteen patients showed no initiation of swallowing toward any stimuli (**Table 3**).

The incidence of the initiation of swallowing differed significantly between the fifth stimulus and the other four stimuli ($Q = 24$, $p < 0.01$) (**Figure 2**), with response rates of 31.58 and 0%, respectively. In addition, the initiation of swallowing had no significant relationship with either etiology or time since injury ($p > 0.05$).

Six months later, the behavioral follow-up data showed that, of the 19 DOC patients, there had been improvement (i.e., MCS− had turned into MCS+ and UWS had turned into MCS−) in several patients. Among the six patients (five MCS− and one UWS) who had a positive response, five (83.3%) had a good outcome. Of the 13 patients who had no positive response, 12 (92.3%) had a poor outcome. Using the 6-month behavioral follow-up data of the 19 DOC patients for prognostic value statistics, the sensitivity and specificity of the initiation of swallowing for DOC patients was 83.33% [95% CIs (36%, 100%)] and 92.31% [95% CIs (64%, 100%)], respectively (**Table 4**). The outcome of whether the consciousness state, as assessed by the CRS-R, of the 19 patients had changed (i.e., MCS− had turned into MCS+ and UWS had turned into MCS−) differed, depending on the initiation of swallowing, which was analyzed by a McNemar's test ($\chi 2 = 7.65$, $P = 0.006$).

DISCUSSION

This study aimed to detect the relationship between the initiation of swallowing and the prognosis of DOC patients. We found that the incidence of patients' movement toward the fifth stimulus (i.e., a spoon filled with water in front of the patient's mouth and the command "there is a spoon with water; open your mouth") was significantly higher than for the other four stimuli; for high-level behavioral interactions, the initiation of swallowing was more sensitive than the stimuli included in CRS-R. More importantly, the patients who showed a positive response to the fifth stimulus had a higher recovery rate (MCS− to MCS+, UWS to MCS−, as assessed by the standardized CRS-R) (83.3%) at the 6-month follow up. These outcomes support our hypothesis that informative and familiar stimuli may better elicit the response of DOC patients and lead to patients' initiation of swallowing. In addition, the initiation of swallowing can be an early indication of conscious behavior and can probably offer evidence for conscious awareness.

The initiation of swallowing, which can indicate the presence of high-level behavioral interactions in DOC patients, appears earlier than either visual or motor movement, which can indicate the high-level behavioral interactions that are recommended in the CRS-R (e.g., a movement in response to a command, non-functioning communication, or intelligible verbalization). In this experiment, no patients showed either movement to a command, non-functioning communication, or intelligible verbalization, but five MCS− and one UWS initiated swallowing, which indicates a high level of awareness in DOC patients (20). A previous study has shown that the first human reflex is the suckling-swallowing reflex in infants (24). Bremare et al. determined that 7 of 11 (63.6 %) severely brain-damaged patients regained oral feeding abilities after an acquired brain injury (18), and Hansen et al. showed that 64% of DOC patients recovered to unrestricted dieting within 126 days (19). Additionally, some functional neuroimaging studies have indicated that the left hemisphere has greater activation in certain sensory and motor-related swallowing regions in patients with cerebral vascular accidents (20, 21), a study have showed a correlation between the improvement of the swallowing function (i.e., eating solid food safely) and brain neuroplastic changes for the patient with brain injury (25), and some studies have suggested that the management of swallowing disorders, whether they are of either short or long duration, for these patients is important (26–29). Our findings were supported by these studies to some extent, which indicated oral movement may recover more quickly than other functions after brain injury because of neuroplasticity and other reasons and emphasized the importance of oral movement in the process of behavioral assessment and the relationship between the initiation of swallowing and the prognosis of DOC patients. In this way, the initiation of swallowing maybe more appropriate than the stimuli included in CRS-R to trigger

TABLE 3 | Different responses to different stimuli and the assessment at the 6-month follow-up evaluation.

Patient	Movement to command (positive response frequency/4 times)					Diagnosis of CRS-R	Diagnosis of CRS-R after 6 months
	Only a command	Only a spoon	A spoon Filled with water	A spoon and a command	A spoon filled with water and a command		
MCS-1	0/4	0/4	0/4	0/4	3/4	MCS−	MCS+
MCS-2	0/4	0/4	0/4	0/4	4/4	MCS−	MCS−
MCS-3	0/4	0/4	0/4	0/4	3/4	MCS−	MCS+
MCS-4	0/4	0/4	0/4	0/4	0/4	MCS−	MCS−
MCS-5	0/4	0/4	0/4	0/4	0/4	MCS−	MCS−
MCS-6	0/4	0/4	0/4	0/4	0/4	MCS−	MCS−
MCS-7	0/4	0/4	0/4	0/4	2/4	MCS−	MCS+
MCS-8	0/4	0/4	0/4	0/4	4/4	MCS−	MCS+
MCS-9	0/4	0/4	0/4	0/4	0/4	MCS−	MCS+
MCS-10	0/4	0/4	0/4	0/4	0/4	MCS−	MCS−
MCS-11	0/4	0/4	0/4	0/4	0/4	MCS−	MCS−
UWS1	0/4	0/4	0/4	0/4	0/4	UWS	UWS
UWS2	0/4	0/4	0/4	0/4	1/4	UWS	MCS−
UWS3	0/4	0/4	0/4	0/4	0/4	UWS	UWS
UWS4	0/4	0/4	0/4	0/4	0/4	UWS	UWS
UWS5	0/4	0/4	0/4	0/4	0/4	UWS	UWS
UWS6	0/4	0/4	0/4	0/4	0/4	UWS	UWS
UWS7	0/4	0/4	0/4	0/4	0/4	UWS	UWS
UWS8	0/4	0/4	0/4	0/4	0/4	UWS	UWS

The first stimulus: only a command (as recommended by the CRS-R); the second stimulus: only a spoon without a command; the third stimulus: a spoon and a command ("There is a spoon; open your mouth"); the fourth stimulus: place a spoon filled with water in front of the patient's mouth without a command; the fifth stimulus: a spoon filled with water in front of the patient's mouth and a command ("There is a spoon with water; open your mouth"). MCS, minimally conscious state; UWS, unresponsive wakefulness syndrome; CRS-R, coma recovery scale-revised.

high-level behavioral interactions in DOC patients in early stages after injury.

A literature review revealed that our findings seemed to be supported by several studies, which suggested that familiar stimuli have been frequently used to capture a patient's attention. Sharon et al.'s study proved that familiar faces succeed in eliciting activations in brain areas, with further limbic and cortical activations in VS patients (30). Di et al.'s study showed that having family members use a patient's name elicits more responses than a neutral voice does (22, 31, 32). Notably, previous studies have suggested that brain lesions may even lead to receptive aphasia (33), the incidence of which has ranged from 15 to 30% (34, 35). In other words, there are probably some aphasic patients in the present study. However, high frequency and the use of familiar words are easier for these aphasic patients to understand (e.g., "Close your eyes"; "Open your mouth") (33). Therefore, a gestural or graphical presentation was suggested after a failed verbal item during the assessment process (36). That is, life-familiar stimuli (i.e., feeding water to patients like a newborn baby) might improve the incidence of the initiation of swallowing. In this study, we chose an object from everyday life (i.e., spoon) and gave the specific characteristics of this object (water in the spoon). The fifth stimulus consisted of a verbal request and a gestural presentation; therefore, this stimulus may be better for patients who have a co-occurring language disorder in consciousness and is more suitable for detecting those underlying aphasic patients. From the reaction results, this stimulus improved the incidence of the initiation of swallowing.

In our results, those six DOC patients who initiated swallowing toward the fifth stimulus were five MCS− and one UWS; in other words, the initiation of swallowing can be more easily elicited in MCS− than that in UWS. This result is in line with some literature showing a low level of arousal to be a negative predictor of oral refeeding and the recovery of swallowing function related to the severity of the brain injury. Hansen et al.'s study showed that 64% of DOC patients recovered to unrestricted dieting within 126 days, and the chance of returning to a total oral diet depended on the severity of the brain injury (19). Terre et al.'s study reported the greater the severity of the TBI according to the outcome scales was, the worse the recovery of swallowing function will be. It also noted that improved deglutition function paralleled improved neurological function and, therefore, dysphagia appears to be a manifestation of greater neurological and functional deficits (37). Moreover, Calabrò et al.'s study proved that dysphagia rehabilitation improved cognitive levels in patients with major neurocognitive sequelae following severe brain injury (25). Linda et al.'s study proved that, as certain cognitive levels improved, patients with severe brain injury were able to achieve greater oral intake (38). Therefore, we have reason to doubt that the

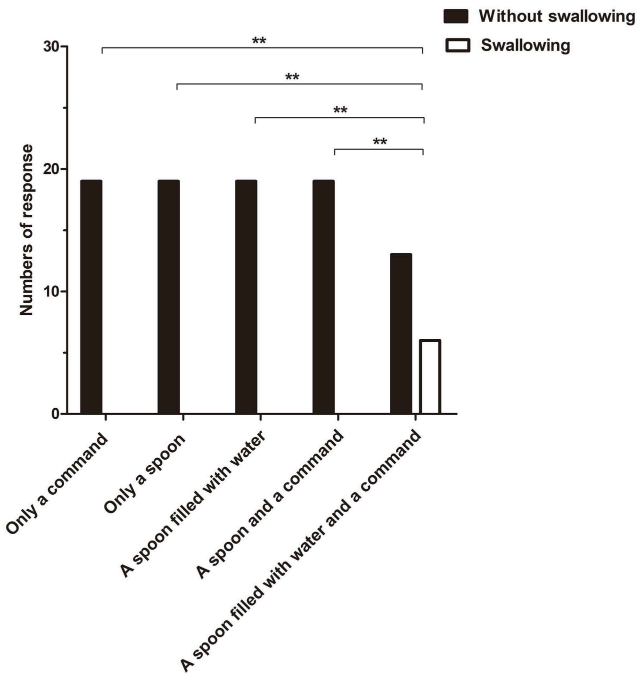

FIGURE 2 | The incidence of the initiation of swallowing to different stimuli differed significantly between the fifth stimulus and the other four stimuli ($Q = 24$, $^{**}p < 0.01$).

TABLE 4 | Prognostic value of initiation of swallowing in DOC patients.

Initiation of swallowing	Initiation of swallowing	No initiation of swallowing	Total
Improved at 6 m	5	1	6
No improvement at 6 m	1	12	13
Total	6	13	19

This study showed the predictive value (sensitivity = 83.33%, specificity = 92.31%) of the initiation of swallowing in DOC patients; five of six (83.3%, [95%CIs (36%, 100%)]) DOC patients who initiated swallowing recovered to either MCS− or MCS+, whereas 12 (92.31%, [95%CIs (36%, 100%)]) of 13 DOC patients with no initiation of swallowing had a poor outcome (remaining in UWS/MCS−). The outcome of whether the consciousness state, as assessed by the CRS-R of 19 patients, had changed (i.e., MCS− turned into MCS+ and UWS turned into MCS−) differed, depending on the initiation of swallowing, which was analyzed by a McNemar's test ($\chi^2 = 7.65$, $P = 0.006$, Fisher's exact testing). DOC, disorders of consciousness.

patients who respond to the fifth stimulus may be misdiagnosed as MCS−, and their correct diagnosis may be MCS+. The cause of this phenomenon might result from the fact that the stimuli recommended by the CRS-R are not so sensitive that patients cannot make a response. Based on these reasons and with improved neurological functions, DOC patients with a positive response to our experiment had a good prognosis after 6 months.

Previous studies have revealed that patients whose etiology was traumatic showed a significantly higher recovery rate than patients whose etiology was non-traumatic (39). In our study, of five patients who had a good outcome, two were traumatic and three were non-traumatic, and the occurrence of the initiation of swallowing had no significant relationship with etiology. On this point, our conclusion seems inconsistent with the previous literature. However, functional magnetic resonance imaging (fMRI) studies have identified anatomic regions that are active during swallowing, including the primary sensory and motor cortex, supplementary motor area, cingulate cortex, insula, operculum, prefrontal and inferior frontal cortex, basal ganglia, thalamus, and cerebellum (21). The use of fMRI has confirmed that neuroplasticity is the mechanism by which the damaged brain relearns "lost behavior" in response to rehabilitation (40). The reason for this phenomenon may be that swallowing is related to many regions of the brain; if some parts are damaged, other parts could compensate to some extent. Therefore, the occurrence of the initiation of swallowing had no significant relationship with etiology, and, perhaps because of this reason, the recovery of swallowing occurs sooner than other physical functions do.

STUDY LIMITATIONS

For the two MCS− patients, the diagnosis was maintained as MCS−, which may be related to the fluctuations of consciousness level that have been mentioned in the literature (7). Although the findings are intriguing, there are several limitations in this study. The sample included only 19 patients, and the follow-up duration was only 6 months. Further investigation with a larger sample needs to be done to validate our findings.

CONCLUSIONS

In conclusion, this study emphasizes that the initiation of swallowing can be an early indication of conscious behavior and can probably provide evidence of conscious awareness in DOC patients. Meanwhile, this study showed that using familiar things is more effective than general stimuli in capturing DOC patients' attention (30, 41).

DATA AVAILABILITY STATEMENT

All datasets generated for this study are included in the manuscript.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Ethics Committee of Hangzhou Normal University. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

JNW, LX, JT, JL, DF, WH, XH, and YS substantially contributed to acquisition of data. JNW, JW, and WH substantially contributed to analysis of data. JNW, HD, SL, and JW substantially contributed to interpretation of data. MH, SL, and HD substantially contributed to study supervision.

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CLINICAL TRIAL
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Activity Performance, Participation, and Quality of Life Among Adults in the Chronic Stage After Acquired Brain Injury—The Feasibility of an Occupation-Based Telerehabilitation Intervention

Aviva Beit Yosef[1]*, *Jeremy M. Jacobs*[2], *Shira Shenkar*[3], *Jeffrey Shames*[4], *Isabella Schwartz*[5], *Yehudit Doryon*[6], *Yuval Naveh*[7], *Fatena Khalailh*[8], *Shani Berrous*[3] and *Yafit Gilboa*[1]

[1] School of Occupational Therapy, Faculty of Medicine, The Hebrew University of Jerusalem, Jerusalem, Israel, [2] Faculty of Medicine, Department of Geriatrics and Geriatric Rehabilitation, Hadassah Medical Center, Hebrew University of Jerusalem, Jerusalem, Israel, [3] Occupational Therapy Department, Maccabi Health Services, Jerusalem, Israel, [4] Medical and Health Professions Division, Maccabi Health Services, Tel Aviv-Yafo, Israel, [5] Faculty of Medicine, Physical Medicine and Rehabilitation Department, Hadassah Medical Center, Hebrew University of Jerusalem, Jerusalem, Israel, [6] Occupational Therapy Department, Medical and Health Professions Division, Maccabi Health Services, Tel Aviv-Yafo, Israel, [7] Maccabi Health Care Services Group, Occupational Therapy Department, Bayit Balev Hospital, Bat Yam, Israel, [8] Occupational Therapy Department, Hadassah Medical Center, Jerusalem, Israel

Edited by:
Lisa Tabor Connor,
Washington University in St. Louis,
United States

Reviewed by:
Candice Osborne,
UT Southwestern Medical Center,
United States
Rachel M. Proffitt,
University of Missouri, United States

***Correspondence:**
Aviva Beit Yosef
aviva.kahan@mail.huji.ac.il

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Objective: Acquired brain injury (ABI) is a leading cause of long-term disability. This calls for effective and accessible interventions to support participation in the community over time. One promising avenue to answer this need is telerehabilitation. Prior to conducting a larger trial, the main objective of this pilot study is to explore the feasibility, acceptability, and preliminary efficacy of a metacognitive occupation-based intervention in a telerehabilitation format with adults and older adults in the chronic phase after ABI.

Methods: Five community dwelling participants (ages 65–72), 6–10 months post-ABI, with scores 2–4 on the modified Rankin scale and without dementia, completed the teleintervention. The intervention included ∼10 weekly videoconferencing sessions administered by an occupational therapist using the Cognitive Orientation to Daily Occupational Performance approach. Each participant defined five functional goals and three were trained and two were not trained during the intervention. Evaluations were conducted at pre, post, and 3-month follow-up. The primary outcome measures included activity performance (The Canadian Occupational Performance Measure; COPM), participation (the Mayo-Portland Adaptability Inventory-4 Participation Index; MPAI-4-P), and quality of life (QoL) (stroke impact scale; SIS). Other measures included a feedback interview, satisfaction questionnaire, field notes, and a treatment fidelity checklist.

Results: The teleintervention was found to be feasible and the participants expressed a high degree of satisfaction with the intervention and the technology use. A Wilcoxon Signed-Ranks test indicated statistically significant improvements post intervention in COPM performance ($z = -2.023$, $p = 0.043$)

and satisfaction ($z = -2.023$, $p = 0.043$) ratings. Additionally, clinically significant improvements (≥2 points) in both performance and satisfaction with performance were found for each participant in at least three of their five defined functional goals. Trends toward significant improvement were found in MPAI-4-P ratings post intervention ($z = -1.826$, $p = 0.068$). Furthermore, clinically significant improvements (≥15 points) post intervention were found for each participant in some subscales of the SIS. Results were partially maintained at 3-month follow-up.

Conclusions: This pilot study demonstrated the feasibility of a metacognitive occupation-based telerehabilitation intervention and its potential benefits in activity performance, participation, and QoL for older adults coping with long-term disability following ABI.

Clinical Trial Registration: www.ClinicalTrials.gov, identifier: NCT03048708.

Keywords: chronic acquired brain injury, activity performance, participation, neurorehabilitation, telerehabilitation, cognitive orientation to daily occupational performance approach, metacognitive approach, occupational therapy

INTRODUCTION

Acquired brain injury (ABI) is a major health issue and a leading cause of disability worldwide (1, 2). ABI is defined as brain injury that occurs after birth, and the most common types of ABI are traumatic brain injury (TBI) and stroke (3). ABI can cause a variety of impairments depending on the affected brain area and the severity of the damage. It may manifest in sensory, motor, cognitive, behavioral, and emotional impairments (4–6) and lead to long-term functional limitations and participation restrictions in daily life (3, 7–11).

There is evidence that home and community-based rehabilitation after ABI is effective in reducing disability (12–14), and that longer-term rehabilitation programs lead to improved global outcomes such as social participation and quality of life (QoL) (15). In addition, there is evidence supporting the use of occupation-based interventions to improve daily activity performance (16). However, most studies currently continue to emphasize measurement and intervention in terms of motor function and mobility. Therefore, further research focusing on achieving meaningful participation and improving QoL, extending beyond impairment remediation approaches, is still needed (10, 17).

Furthermore, most rehabilitation resources are invested in the first weeks and months following the ABI, at the sub-acute stage, while less emphasis is placed on long-term interventions (3, 6, 18). There is a lack of sufficient rehabilitation services in the community offering continued support in the chronic stage (6, 12, 19–21). This might be explained by low accessibility and availability as well as numerous barriers to community-based rehabilitation services, while high costs and reimbursement issues limit the possibility of receiving in-home rehabilitation services (20, 22–24). Many ABI survivors therefore continue to live in the community with limited participation in meaningful daily activities (8, 25–27). Accordingly, there is a growing understanding that ABI is a chronic health condition that requires long-term attention, and necessitates the improved continuity of both short and long-term rehabilitation services in the months and years following brain injury (11, 18, 28–32).

This need for developing cost-effective and accessible intervention models for people in the chronic phase following ABI in order to facilitate participation and community reintegration (6, 29) can be addressed by telerehabilitation. Telerehabilitation is defined as the use of information and communication technologies to provide remote rehabilitation services to people in their homes or other environments (33). Telerehabilitation has a wide range of delivery modes from texting or talking on mobile phones to video conferencing and to more complex systems like virtual reality video games. One strong advantage of telerehabilitation is that it allows services to be delivered to people in their homes without the therapist being physically present with them. This can clearly improve accessibility and cost effectiveness. However, there may also be challenges such as difficulties using the technologies, privacy issues, and the attitudes of patients and clinicians (23, 34–36).

Supporting evidence can be found in the literature for telerehabilitation interventions with adults after ABI in terms of feasibility and patient satisfaction (37–40). A recently published systematic review that evaluated the efficacy of telerehabilitation interventions among stroke survivors concluded that it may have equal or even better outcomes than face-to-face interventions in motor function, cognitive function, and emotional state (41). However, other systematic reviews and meta-analyses concluded that the evidence available is inconclusive and insufficient (22, 42–44). It should be noted that most studies that examined the efficacy of telerehabilitation programs included interventions that focused on body functions on the impairment level such as balance, upper-extremity function, and cognitive and language skills (37, 38, 41, 45–51).

To the best of our knowledge, there have not been many studies that have examined telerehabilitation interventions for individuals in the chronic phase after ABI that focused directly on the activity and participation level. Chumbler et al. (52) evaluated a telerehabilitation program that focused on improving functional mobility among 52 veterans post-stroke. Results indicated that the intervention significantly improved physical function. However, the focus of the intervention was limited to functional mobility, and it did not address broader domains of daily function. Another trial (53) evaluated the efficacy of a telephone-delivered problem-solving treatment. The results suggested this intervention offers the promise of reducing psychological distress after combat-related mild TBI. The sample in this study included 356 young soldiers (mean age 29.35) who had been exposed to stressful combat situations, thus not allowing the generalization of the results to a broader ABI population. A third randomized controlled study ($N = 38$) evaluated the effects of an errorless learning training approach in comparison with a didactic strategy instruction approach, both delivered over the telephone, on the reported everyday memory problems of adults with chronic TBI. Results demonstrated that both of these treatment approaches improved reported everyday memory functioning (54). This study was limited to memory-related goals with a focus on a specific technique of errorless learning. Other studies included a feasibility study (55), case-study (56), and pilot studies (24, 57, 58).

Ng et al. (24) used the Cognitive Orientation to Daily Occupational Performance (CO-OP) approach via video sessions in their study with three adults after TBI (ages 34–55). The results demonstrated a high level of satisfaction among the participants, an improvement in their level of performance and satisfaction in functional goals, and a trend toward greater community participation. Despite the preliminary nature of this evidence (24), it sparked our interest due to the occupation-based, client-centered intervention approach that was used. The CO-OP approach is a metacognitive approach that focuses on strategy training and problem solving to improve the performance of daily activities, as opposed to training directed at improving the underlying impaired body functions. Essential elements of this approach are client-chosen functional goals, dynamic performance analysis, use of global and domain-specific strategies, and a process of guided discovery with enabling principles. The approach uses a global problem-solving strategy, “Goal-Plan-Do-Check,” that outlines four steps toward achieving goals: setting a specific functional goal, creating a plan that includes steps to achieve the personal goal, executing that plan, and checking if the plan was executed and if it worked (59). The CO-OP was adapted for use in different populations including adults with ABI (60). Several studies have demonstrated the efficacy of using the CO-OP approach to promote functional goals for individuals during the chronic phase after ABI (60–65).

To summarize, there is a need for an improvement in the continuum of rehabilitation services provided to ABI survivors that will enable meaningful participation and community reintegration (6, 10, 17, 29). The CO-OP approach is an appropriate treatment option to meet this need, consistent with existing recommendations for practice guidelines in the chronic phase after ABI (12, 16, 30). The use of the CO-OP approach through remote rehabilitation enables the application of the intervention in an accessible manner in the home environment, with potential for long-term, cost-effective treatment (66). Although this has been shown in a small pilot study to be both feasible and potentially effective (24), it should be noted that the evidence is preliminary and limited to younger adults with a diagnosis of TBI. It is likely that a more comprehensive and definitive understanding of this innovative treatment modality would be gained by undertaking a sufficiently powered randomized controlled study. Therefore, prior to conducting a larger trial, the main objective of this pilot study is to explore the feasibility, acceptability, and preliminary efficacy of the CO-OP approach in a telerehabilitation format with adults and older adults in the chronic phase after various types of ABI. We had three specific research questions: (1) Is the intervention feasible in terms of recruitment, retention and intervention adherence, fidelity of treatment, and technology delivery? (2) Will the intervention be acceptable to the participants and their significant others? and (3) What is the effect of the intervention program in improving activity performance, participation, and QoL?

MATERIALS AND METHODS

Design

This study was a quasi-experimental pilot study. The study protocol was approved by the research ethics committees of Hadassah-Hebrew University Medical Center, Jerusalem, and Maccabi Healthcare Services, Bat-Yam, Israel (ethical committee registration numbers: 0689-15-HMO and 192016, respectively).

Participants

Community-dwelling adults with ABI were recruited between February 2017 and April 2018 from a day-rehabilitation hospital unit and from 2 day-rehabilitation clinics in and around Jerusalem and Bat-Yam, Israel. There were several inclusion criteria: (1) at least 6 months post-ABI, reflecting the chronic rehabilitation phase, (2) aged 18 years and over, (3) sufficient proficiency in Hebrew or English to undertake the study, (4) slight to moderately severe disability in daily function, based on the modified Rankin scale (mRS) scores of 2–4 (67, 68), (5) ability to identify at least 3 day-to-day functional difficulties that they experienced on which to base treatment goals, (6) internet access in their home, and (7) having a significant other who knows the participant well, is at least 18 years old, and who expressed a willingness to be involved in the study. The presence of the significant other in the sessions was not an eligibility criterion. There were some exclusion criteria: (1) dementia diagnosis or Mini Mental Status Examination (MMSE) < 24 (69) or Montreal Cognitive assessment (MoCa) < 19 (70), (2) moderate or severe aphasia, and (3) an acute or chronic illness that has a significant impact on the ability to cooperate in the study.

Procedure

After obtaining the approval of the research ethics committees, potentially eligible participants were identified by occupational therapists (OTs) who worked in the rehabilitation departments. Patients who were interested in participating were referred to the research coordinator (Author ABY) who contacted them and further screened for eligibility. The participants and significant others were informed about the study process as well as the technology requirements. Eligible patients who agreed to participate gave written informed consent in accordance with the latest declaration of Helsinki. The study period lasted ∼6 months for each participant and started after the completion of the occupational therapy treatment in the day-rehabilitation clinics. The study procedure included different steps: (1) baseline assessment, (2) 3-month intervention period, (3) post intervention assessment, and (4) 3-month follow-up assessment.

The baseline assessment was performed in two sessions (∼2 h overall). These sessions were conducted by the same OT that provided the intervention and were done face-to-face in the participant's home in order to establish a therapeutic relationship as the basis for the remote intervention sessions that followed. In addition, the baseline assessment meeting ended with training in the use of the technological equipment. The post intervention assessment and 3-month follow-up assessment were also conducted face-to-face at the participants' homes, with the exception of participant 1 who did these assessments via a phone call. Assessments and intervention sessions were performed by licensed OTs (authors ABY and SS) with more than 5 years of experience in geriatric and neurological rehabilitation. Both OTs are certified in the CO-OP approach after attending the standard CO-OP workshop, and they trained together in the administration of the measures. For each participant, the OT who carried out the baseline assessment was the same one who performed the intervention program. The post intervention and follow-up assessments were conducted by the other OT in order to prevent bias.

Intervention

The intervention program included up to 15 remotely delivered CO-OP sessions, 1–2 times a week (∼45 min per session), and they were spread out over a 3-month period. The intervention was administered in a telerehabilitation format via video conferencing using Skype^{TM} software. Skype^{TM} is free, available and easy to use, and security for the users is insured by encryption of this software program (71). The video sessions occurred while the participant was at home, in a location they preferred, and the OT was alone in her office to ensure privacy. At the beginning of the process the OT explained that the significant other's involvement was important for two aspects of the process. The first aspect was supporting the therapeutic process in line with the CO-OP principles (59). This was especially significant in both facilitating the execution of plans during the week between the sessions and the generalization and transfer of strategies and skills to the participants' daily routines. In some cases, the significant other was part of a plan the participant formulated for achieving a goal (e.g., my wife will drive me to the community center). The second aspect was supporting the logistics of the intervention. Since the therapist is not physically present in the room, the presence of another person is necessary for safety reasons in cases of actual performance of specific activities during the sessions (e.g., cutting vegetables in the kitchen). In addition, in some cases, the significant other assisted with the use of the telerehabilitation technology. The video sessions were recorded using TalkHelper Call Recorder for Skype software and were stored in a local secured hard drive. In addition, after each session, the OT documented key points in field notes. Participants who did not have a computer or tablet at home were provided with iPads.

The first phase of CO-OP intervention is defining client-chosen functional goals (59). In this study, each participant identified five functional goals during the baseline assessment using the Canadian Occupational Performance Measure (COPM), of which three were the focus of the intervention (trained goals). The other two goals were not addressed directly during the intervention sessions (untrained goals), to allow assessment of generalization and transfer of learning. At the first intervention session, the OT and participant reviewed and re-discussed the goals, and the OT taught the participant the global problem-solving strategy (Goal-Plan-Do-Check). In the proceeding sessions the OT guided the participant in the use of this strategy to help them discover their performance problems as well as potential task-specific strategies to improve their performance and enable goal attainment. Rather than providing the participant with the solutions, the OT facilitated this process with questions and feedback. The CO-OP is a performance-based approach. Therefore, the participants actually performed some of the activities during sessions if it was possible, and the OT observed that actual performance in the participant's natural environment via video conferencing. In some cases, it wasn't possible to perform the activity online, either because it was done in other settings (e.g., a community center), due to privacy issues (e.g., dressing), or for safety reasons (e.g., peeling vegetables while the significant other was not present). In these cases, the sessions included discussing the performance, the plans, and strategies. Each participant received a folder with materials to support the intervention. To ensure adherence to the CO-OP protocol, meetings were held regularly between ABY, SS, and YG to review and discuss the intervention sessions.

Outcome Measures

Socio-Demographic and Clinical Characteristics

Participants' socio-demographic characteristics were documented and included information such as age, years of education, and the identity of the significant other. Clinical information included the type and side of the ABI, time since the ABI, cognitive screening test scores, and functional status. The information was collected through a review of the medical records and through a conversation with the participants at the baseline assessment. Reports regarding other outpatient treatments were documented at post intervention and follow-up assessments.

Feasibility

Therapists' field notes and recordings from the intervention sessions were used to assess feasibility aspects. Information regarding eligibility, recruitment, and retention rates was documented. In addition, intervention adherence was described by the number of participants who completed the intervention program (with a minimum of eight sessions), the number of sessions completed, and the duration of each intervention session. To assess fidelity of treatment, video-recordings and field notes from three sessions for each participant were reviewed and scored using the CO-OP fidelity checklist (72, 73). In addition, the quality of the online communication as well as specific technical problems that arose (e.g., video and audio disruptions, the need of assistance to operate the software and equipment, and problems with the internet connection) were also documented.

Acceptability

Acceptability of the intervention was assessed at post intervention by a satisfaction questionnaire completed by the participants and a short semi-structured feedback interview with the participants and their significant others. The questionnaire was developed for this study and included 13 statements (detailed in **Supplementary Figure 1**) that were rated on a 5-point scale (from 1, being very low, to 5, being very high). The questionnaire assessed satisfaction with the intervention in general and other aspects such as the remote delivery, the technology use, and the therapeutic relationship. The short semi-structured feedback interview included two main questions: (1) What are the main benefits you experienced while participating in the program? and (2) What are the main challenges you experienced while participating in the program? Follow-up questions were added to encourage elaboration on these topics. The interviews were audio-recorded and later transcribed.

Preliminary Efficacy

Primary outcome —activity performance in participant-chosen goals

Activity performance was measured with the Hebrew version of the Canadian Occupational Performance Measure (COPM) (74). The COPM measures the client's perceptions of their performance of daily activities over time and facilitates client-centered goal setting as the basis of the intervention process. It is a semi-structured interview that helps the client identify occupational performance problems and then prioritize them using an importance rating scale (1: not important at all, 10: extremely important). The client then rates the five most important goals on 10-point rating scales of performance and satisfaction (1: not able to do it/not satisfied at all, 10: able to do it extremely well/extremely satisfied). Changes in the client's perception of their performance and satisfaction of two points or more is considered a clinically significant change. The COPM has demonstrated good validity, test–retest reliability, and sensitivity to change in many studies, and it is widely used as an outcome measure with various populations including adults after ABI (74–78). In this study, the COPM was administered as part of the baseline assessment and served as the basis for setting five goals. Three of these goals were directly addressed in the intervention process, and the other two goals were not.

Secondary outcomes—participation and quality of life

Participation was measured with the Mayo-Portland Adaptability Inventory-Participation index (MPAI-4-P) (79), using the Hebrew version (80). The MPAI-4 is a questionnaire widely used among rehabilitation professionals to evaluate the recovery progress among people after ABI (81). The MPAI-4 includes 29 items divided into three indexes: (a) Ability (e.g., motor, sensory and cognitive abilities), (b) Adaptation (e.g., emotional state and social interactions), and (c) Participation (e.g., leisure activities, work, and use of transportation). In this study, we used the participation index (includes eight items), which was completed by the participants. The items are ranked on a scale of 0–4, with a higher score indicating more participation difficulties and limitations. Item scores are calculated and converted to a standardized T-score that represents different levels of participation limitation: scores below 30 denote relatively good participation; 30–40 denote mild participation limitations; 40–50 denote mild to moderate participation limitations; 50–60 denote moderate to severe participation limitations; and scores above 60 denote severe participation limitations. The MPAI-4 has well-documented psychometric properties. Previous studies have described good internal consistency, construct and concurrent validity, as well as predictive validity (15, 81–83). In addition, the MPAI-4 was found to be sensitive to clinical change following rehabilitation (84, 85).

Quality of life was measured with the Stroke Impact Scale (SIS) (86) using the Hebrew version (87). The SIS is a questionnaire for evaluating the self-perceived effect of stroke on a wide range of domains and is commonly used as a measure of QoL. The questionnaire includes 59 items divided into eight subscales: limb strength on the affected side, memory and thinking, mood, communication, daily activities, mobility, hand function, and participation. The patient rates each item on a scale of 1–5, with a low score indicating more difficulty or limitations. In addition, there is another subscale with one item measuring general recovery on a scale of 0 (no recovery) to 100 (full recovery). The SIS does not have a total score, but rather a score for each subscale. Raw scores are converted to standard scores (between 0 to 100). A change of 15 points or more is considered a clinically significant change (88, 89). The SIS is widely used in research and is reliable, valid, and sensitive to changes (86, 88, 90–92). It had been used previously with individuals after stroke and TBI (93).

Statistical Analysis

Statistical analyses were conducted using SPSS version 24.0 (IBM Corp., Chicago, IL, USA). Due to the small sample size, the results are presented for each participant separately as well as for the group, and both statistically and clinically significant changes are noted. Descriptive statistics were used to describe the participants' characteristics and the feasibility aspects of the study. Acceptability of treatment was analyzed with a combination of descriptive statistics and qualitative analysis of the feedback interviews with the participants and their significant others.

To analyze the preliminary efficacy of the intervention, we calculated the median and interquartile range (IQR) scores of the outcome measures at baseline, post intervention, and 3-month follow-up. Since the sample was small, non-parametric Wilcoxon signed-rank tests were used to detect statistically significant changes from baseline to post intervention and from baseline to follow-up with the p-value set at <0.05. In addition, an effect size (r) was calculated from the z-value of Wilcoxon signed-rank test

($r = z/\sqrt{n}$) (94) and can be interpreted as a small ($r \leq 0.10$), medium ($r = 0.30$), and large ($r \geq 0.50$) effect size (95).We did not make adjustments for multiple testing because in a pilot study there is more of a concern for a type II error than a type I error (65, 96).

RESULTS

Socio-demographic and clinical characteristics of the participants are presented in **Table 1**. The sample included older adults (age range 65–72 years), 6–10 months post-ABI, with stroke being the most common type of injury (80%). MRS scores ranged between 2 (slight disability) and 4 (moderately severe disability). The participants had 2–15 years of education, and they did not have dementia. Three participants had prior experience using a computer and/or tablet, and the other two participants did not. Three of the participants were first-time Skype$^{\text{TM}}$ users. We supplied an iPad for the intervention period for two participants who did not own a computer or a tablet. None of the participants received additional occupational therapy during the intervention period.

TABLE 1 | Socio-demographic and clinical characteristics of the participants (N = 5).

Characteristics	*N* (%)	Mdn (IQR)
Age		67 (65.5–69.5)
Sex		
Female	3 (60%)	
Male	2 (40%)	
Education (years)		11 (5.0–14.5)
Significant other		
Spouse	3 (60%)	
Child	2 (40%)	
Living situation		
Alone	2 (40%)	
With spouse	3 (60%)	
Previous use experience		
Computer/tablet	3 (60%)	
Skype$^{\text{TM}}$	2 (40%)	
Type of ABI		
Hemorrhagic stroke	2 (40%)	
Ischemic stroke	2 (40%)	
Subdural hematoma	1 (20%)	
Side of ABI		
Right	1 (20%)	
Left	4 (80%)	
Time since ABI (months)		8 (6.5–9.0)
Cognitive status		
MMSE (n = 4)		26 (25.0–28.5)/30
MoCA (n = 1)		24/30
mRS scores		
Score 2	2 (40%)	
Score 3	1 (20%)	
Score 4	2 (40%)	

Mdn, Median; IQR, interquartile range; ABI, acquired brain injury; MMSE, Mini Mental State Examination, cutoff score in this study was 24 (69); MoCA, Montreal Cognitive Assessment, cutoff score in this study was 19 (70); mRS, the modified Rankin Scale (97, 98), the scale runs from 0 to 6, running from perfect health without symptoms to death—0: no symptoms; 1: no significant disability; 2: slight disability; 3: moderate disability; 4: moderately severe disability; 5: severe disability; 6: dead. In this study we included participants with scores of 2–4.

Feasibility

Recruitment, Retention, and Intervention Adherence

The flow diagram (see **Figure 1**) provides details regarding the process of enrolment, intervention, and assessments. During the recruitment period, 18 potentially eligible ABI patients were referred to the research director by clinical coordinators in the day-rehabilitation clinics and assessed for eligibility. Eight patients were excluded from the study; two declined to participate, five were found not eligible and one did not reply to the researcher's contact efforts (via phone calls and text messages). Among those referred, 55% (10/18) were eligible, agreed to participate, and started the study procedure. Two of the 10 consenting participants dropped out during baseline assessments. Five of the eight remaining participants completed the 3-month tele-intervention program and the post intervention assessments (62% retention rate). Those who discontinued the intervention withdrew from the study after one, three, and six sessions. The reasons for discontinuing the intervention are detailed in **Figure 1**. Participants who completed the CO-OP program received 8–14 intervention sessions (mean 10.6 ± 2.2 sessions). Four participants received the sessions over 3 months, while the fifth participant's intervention (participant 4) was extended to 8 months due to several hospitalizations unrelated to the study that led to breaks in the intervention program. Despite these breaks, the participant expressed high motivation to continue the program and good recovery after the hospitalizations. Therefore, he continued to participate in the intervention process. The average session length was 46.3 ± 12.4 minutes. Of the five participants who completed the intervention period, four participants completed the 3-month follow-up assessment. No adverse events related to the intervention were reported.

Fidelity of Treatment

In order to evaluate the treatment fidelity to the CO-OP approach, the CO-OP Fidelity Checklist was used (72, 73). This questionnaire was completed based on observing video recordings (that due to technical and ethical issues were available only for participants 3, 4, and 5) and reading the therapist's field notes of sessions three, six, and nine (in the case of participant four, who had eight treatment sessions, we used sessions three, five, and seven). Based on the fidelity checklist, it was demonstrated that all the CO-OP principles listed in the checklist were addressed for each participant across sessions, indicating high treatment fidelity.

Technology Delivery

Two of the participants had no prior experience using a computer or tablet, and three of the participants were first time Skype$^{\text{TM}}$ users. In general, we were able to successfully communicate with the participants using the technology to carry out the intervention sessions as planned. Nevertheless,

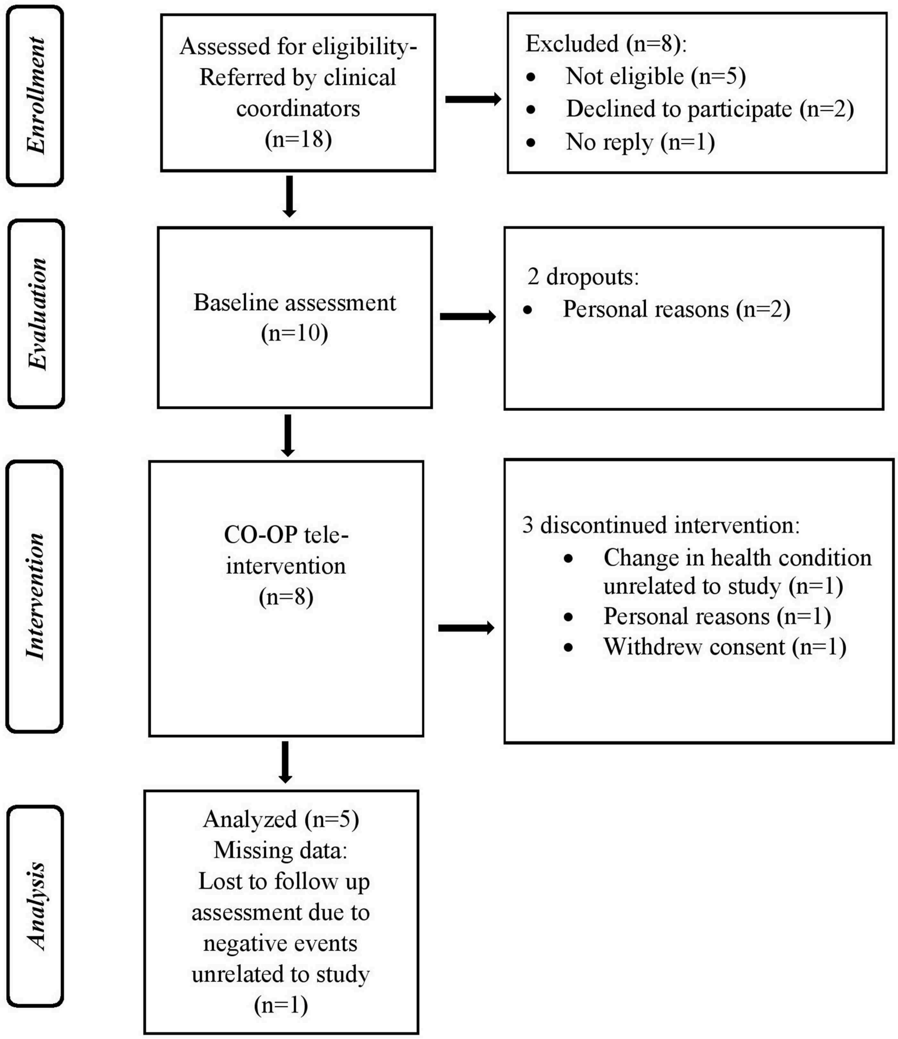

FIGURE 1 | Flow diagram of the study enrollment, evaluation, intervention, follow-up, and analysis.

there were various technical problems we dealt with during the study. Skype^{TM} and TalkHelper Call Recorder for Skype were not consistently reliable. The main issues were inadequate internet connection, and the difficulty some participants had of using the equipment and video conference software independently. Overall, of the total number of intervention sessions of all participants (53 sessions), there were video and/or audio disruptions in 14 sessions (26%), and only three sessions (6%) were either canceled or carried out via phone call due to severe technical issues. In order to solve the technical problems that arose during sessions, the OT provided technical support via telephone or was assisted by the participants' family members. Additionally, in two cases, the OT went to the participant's home and tried to solve the internet connection problem using Wi-fi amplifiers. Despite the technical issues described, all of the participants found the technological aspect of the intervention to be acceptable as described in the following acceptability section.

Acceptability

Acceptability of the intervention was based on a satisfaction questionnaire and short feedback interviews post intervention. Overall, the participants were satisfied with the intervention. All five participants (100%) expressed high to very high satisfaction with the intervention in general and the therapeutic relationship. They all expressed their desire to continue the treatment if possible and stated that they would recommend this treatment to others with a similar health condition. Four out of five participants (80%) expressed high to very high satisfaction with the treatment process, which included the number, length, and frequency of sessions. Regarding the remote aspect of the intervention implementation, three participants (60%) expressed high to very high satisfaction with the remote nature of the treatment, and 80% were highly or very highly satisfied with the Skype^{TM} software in terms of ease of use and quality of image and sound. Participant 2 expressed moderate satisfaction with the use of the software. It should be noted that despite the high satisfaction with the intervention, three of the five participants would have strongly preferred that the treatment be done face-to-face. Four participants (80%) expressed high to very high satisfaction with having a significant other involved in the treatment program and very high satisfaction with the level of involvement of their significant other. It should be noted, however, that one participant expressed very low satisfaction with having a significant other involved in the treatment program and medium satisfaction with the level of involvement of their significant other in the intervention process.

Some sample quotes from the feedback interviews illustrate the experience of participating in the intervention and give possible reasons for satisfaction with the intervention. When asked about the advantages of the intervention, one theme that was repeated was the functional improvements that followed the treatment. As participant 5 stated, “I [now] manage to put on clothes by myself… and it’s true that it takes me 15 minutes to get dressed, but I don’t get so frustrated.” Participants also reported an improvement in their sense of self-efficacy, as in this quote of participant 5, “[Now] I know that I can try it... [I know] that it’s possible to get to where I need to go, to do what I need to do.” Participants and their significant others also positively described the process of guided discovery in the intervention. As the wife of participant 3 said, “She [the OT] told him, is it right or not? And what could he do to help himself?” Similarly, participant 5 explained, “If you ask and say, what is the difficulty? What can you do? What can we do to make it better?—this is very good. If at first, I don’t succeed one way, I try another way, and maybe it will work.” When asked about the disadvantages of the intervention, participant 3 and the spouse of participant 5 mentioned that they would have liked to continue the intervention for a longer period of time. In addition, participant 1 reported that she felt that the required involvement of her significant other (her son) in the sessions was a burden to him.

When asked about their experience regarding the remote aspect of the intervention, Participant 3 stated, “[It] feels like face-to-face... in fact it is almost the same treatment [as face-to-face] because she saw me and I saw her.” Participant 5 said, “I think it would be nicer if it was face-to-face, but if you don’t have the person face-to-face - it [the treatment] felt like face-to-face.” Participants mentioned that the use of the video conferencing provided an opportunity for the OT to see them performing activities in their natural environment. Participant 5 stated, “She watched it [what I did]... so I knew there was someone there who saw what I needed.” Participant 2 was the only one who reported during the feedback interview that there were technical issues which interfered with the treatment. Regarding the remote therapeutic relationship, participants expressed that they felt the OT gave them support that strengthened them and encouraged them to take action. Participant 1 said, “It gave me strength to do things that I could have postponed a lot more and maybe even given up on.” Participant 3 explained, “There is someone that is watching and looking out for you and trying to help with things that you find difficult and don’t understand”.

Preliminary Efficacy

Primary Outcome—Activity Performance in Participant-Chosen Goals

At baseline assessment, each participant identified five goals related to their daily function (see **Table 2**) and rated the importance of each goal they identified on a 10-point scale. Participants’ chosen goals were in four main life domains according to the International Classification of Functioning, Disability and Health (ICF) activities and Participation component: (a) self-care, (b) domestic life, (c) major life areas, and (d) community, social, and civic life (99). Each Participant had goals in a few life domains with different variations. It should be noted that all participants chose at least one goal in the domain of community, social, and civic life.

During the intervention sessions, three of the five goals were trained directly using the CO-OP approach. The other two goals were not trained, thus enabling us to assess generalization and transfer of learning. One exception was participant 4, who worked directly on all five goals during the intervention sessions due to rapid progress with the first three goals. This participant was lost to follow-up due to an unstable medical condition unrelated to the study intervention. The goals are detailed in **Table 2**, and goals for which clinically meaningful improvements ($\geq$2 points) were achieved based on participants’ performance ratings on the COPM are indicated with an asterisk (*).

We found that clinically meaningful improvements in performance and satisfaction ratings were achieved at post intervention and at follow-up in both trained and untrained goals. Overall, each participant improved in three to five of their five identified goals in both performance (see **Figure 2**) and satisfaction with performance (see **Figure 3**). Examination of the total clinically meaningful improvements indicates three main findings. First, the performance and satisfaction improvements that were achieved at post intervention were partially maintained at follow-up. The improvements of participants 1, 2, and 5 were maintained. However, few of participant 3’s improvements were maintained. Second, satisfaction improvements were greater than performance improvements at both post intervention and at follow up and for both trained and untrained goals. Third, interestingly, a greater proportion of untrained goals than of trained goals showed improvements at both post intervention and at follow-up (see **Table 3**).

Wilcoxon Signed-Ranks test results (see **Table 4**) indicated statistically significant improvements from baseline to post intervention in COPM performance scale ratings on trained goals ($z = -2.032$, $p = 0.042$) and on all five goals (trained and untrained goals together, $z = -2.023$, $p = 0.043$). We found a near-significant improvement on the untrained goals ($z = -1.841$, $p = 0.066$). At follow-up, the COPM performance scores remained higher in comparison to baseline, and we found a near-significant improvement in trained goals and all goals (trained and untrained goals together, $z = -1.826$, $p = 0.068$ for both improvements). We found similar patterns for changes in satisfaction ratings at all time points. In addition, large effect sizes were demonstrated on changes in performance and satisfaction at post intervention and at follow-up.

TABLE 2 | Participants' selected goals, importance ratings, and classification according to the ICF.

		Goals	IR	Life domain-ICF
P1	Trained	1. Exercise 1–2 times a week	10*	d5: Self-care- d5701: Managing diet and fitness
		2. Manage doctor appointments	10*	d5: Self-care- d5702: Maintaining one's health
		3. Finish embroidery artwork on blanket	10	d9: Community, social, and civic life- d920: Recreation and leisure
	Untrained	4. Manage bank account on-line	10*	d8: Major life areas- Economic life (d860-d870)
		5. Participate in a social leisure class	10*	d9: Community, social, and civic life- d920: Recreation and leisure, d9205: Socializing
P2	Trained	1. Return to community center	10	d9: Community, social, and civic life- d9205: Socializing, d920: Recreation and leisure
		2. Start cooking again	10*	d6: Domestic life- d630: Preparing meals
		3. Dress independently	10	d5: Self-care- d540: Dressing
	Untrained	4. Shower independently	10*	d5: Self-care- d510: Washing oneself
		5. Make a ponytail independently	10*	d5: Self-care- d5202: Caring for hair
P3	Trained	1. Start going to a community center	10*	d9: Community, social, and civic life- d9205: Socializing, d920: Recreation and leisure
		2. Dress lower body independently	10*	d5: Self-care- d540: Dressing
		3. Dry body after a shower independently	10*	d5: Self-care- d510: Washing oneself
	Untrained	4. Be more involved in managing health care	10	d5: Self-care- d5702: Maintaining one's health
		5. Independence in grocery shopping	10*	d6: Domestic life- d620: Acquisition of goods and services
P4	Trained	1. Do minor repairs at home	10*	d6: Domestic life- d6501: Maintaining dwelling and furnishings
		2. Find volunteer work	6*	d8: Major life areas- d855: Non-remunerative employment
		3. Go to lectures	8*	d9: Community, social, and civic life- d920: Recreation and leisure
		4. Go out with spouse for fun	10*	d9: Community, social, and civic life- d920: Recreation and leisure
		5. Visit children and grandchildren	10*	d9: Community, social, and civic life- d9205: Socializing
P5	Trained	1. Peel and cut vegetables	9*	d6: Domestic life- d630: Preparing meals
		2. Dress independently	10*	d5: Self-care- d540: Dressing
		3. Play with grandchildren on the floor	10*	d9: Community, social, and civic life- d9200: Play, d9205 Socializing
	Untrained	4. Go out with friend once a month	6*	d9: Community, social, and civic life- d920: Recreation and leisure, d9205: Socializing
		5. Exercise 1–2 times a week	5*	d5: Self-care- d5701: Managing diet and fitness

P, participant; IR, importance rating, rated by participants on a 10-point scale (1: not at all important, 10: very important) (74); ICF, the International Classification of Functioning, Disability and Health (http://apps.who.int/classifications/icfbrowser/).

**Indicates goal improved to criterion (≥2 points) at post intervention and/or follow-up based on participants' COPM performance ratings (74).*

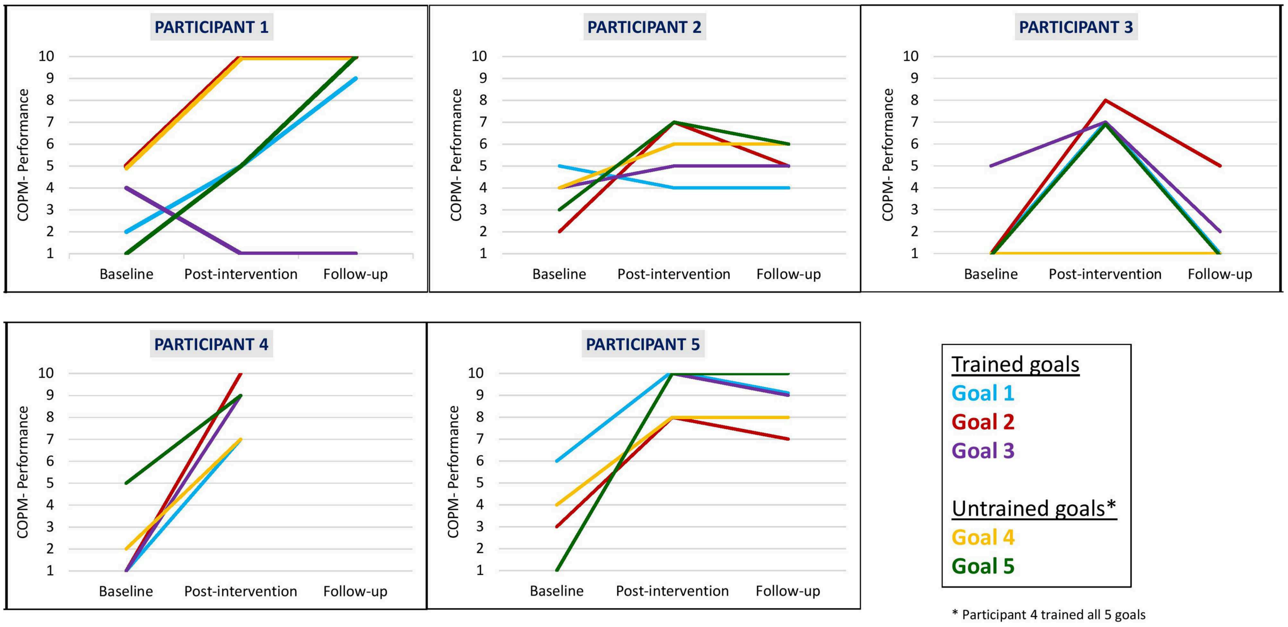

FIGURE 2 | Participants' COPM performance scale ratings at baseline, post intervention, and 3-month follow-up.

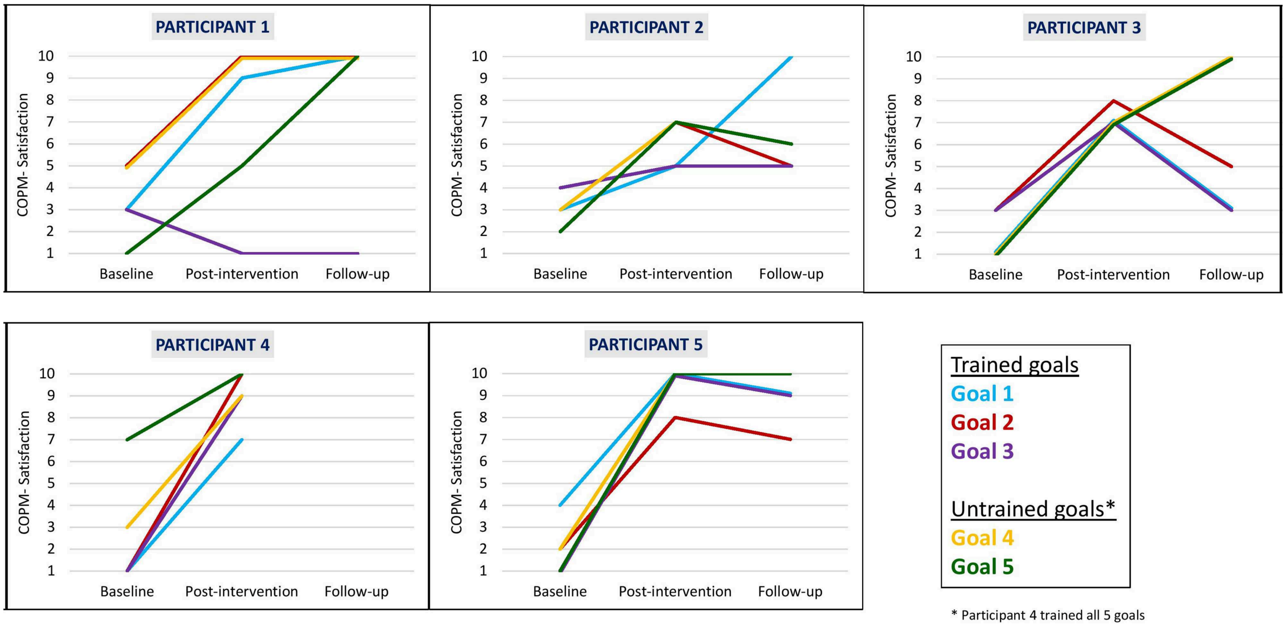

FIGURE 3 | Participants' COPM satisfaction with performance scale ratings at baseline, post intervention, and 3-month follow-up.

TABLE 3 | The number of goals that reached a clinically significant improvement (≥2 points) on the COPM performance and satisfaction scales.

		Trained goals		Untrained goals		All goals	
		Baseline-post	**Baseline-FU**	**Baseline-post**	**Baseline-FU**	**Baseline-post**	**Baseline-FU**
Performance ratings	P1	2/3	2/3	2/2	2/2	4/5	4/5
	P2	1/3	1/3	2/2	2/2	3/5	3/5
	P3	3/3	1/3	1/2	0/2	4/5	1/5
	P4	5/5	–	–	–	5/5	–
	P5	3/3	3/3	2/2	2/2	5/5	5/5
	Total	14/17 (82.4%)	7/12 (58.3%)	7/8 (87.5%)	6/8 (75%)	21/25 (84%)	13/20 (65%)
Satisfaction ratings	P1	2/3	2/3	2/2	2/2	4/5	4/5
	P2	2/3	2/3	2/2	2/2	4/5	4/5
	P3	3/3	2/3	2/2	2/2	5/5	4/5
	P4	5/5	–	–	–	5/5	–
	P5	3/3	3/3	2/2	2/2	5/5	5/5
	Total	15/17 (88.2%)	9/12 (75%)	8/8 (100%)	8/8 (100%)	23/25 (92%)	17/20 (85%)

COPM, the Canadian Occupational Performance Measure (74); Post, post intervention; FU, follow-up; P, participant.

Secondary Outcomes—Participation and Quality of Life

Participation was measured with the MPAI-4-P (79). Participation scores decreased (participation improved) from baseline (Mdn = 46.00, IQR = 42.25–59.50) to post intervention (Mdn = 33.50, IQR = 22.00–51.00). This improvement was near statistical significance ($z = -1.826$, $p = 0.068$). A similar trend was also observed when examining the changes in the participants' median MPAI-4-P scores at follow-up (Mdn = 36.00, IQR = 28.00–55.00), although the Wilcoxon Signed-Ranks test did not reveal a statistically significant difference from baseline ($z = -1.604$, $p = 0.109$). In addition, effect sizes were large at post intervention ($r = -0.913$) and at follow-up ($r = -0.927$).

Figure 4 shows participants' individual profiles of MPAI-4-P scores at baseline, post intervention, and follow-up. Participant 2 did not fill in the questionnaire due to technical issues and participant 4 was lost to follow-up due to an unstable medical condition unrelated to the study intervention. Participant 3 had the highest participation limitation at baseline (T score 64- reflecting severe participation limitation). The other three participants started at a similar level of participation limitation (T scores between 30 and 40, reflecting mild to moderate participation limitations). A decrease in MPAI-4-P scores was

TABLE 4 | Changes in COPM median ratings from baseline to post intervention and from baseline to 3-month follow up (including effect size)$^{\Theta}$.

Outcome measure (possible range of scores)	Baseline	Post-intervention	Baseline to post intervention ($n = 5$)			Follow-up	Baseline to follow-up ($n = 4$)‡		
	Mdn (IQR)	Mdn (IQR)	z	p	r (ES)	Mdn (IQR)	z	p	r (ES)
Performance (1–10) Trained goals ($n = 5$)	3.33 (2.17–3.67)	7.33 (5.33–8.87)	−2.032*	0.042	−0.909	5.67 (3.17–7.92)	−1.826†	0.068	−0.913
Untrained goals ($n = 4$)‡	2.75 (1.38–3.38)	7.00 (4.63–8.63)	−1.841†	0.066	−0.921	7.50 (2.25–9.75)	−1.604	0.109	−0.802
All goals ($n = 5$)	3.00 (1.90–3.50)	6.20 (5.90–8.80)	−2.023*	0.043	−0.905	6.60 (2.80–8.45)	−1.826†	0.068	−0.913
Satisfaction (1–10) Trained goals ($n = 5$)	2.60 (2.33–3.33)	7.33 (6.17–9.17)	−2.023*	0.043	−0.905	6.83 (4.42–8.00)	−1.826†	0.068	−0.913
Untrained goals ($n = 4$)‡	2.00 (1.13–2.88)	7.25 (7.00–9.38)	−1.841†	0.066	−0.921	10.00 (7.00–10.00)	−1.826†	0.068	−0.913
All goals ($n = 5$)	2.60 (1.90–3.10)	7.20 (6.60–9.30)	−2.023*	0.043	−0.905	7.30 (6.25–8.80)	−1.826†	0.068	−0.913

COPM, the Canadian Occupational Performance Measure. Higher score reflects higher perceived performance/satisfaction with performance (74); Mdn, Median; IQR, interquartile range; EF, effect size.

$^{\Theta}$*An effect size (r) was calculated from the z value of Wilcoxon signed-rank test* ($r = z/\sqrt{n}$) *(94) and can be interpreted as a small* ($r \leq 0.10$)*, medium* ($r = 0.30$)*, and large* ($r \geq 0.50$) *effect size (95).*

*$p < 0.05$; †*near statistical significance;* $0.05 \leq p < 0.1$.

‡*Participant 4 was not included in this analysis (of untrained goals) because all his goals were trained during the intervention process; therefore, he had no untrained goals. In addition, this participant was lost to follow-up due to an unstable medical condition unrelated to the study intervention, and he was therefore not included in the baseline to follow-up analysis.*

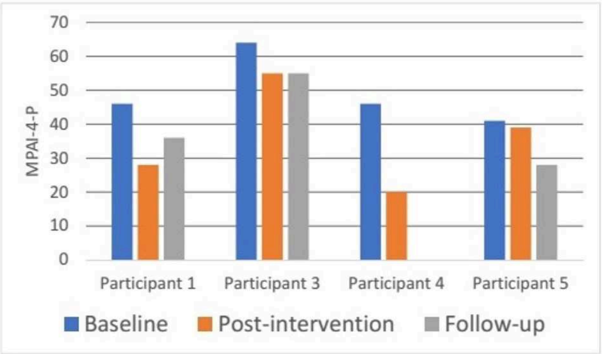

FIGURE 4 | Participants' MPAI-4-P ratings at baseline, post intervention, and 3-month follow-up. MPAI-4-P, Mayo-Portland Adaptability Inventory-4, Participation Index (82).

found for each participant from baseline to post intervention and from baseline to follow-up, suggesting greater participation and independence in community living. Furthermore, these differences reflect a clinical improvement in level of participation as described in the MPAI-4 manual (79).

Quality of life was measured with the SIS (82) at baseline, post intervention and follow up (see **Table 5**). Generally, no statistically significant improvement was found in the SIS subscales. However, near-statistically significant improvement was found on the "memory and thinking" subscale from baseline to post intervention and from baseline to follow-up ($z = -1.841$, $p = 0.066$ and $z = -1.826$, $p = 0.068$, respectively) with large effect sizes ($r \geq 0.80$ for both). A near-significant improvement ($z = -1.826$, $p = 0.068$) was found on the "communication" subscale from baseline to post intervention, with a large effect size ($r = -0.817$); however, there was a decrease in follow-up scores, and these were not significantly different compared to baseline ($z = -0.365$, $p = 0.715$) and had a small effect size ($r = -0.183$).

On an individual level, each participant achieved a clinically meaningful improvement of 15 points or more (88, 89) in one to seven (out of nine) subscales at post intervention and/or follow-up, suggesting improvement in different aspects of QoL. It should be noted that two participants reported clinically meaningful decreases in one or two subscales compared to baseline (along with improvements in other subscales).

DISCUSSION

This pilot study assessed the feasibility, acceptability, and preliminary efficacy of the CO-OP approach in a telerehabilitation format with adults in the chronic phase after ABI, prior to conducting a larger trial. Our findings indicated that implementation of the approach via videoconferencing is feasible and was found to be highly acceptable to the participants and their significant others. In addition, the study provided preliminary evidence of the intervention's efficacy. The most prominent improvements were found in the primary outcome of activity performance in the personal functional goals. Clinically meaningful improvements were also found in participation and QoL measures. Improvements were partially maintained at 3-month follow-up.

Feasibility and Acceptability of the Intervention

We found that it was feasible to deliver the intervention remotely, while generally adhering to the essential elements of the CO-OP approach, and received reports of high satisfaction of participants. However, regarding the aspect of technology use for treatment delivery, there were difficulties similar to those reported in previous internet-based telerehabilitation

TABLE 5 | Changes in SIS median ratings from baseline to post intervention and from baseline to 3-month follow-up (including effect size)$^{\Theta}$.

Outcome measure (possible range of scores)	Baseline	Post-intervention	Baseline to post intervention (*n* = 5)			Follow-up	Baseline to follow-up (*n* = 4)‡		
	Mdn (IQR)	Mdn (IQR)	*z*	*p*	*r* (ES)	Mdn (IQR)	*z*	*p*	*r* (ES)
SIS domains (0–100)									
Strength	50.00 (28.50–75.00)	50.0 (34.50–78.50)	−0.0680	0.496	−0.030	47.00 (38.75–87.50)	−0.535	0.593	−0.268
Memory and thinking	68.00 (43.00–89.50)	89.00 (68.00–93.00)	−1.841†	0.066	−0.823	82.00 (52.25–98.25)	−1.826†	0.068	−0.913
Emotion	81.00 (54.50–94.00)	86.00 (71.00–90.00)	−0.535	0.593	−0.239	79.00 (63.75–94.25)	0.000	1.000	0.000
Communication	89.00 (73.50–96.50)	96.00 (89.00–98.00)	−1.826†	0.068	−0.817	80.00 (64.75–98.25)	−0.365	0.715	−0.183
ADL/IADL	80.00 (41.50–90.50)	75.0 (52.50–93.00)	−0.813	0.416	−0.364	70.0 (51.75–90.50)	−1.095	0.273	−0.548
Mobility	64.00 (44.50–86.00)	75.00 (69.50–86.00)	−1.289	0.197	−0.577	72.00 (61.75–90.50)	−0.736	0.461	−0.368
Hand function	50.00 (15.00–85.00)	70.00 (30.00–90.00)	−1.490	0.136	−0.666	55.00 (21.25–85.00)	−0.184	0.854	−0.092
Participation	69.00 (31.00–94.00)	84.00 (34.50–97.00)	−1.095	0.273	−0.490	56.00 (53.00–85.25)	−1.089	0.276	−0.545
General recovery	65.00 (45.00–85.00)	70.00 (45.00–82.50)	0.000	1.000	0.000	60.00 (27.50–92.50)	−0.365	0.715	−0.183

SIS, the stoke impact scale, higher scores reflect better QoL (82); QoL, quality of life; Mdn, Median; IQR, interquartile range; EF, effect size.

$^{\Theta}$*An effect size (r) was calculated from the z value of Wilcoxon signed-rank test* ($r = z/\sqrt{n}$) *(94) and can be interpreted as a small* ($r \leq 0.10$)*, medium* ($r = 0.30$)*, and large* ($r \geq 0.50$) *effect size (95).*

†*near statistical significance;* $0.05 \leq p < 0.1$.

‡*Participant 4 was lost to follow-up due to an unstable medical condition unrelated to the study intervention, and he was therefore not included in the baseline to follow-up analysis.*

studies (51, 52, 57, 100) and with tele-CO-OP specifically (24). Some difficulties might have been more prominent in the current study as the participants were relatively older adults with little experience in technology use and needed assistance to operate it (35, 101). Nevertheless, despite the technical challenges, all of the participants reported positive attitudes toward telerehabilitation, and this was in line with previous studies (102, 103). It is possible that these challenges affected recruitment rates and contributed to the relatively high dropout rates. In light of these issues, special consideration should be given to developing efficient ways of providing appropriate guidance and adequate technical support for various populations when planning telerehabilitation programs.

Four of the five final participants that completed the intervention showed good adherence rates, with appropriate numbers and duration of sessions. One exception is participant 4 who had several hospitalizations that led to breaks in the intervention process resulting in the extension of the intervention period to 8 months. Following the hospitalizations, the OTs debated whether to stop the intervention process. However, due to the participant's high motivation to take part in the home-based teleintervention and his recovery between hospitalizations, it was decided to continue the intervention. This case demonstrates the potential of the intervention to make a positive impact even in a case involving an unstable health condition, something that is prevalent in ABI survivors (104–106). This is particularly relevant for interventions with older adults who are considered a more vulnerable population (107).

Another factor that can affect the treatment process is the involvement of the significant other in the intervention program (108–110). In the current study, the significant others' involvement varied based on the participation needed in the participants' formulated plans as well as the willingness of the participants and the significant others to be involved. In some cases, the significant other mainly assisted in providing technical support, while in other cases they were involved in supporting the execution of the participants' plans. In addition, there was variation regarding the satisfaction of the participants with the involvement of the significant other in the treatment process. This highlights the complexity of this issue, as similarly discussed by Ng et al. (24). Despite the importance of the significant others' involvement in the rehabilitation process of adults with ABI and its potential positive effects, there are also barriers to this involvement, such as a lack of availability (108, 111, 112). When reflecting on the participants who dropped out during the study process, our impression was that they had less involvement or support from their significant others in regard to participating in the study.

Preliminary Efficacy of the Intervention

Improving daily activity performance and participation is a valued and desired outcome in ABI rehabilitation, and there is a call to emphasize this aspect in outcome measures and as a focus of interventions (6, 10, 17). Accordingly, the primary outcome in our study was perceived performance and satisfaction on participant-chosen functional goals. Despite the small sample, significant statistical and clinical improvements were found in trained goals at post intervention and were partially maintained at follow up. These results are in line with previous studies that evaluated the efficacy of traditional face-to-face CO-OP approach among adults in the chronic stage post-ABI (113, 114). This improvement can be attributed to the client-centered, occupation-based nature of the intervention that focused directly on improving the performance of self-chosen goals. The intervention delivery to the participants in their natural environment, which is considered the ideal setting to address specific functional issues (20), may also have contributed to the gains in activity performance. Our results also indicated gains in the untrained goals suggesting the transfer of learning, similar to results in previous CO-OP studies (60, 61, 63, 73). These results can be explained by the metacognitive aspects of the approach and the emphasis on generalization and transfer during the sessions. This is assumed to facilitate participants' independent use of the global and domain-specific strategies in various life situations (115). In addition, participants' active involvement in the goal setting process is considered a motivational incentive that can promote goal attainment (116, 117). The improvements in activity performance and satisfaction were partially maintained at follow-up, as also reported in previous CO-OP studies that included adults with ABI (24, 60). Although activity participation and satisfaction improvements were maintained for participants 1, 2, and 5 at follow-up, participant 3 showed decreases in most of his goals at follow-up. These results might suggest that some participants require a longer intervention period or additional maintenance sessions to support achievements over time.

In relation to global outcomes of participation and QoL, the results were positive on the clinical level, yet less conclusive. This is similar to other studies that evaluated telerehabilitation interventions that target daily activities directly with ABI survivors, which have presented inconsistent or insufficient results regarding these outcomes (24, 52, 53, 55, 57). A possible explanation for this, in addition to the small sample size, is the rather short duration of the intervention, as well as the relatively low intensity of one weekly session (12, 117). Moreover, the current intervention focused on specific personal activities; consequently, the specific improvements in activity performance may not have been reflected significantly in the global participation and QoL measures, which include a broad range of life domains (52, 117).

Limitations

The results need to be interpreted, taking into account the limitations of the study. First of all, these analyses were exploratory, and interpretation of the results was done with caution due to the small sample size and the possibility that the significant changes were found only by chance. Furthermore, the current study is a pilot study without a control group, which means we cannot attribute the improvements at post intervention solely to the treatment. However, it should be noted that none of the participants received additional occupational therapy during the intervention period. Therefore, we can assume that the activity performance improvements in the participant-chosen goals may be related to the studied intervention in general. Finally, we included a heterogenous group of participants with stroke and TBI with different levels of disability. While this limits the clear applicability to one group or the other, the fact that we found improvements in all patients suggests that this intervention has potential as a treatment for community dwelling individuals with chronic neurological conditions. In light of these limitations, further research is warranted with a larger sample and a control group. Additional outcome measures should be used to evaluate the effect of the intervention as perceived by the significant others and/or clinicians, as well as to deepen our understanding of who are the best candidates for this intervention.

CONCLUSIONS

Improved functional performance is a main issue for many ABI survivors who continue to experience disability in a broad range of daily activities, and it is an important and desired outcome of rehabilitation. Our findings suggest that the delivery of the CO-OP approach via videoconferencing is feasible, acceptable, and beneficial to older adults in the chronic phase after TBI and stroke. Despite, the small and heterogeneous sample, we found significant improvements in activity performance as well as clinically meaningful improvements in activity performance, participation, and QoL for all of the participants. These improvements were partially maintained at 3-month follow up. Given accessibility barriers for receiving treatment in community-based clinics and the limited resources available for community in-home rehabilitation for ABI survivors, remotely delivered CO-OP could be a useful supplement to traditional rehabilitation options and could enable continued treatment for a longer period. Our encouraging results strengthen the evidence of the potential benefits occupation-based telerehabilitation interventions have in promoting activity performance, participation, and QoL among community dwelling ABI survivors in the long term. Based on these findings we are currently conducting a sufficiently powered randomized controlled study to further our understanding and strengthen the evidence of this intervention and its benefits.

DATA AVAILABILITY STATEMENT

The datasets analyzed in this manuscript are not publicly available. Requests to access the datasets should be directed to AB, aviva.kahan@mail.huji.ac.il.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the research ethics committees of Hadassah-Hebrew University Medical Center, Jerusalem and Maccabi Healthcare Services, Bat-Yam, Israel (ethical committee registration numbers: 0689-15-HMO and 192016, respectively). The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

YG, JJ, AB, JS, YD, and IS conceived and designed the experiments. AB, SS, JS, FK, YN, and SB performed recruitment and data collection. AB, SS, and YG performed data analysis. AB wrote the manuscript. YG critically revised the manuscript. All the authors read and approved the final manuscript.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2019.01247/full#supplementary-material

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Interdisciplinary Stroke Recovery Research: The Perspective of Occupational Therapists in Acute Care

Jessica Ranford[1]*, Jessica Asiello[1], Alison Cloutier[2], Kimberly Cortina[1], Helena Thorne[1], Kimberly S. Erler[1,3], Natasha Frazier[1], Caitlin Sadlak[1], Abigail Rude[1] and David J. Lin[2]

[1] Department of Occupational Therapy, Massachusetts General Hospital, Boston, MA, United States, [2] Center for Neurotechnology and Neurorecovery, Department of Neurology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, United States, [3] Department of Occupational Therapy, MGH Institute of Health Professions, Boston, MA, United States

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Ulster University, United Kingdom

****Correspondence:***
Jessica Ranford
jranford@partners.org

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As acute stroke treatments advance, more people survive the initial stroke event and live with long-term neurological impairments that impact functional outcomes and quality of life. In accordance with International Classification of Functioning (ICF), living with long-term neurological impairments can limit survivors' activity performance and restrict participation in valued life roles and routines. Research focused on longitudinal analysis of functional measures and outcomes after stroke are critical for determining early indicators of long-term participation and quality of life and guiding rehabilitation resource allocation. As core members of the interdisciplinary stroke recovery treatment team throughout the post-acute care continuum, occupational therapists (OTs) directly address stroke survivors' ability to participate in meaningful daily activities to promote function and quality of life. Just as in clinical care in which multidisciplinary, team-based perspectives are vital, OTs provide invaluable perspectives for stroke recovery research. Here we describe OTs' role in a collaborative, interdisciplinary research study aimed at comprehensively understanding upper extremity motor recovery after stroke and its impact on individuals across the post-acute care continuum. This article discusses the importance of the OTs' perspectives in conducting interdisciplinary, longitudinal stroke recovery research. The challenges, strategies and recommendations for future directions of advancing the role of OTs in multidisciplinary stroke recovery research are highlighted. We use this perspective as a call to action to the stroke recovery field to incorporate OTs as members of the research team and for OTs to provide their perspectives on ongoing stroke recovery research.

Keywords: occupational therapy, stroke recovery, acute care, neurorehabilitation, participation

INTRODUCTION

Despite continuous advances in acute interventions, stroke remains the leading cause of disability worldwide (1). Given the aging population and increased rates of survival, the global burden of stroke is expected to continue to increase in the coming years. Although the World Health Organization International Classification of Functioning (ICF) identifies impairments, activity limitations and participation restrictions as components of functioning and disability in the setting of a health condition, much of stroke recovery research occurs in silos (2, 3). All too often research studies are focused only on one axis of the ICF or are restricted to one professional perspective— the neurologist, the rehabilitation scientist, the therapist, etc. There is limited attention toward the interconnectedness of impairment, activity and participation in stroke recovery research. A multidisciplinary approach to stroke research broadens the lens with which we view recovery and provides a multidisciplinary context from which interdisciplinary communication can occur.

The clinical care of patients with stroke employs an interdisciplinary approach. This approach should also be emphasized in stroke research, starting in the acute care setting and across the post-acute care continuum. Occupational therapists (OTs) are essential members of the interdisciplinary team who address all domains of the ICF after stroke across the continuum of care. The overarching goal of occupational therapy is to improve a stroke survivor's ability to engage in meaningful activities, promoting function and quality of life (4). Here we discuss the role of OTs in interprofessional stroke recovery research with a focus on the acute care setting.

This perspective discusses the feasibility of conducting stroke recovery research through the lens of an inpatient occupational therapy department. We highlight the example of clinical OTs (full-time clinicians) in a busy academic, acute care, clinical department participating in stroke-recovery research and becoming integral members of a clinical-research study team. The context of this research, challenges, strategies, and recommendations for future directions are highlighted.

CONTEXT

Stroke Motor Rehabilitation and Recovery Study

The Stroke Motor Rehabilitation and Recovery Study (SMaHRT) is a neurology, physician-scientist led longitudinal, single site study aimed at understanding the natural history of upper extremity motor recovery after ischemic stroke. Participants are enrolled during their acute stroke hospitalization at Massachusetts General Hospital (MGH) in Boston, MA with the aim of rigorously examining the behavioral, neuroanatomic, and neurophysiologic underpinnings of recovery. The ultimate goal is to develop personalized strategies and neuro-technologies to facilitate neurorehabilitation and enable better recovery for our patients. Launched in June 2017, OTs on the inpatient service at MGH participated in study design and became an integral part of this interdisciplinary research team. The team of OTs perform standardized clinical assessments in the acute care setting as baseline measures. These assessments were paired with longitudinal follow-up in a neurologist-led integrated clinical research outpatient clinic at 6 weeks, 3 months, 6 months and 1-year post stroke. All participants in the study provided written informed consent. The Institutional Review Board at Partners Healthcare approved the study.

Comprehensive Stroke Center

MGH is recognized as a Comprehensive Stroke Center by the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) for its specialized ability to treat the most complex stroke patients. The MGH Inpatient Occupational Therapy Department leadership team includes a clinical director and four clinical specialists with advanced knowledge and experience in specialized areas of clinical care. The clinical specialists oversee clinical practice, support professional development amongst staff and perform quality process improvement initiatives. There are 28 licensed OTs with 6 assigned to the neurology units (i.e., the neuroscience intensive care unit and two neuroscience hospital floors). OTs rotate through neurology units every 12–15 months and work closely with the occupational therapy clinical specialist in neurology to develop expertise related to this population. In addition to the licensed clinicians, the department also includes one rehabilitation aide who assists with hands-on support and environmental set up for occupational therapy interventions.

Interdisciplinary Approach to Research

The physician-scientist investigators included occupational and physical therapy leadership in the design phase of this study to select appropriate assessments. The study was initially focused on arm motor impairment but, with perspectives of the occupational therapy team, the aims were refocused to understand how arm impairment influences activity and participation restrictions. Qualifications for OTs to act as study staff included completion of a rotation on the neurology service, commitment to a 2-year time period of data collection, maintenance of typical clinical caseload and productivity expectations, and participation in study trainings. Six OTs were selected to perform inpatient testing. OTs who administered assessments to study participants were sometimes involved in the clinical care of the study participants but did not bill for the study visit since it was not considered standard clinical care.

Research Test Selection

A series of meetings were held between physicians and occupational and physical therapists to decide on the best research tests to capture not only arm impairment but also activity limitations and participation restrictions. Decisions regarding test selection were based on goals of the study, commonly accepted research measures, clinical relevance, psychometric properties, practicality, and time to complete. Each assessment needed to be administered in an efficient timeframe on an inpatient acute hospital unit with minimal equipment. The interdisciplinary research group selected the final battery of assessments (**Table 1**). The OTs in the study played a critical role in determining final test battery selection. The MGH Occupational Therapy department advocated to serve as the primary data collectors during the acute stroke inpatient stay. Their clinical expertise in upper extremity motor function, familiarity with several of the assessments and background training in supporting patient performance via environmental set up were key in this regard. The entire test battery was anticipated to take a maximum of 1 h to complete. All research OTs participated in standardized training to ensure inter-rater reliability. Standard operating procedures with written

TABLE 1 | Outcome measures administered in MGH Stroke Motor Rehabilitation and Recovery Study (SMaHRT) spanning International Classification of Functioning Domains.

WHO ICF domain	Outcome measure	Assessment type
Structure-function	Fugl-meyer motor assessment	Upper extremity impairment
	Dynamometer	Grip strength
	NIH stroke scale	Overall stroke severity
Activity	Box and blocks	Gross motor function
	9-Hole peg	Fine motor function
	Barthel index	Performance of ADLs/iADLs
	Modified rankin scale	Functional independence
	Timed up and go	Mobility and fall risk
	Gait velocity	Mobility and fall risk
Participation	Stroke impact scale 16 (ADLs/iADLs)	Stroke impact on function
	Patient reported outcome measure (PROMIS-10)	Self-assessment of overall health

scripts and visual illustrations were developed and used for the assessments in order to ensure assessors' fidelity to standardized testing procedures.

Outcome

One hundred patients with stroke consented and enrolled in SMaHRT between June 2017 and April 2019 and continue to be followed as outpatients for integrated clinical research visits. Of the 100 participants, 55 were assessed by OTs. The first 30 participants were enrolled and tested prior to the OTs receiving formal training on the battery of assessments. Due to time constraints of the inpatient occupational therapy group, another 15 participants' assessments were completed by non-OT members of the research team. The reasons for this included therapist availability for participants enrolled on the weekend or after work hours and time sensitivity related to impending discharge.

Contributions of Occupational Therapists to Stroke Recovery Research

Ongoing discussions with leaders of the SMaHRT research team have highlighted the critical role of OTs in this ongoing stroke recovery research study. First, with regard to study design, stroke recovery research studies do not often account for how stroke affects the individual comprehensively. In this study, given the involvement of OTs in even the beginning stages of study design, all aspects of the ICF were included in study outcome measures. The study continues to benefit from never losing the perspective of the comprehensive ICF framework. Second, with regard to study implementation, OTs are familiar with standardized upper extremity motor assessments, as well as cognitive assessments from their clinical work. Having these perspectives are invaluable to inform the feasibility of research outcomes. The OTs specifically contributed to identifying a combination of outcome measures for UE motor function that are both meaningful and practical. This practical application of clinical practice and knowledge added to the efficiency of research testing which is critical for feasibility in the acute care setting. Third, performing clinical research on patients during the acute phase of stroke recovery poses challenges to a patient's limited physical, emotional, and mental endurance for tolerating activity. To this end, OTs' expertise at providing clinical care to patients with impaired arousal and attention allowed for discussion amongst research staff on how to best optimize participation in outcome assessments. Recommendations for environmental set-up and strategies to facilitate arousal and attention were also important contributions to efficiently and safely enable patient testing in the dynamic acute hospital setting.

SUCCESSES, CHALLENGES, AND STRATEGIES

There are many factors that contributed to the ongoing success of inpatient OTs participating in clinical research and data collection during acute hospitalization for stroke. These include the infrastructure of the inpatient occupational therapy department and hospital culture regarding OT's contribution to the multidisciplinary team, the value placed on research, interdisciplinary approach to stroke care and a strong relationship with academic rehabilitation science researchers. These factors are discussed below.

Infrastructure

The size and structure of the MGH Inpatient Occupational Therapy Department contributes to the ability to have 1-year rotations on specific service areas, such as neurology, where OTs have exposure to sub-groups of patient populations over time. This model allowed for clinicians involved in the study to use their advanced clinical skills and knowledge to assist in developing guidelines for the research assessment battery. The advanced knowledge of stroke recovery and stroke unit systems allowed clinicians to problem solve research participation and coordination of care issues. There was a large enough pool of clinicians both interested in contributing to research and qualified to serve as study staff who joined the study to prevent burnout among study staff. The OT Clinical Specialist in neurology at MGH has a unique role which includes overseeing clinical practice, supporting professional development of staff and leading quality process improvement initiatives on the neurology service. The OT Clinical Specialist's clinical care expectations is only 70%, allowing for the flexibility in the remaining 30% time to participate in weekly research meetings and to develop roles and responsibilities for other OTs within the study. This role was imperative to maintaining successful operations both within the interdisciplinary research team as well as the research OT group.

Shared Value of Research

There is a strong value placed on research at MGH as an institution as well as within the occupational therapy department. Research OTs volunteered their time to complete the assessments, often needing to extend their work day to meet their clinical productivity expectations. Although this highlights one of the significant challenges, it also demonstrates the powerful commitment of these OTs to research and the motivation to contribute to the evidence that promotes stroke recovery for patients. The MGH Inpatient Occupational Therapy Department has a strong relationship with the OT faculty at the MGH Institute of Health Professions. This academic-practice partnership blends clinical and research expertise to maximize OT involvement and contribution to this study. The research expert for stroke UE motor recovery on the occupational therapy faculty at the MGH Institute of Health Professions was critical to the development of training protocols. These training protocols ensured occupational therapy research staff demonstrated continued proficiency in standard administration of tests. The physician-scientists who had the vision to create the interdisciplinary research team are to be commended for their commitment to an approach that recognizes and values the contribution of each discipline in caring for patients with stroke. This emphasis on interdisciplinary research is critical for moving the rehabilitation field forward to optimize outcomes for individuals who experience stroke.

Training

Before initiating data collection, there was dedicated time for training and educating clinicians on the overview of the research study and the various assessments being administered. The demands of training six clinicians to ensure proficiency in administering tests was spread across two four-hour sessions. These sessions primarily addressed the Upper Extremity Fugl-Meyer to ensure standardization of the assessment across clinicians (5–7). OT and non-OT members of the research team participated together in these sessions. Approximately 1 year after study launch, an inter-rater reliability session was held. A two-way mixed-effect model with single ratings and absolute agreement was used to assess the intra-class coefficient (ICC) on proximal/distal/and speed coordination aspects of the Upper Extremity Fugl-Meyer among study staff (both OT and non-OT members). The ICC was calculated to be 0.80 [95% CI from 0.43 to 0.99, $F_{(2,13.5)} = 49.5$, $p < 0.001$], confirming prior reports of the high inter-rater reliability of the Fugl-Meyer (8, 9). A one-time hour-long training session covered testing for the Box and Blocks Test and Nine Hole Peg Test. Once clinicians began participating in data collection, it was important to establish a structure to ensure that the assessment burden was equally shared amongst clinicians as well as to ensure all participants would be systematically assigned. The OT team established a rotation system to minimize burnout and share the workload burden. This was helpful to provide structure; however, flexibility was key in the success of the system. If a clinician was not present or had other commitments limiting their ability to perform the assessments, we had a coverage system where another clinician would substitute.

Communication

Critical to the sustainability of interdisciplinary research in an acute care setting is ongoing communication regarding issues impacting feasibility. Understanding the severity of participants' deficits as well as the trajectory of the acute hospital course are influential factors in determining discharge and timeline for test completion. One of the biggest challenges was coordinating testing time in the context of an acute hospitalization. In the acute care setting where the focus is on diagnostic work-up of the current stroke and future stroke prevention, research OTs were vying for valuable time along with the primary team, consultative services, testing, imaging and clinical therapy. Finding research time that did not compete with the clinical needs of the patient required deliberate communication to coordinate. Since this is also necessary in clinical care coordination, we were able to use systems already available for quick and efficient communication. For example, a unique feature that our clinicians have access to are hospital-based cell phones where they can individually call and text nurses and other therapists to discuss plans for the day regarding the participant. In the electronic medical record, the therapists can view the participant's current location and thus avoid traveling to perform testing when participants are off the floor at a test or procedure.

Efficiency

Balancing time to perform the study tests with clinical efficiency was a substantial issue. The OTs involved in the study all had busy, full-time clinical commitments. Many of the clinicians were on different rotations (outside of stroke) during their time on the study, which brought up challenges for coordinating care as they were often treating patients on services located in different buildings throughout the hospital. Study staff found that with increased experience performing the assessment battery, their proficiency in administering the assessments improved which had a direct and positive impact on efficiency. Another challenge to efficiency is the preparation prior to and just after test administration, which includes gathering/putting away testing materials, scoring and inputting results, environmental set-up and positioning needed to maximize participation. To combat this challenge, we utilized exercise physiology students and our occupational therapy aide to assist with care coordination, environmental set-up/clean up, gathering/putting away testing materials and electronic entry of test scores.

Client Factors

Given the often fluctuating medical status of acute stroke patients and variability of post-stroke deficits, OTs with previous experience working with this complicated and heterogeneous population of patients were critical to successful data collection. In the early stages of recovery, a participant's cognitive status can often fluctuate and may interfere with their ability to effectively engage in assessments. At times, some participants' deficits in arousal, attention, and short-term memory required graded cueing or arousal stimulation. In addition, visual attention and processing, spatial awareness, praxis, postural control, and motor deficits might require adaptations to the environment and/or positioning of the patient. Participant fatigue, especially after stroke, is also an important factor influencing research testing. Having worked specifically with the stroke population for at least a 1-year rotation prior to joining the study, our research OTs

BOX 1 | Summary of perspectives of acute care occupational therapists on stroke recovery research.

- Stroke recovery research too often occurs in silos, focused on one domain of the ICF and one professional perspective.
- To advance stroke recovery research, all aspects of the ICF should be accounted for in research studies. Clinical occupational therapists, core members of the interdisciplinary stroke recovery team, have unique perspectives on stroke survivors' ability to engage in meaningful activities to promote functioning and quality of life.
- Occupational therapists with full-time clinical commitments participated in a physician-scientist led stroke recovery research study at Massachusetts General Hospital, becoming integral members of the multidisciplinary study team and shaping all aspects of the study from study design to data collection and analysis.
- Unique contributions of OTs to the stroke recovery research study include addition of outcome measures measuring different domains of the ICF beyond body-structure/function, valuable perspectives on the feasibility of outcome measures, and unique qualifications for day-day research data collection in a busy inpatient stroke unit.
- Factors contributing to the success of OTs becoming integral members of the stroke recovery research team include (1) the infrastructure of the OT department, (2) the value placed on research in both the department and the institution, (3) the interdisciplinary approach to clinical stroke care translated into research, and (4) a strong relationship with academic rehabilitation science researchers.
- Potential barriers to clinical OTs participating in research are (1) time required for research assessment training and maintaining proficiency in tests (inter-rater reliability) (2) coordinating time for research testing for patients in the context of a busy acute stroke hospitalization (3) study staff balancing time for research with a busy clinical schedule and (4) complex and rapidly changing medical status of stroke patients.
- Strategies for success to overcome these barriers include (1) designing flexibility into the research schedule (2) ensuring regular communication between research and clinical staff (3) utilizing students and aides to maximize research testing efficiency and (4) applying clinical knowledge of patient factors to maximize research assessments.

could efficiently and effectively provide these adaptations as well as verbal and visual cues to maximize the patient's ability to perform the desired movement patterns for research testing. It is important to understand stroke impairments' effects on test performance and scoring criteria to maintain fidelity to testing instructions, maintain inter-rater reliability and document any interventions that may have affected these. OT study staff also utilized their advanced understanding and knowledge to assess patient's appropriateness for engaging in the assessment battery and recognizing when timing may improve test performance. If participants reported fatigue, study staff would terminate research testing and return later to complete assessments. Flexibility here was again key. Appreciating and understanding the acuity and fragility of this population in the acute hospital setting impacts the many factors that make research in this setting feasible.

RECOMMENDATIONS FOR FUTURE INTERDISCIPLINARY STROKE RESEARCH

To advance stroke rehabilitation research and approaches to improve recovery after stroke, it is clear that an interdisciplinary approach that addresses all domains of the ICF and spans the post-acute care continuum must be used. Stroke recovery research, starting in the acute phase after stroke, is challenging due to the need for coordination between research staff with clinical teams as well as the complexity and medical needs of acute stroke patients. OTs have distinct expertise in ICF domains as well as in stroke client factors and can be invaluable assets to the research team. Due to the heterogeneity of stroke, large sample sizes are needed to address important research questions; therefore, challenges identified must be addressed in order to support ongoing, multi-site data collection. This perspective is a call to action to the field for stroke recovery researchers to integrate clinical OT perspectives into ongoing research and for OTs to participate and lend their perspectives to ongoing studies. A summary of the perspectives of MGH acute care OTs on stroke recovery research is outlined in **Box 1**. Future studies may seek to establish a standardized, stroke recovery assessment battery, deployed as the standard of care in occupational therapy across healthcare systems and further across the United States and internationally. Such a battery will overcome many of the current challenges that straddle the clinical-research divide and may advance some of our research insights into clinical evidence-based practice.

AUTHOR CONTRIBUTIONS

JR, JA, AC, KC, HT, NF, CS, DL, and AR contributed to initial concept and perspectives. JR, JA, KC, HT, NF, CS, and AR developed the initial version of the manuscript. KE, CS, JR, and DL critically revised the manuscript. AC and DL provided objective data. All authors read and approved the final manuscript.

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Participation Following Inpatient Rehabilitation for Traumatic Disorders of Consciousness: A TBI Model Systems Study

Christopher Malone[1,2], **Kimberly S. Erler**[3], **Joseph T. Giacino**[1,2], **Flora M. Hammond**[4], **Shannon B. Juengst**[5], **Joseph J. Locascio**[6], **Risa Nakase-Richardson**[7,8], **Monica Verduzco-Gutierrez**[9], **John Whyte**[10], **Nathan Zasler**[11] **and Yelena G. Bodien**[1,2,6]*

[1] *Department of Physical Medicine and Rehabilitation, Harvard Medical School, Boston, MA, United States,* [2] *Neurorehabilitation Laboratory, Spaulding Rehabilitation Hospital, Boston, MA, United States,* [3] *Department of Occupational Therapy, MGH Institute of Health Professions, Boston, MA, United States,* [4] *Department of Physical Medicine and Rehabilitation, Indiana University School of Medicine, Indianapolis, IN, United States,* [5] *Department of Physical Medicine and Rehabilitation, University of Texas Southwestern Medical Center, Dallas, TX, United States,* [6] *Department of Neurology, Massachusetts General Hospital, Boston, MA, United States,* [7] *Mental Health and Behavioral Science, Defense and Veterans Brain Injury Center, James A. Haley Veterans Hospital, Tampa, FL, United States,* [8] *Division of Pulmonary and Sleep Medicine, Department of Internal Medicine, University of South Florida, Tampa, FL, United States,* [9] *Department of Physical Medicine and Rehabilitation, McGovern Medical School at the University of Texas Health Science Center at Houston, and TIRR Memorial Hermann, Houston, TX, United States,* [10] *Moss Rehabilitation Research Institute, Elkins Park, PA, United States,* [11] *Department of Physical Medicine and Rehabilitation, Concussion Care Centre of Virginia, Ltd. and Tree of Life Services, Virginia Commonwealth University, Richmond, VA, United States*

Edited by:
Naomi Josman,
University of Haifa, Israel

Reviewed by:
Meg E. Morris,
La Trobe University, Australia
Alessio Baricich,
Università degli Studi del Piemonte Orientale, Italy

***Correspondence:**
Yelena G. Bodien
ybodien@mgh.harvard.edu

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Severe traumatic brain injury (TBI) may result in a disorder of consciousness (DoC) and lead to substantial long-term disability. While level of independence with activities of daily living, especially for persons who recover consciousness during inpatient rehabilitation, generally improves over time, the degree of change in participation remains unknown. We determined level of participation among persons with TBI between 2005 and 2017 who were admitted to inpatient rehabilitation unable to follow commands and subsequently enrolled in the TBI Model Systems National Database. Participation on the Participation Assessment with Recombined Tools-Objective (PART-O) Productivity, Social Relations, and Out and About subscales was evaluated at 1–5 years post-injury. We used a mixed-effects model to longitudinally compare participation between persons who did and did not regain command-following during inpatient rehabilitation. We further explored the level of participation associated with increasing levels of functional independence (FIM). The analysis included 333 persons (229 recovered command-following during rehabilitation, mean age = 35.46 years, 74.9% male). Participation across groups, at all follow-up time points, on all PART-O subscales, was remarkably low (mean range = 0.021–1.91, maximum possible score = 5). Performance was highest on the Social Relations subscale and lowest on the Productivity subscale. Longitudinal analyses revealed no difference in level of participation or change in participation across time for persons who regained command-following during rehabilitation compared to those who did not. While productivity increased over time, social participation did not and participation outside the home increased more for younger than for older persons. Across all three PART-O subscales, FIM Motor scores positively predicted participation. FIM Cognitive scores positively predicted level of participation on the Productivity and Social Relations subscales. Exploratory analyses revealed that even persons who achieved independence on the FIM Motor and Cognitive subscales had low levels of participation across domains and follow-up years. In summary, persons with severe TBI who were admitted to inpatient rehabilitation unable to follow commands were found to be unlikely to participate in productive tasks, social endeavors, or activities outside of the home up to 5 years post-injury, even if functional independence was recovered.

Keywords: traumatic brain injury, minimally conscious state, participation, rehabilitation, outcome

INTRODUCTION

Medical advances have improved the ability of healthcare providers to prevent early death among persons with severe traumatic brain injury (TBI) (1). Surviving persons may experience a disorder of consciousness (DoC), which includes the vegetative state, characterized by periods of eye-opening but no behavioral evidence of conscious awareness, and minimally conscious state, characterized by clearly-discernible but inconsistent behavioral signs of conscious awareness (2). Recovery of command-following (e.g., the ability to accurately respond to a spoken or written prompt such as "look up," "make a fist," "kick your leg") is a critical clinical milestone in the recovery from a DoC, as it demonstrates increased situational awareness (3). For persons admitted to inpatient rehabilitation without command-following, restoration of independence across domains of self-care, mobility, and to a lesser extent, cognition, is possible for up to 10 years post-injury, especially for those who regain command-following during rehabilitation (4–6). However, less is known about whether these individuals eventually participate in social and productive activities. In fact, many studies of participation after TBI exclude persons with the most severe impairments and lower levels of function for logistical reasons (e.g., inability to complete self-report questionnaires or primary residence in a non-community setting) (7, 8). Alternatively, patients with severe TBI and prolonged impairments may be grouped with less severe patient populations (e.g., moderate TBI) (9), thus potentially masking cohort-specific effects (10, 11). Prior studies of severe TBI have focused on emergence from a DoC, global function, or recovery of basic cognitive abilities as primary outcome metrics; however, participation in community-based activities is also considered a measure of successful recovery after TBI. A more comprehensive understanding of participation across the trajectory of recovery from traumatic DoC may provide targets for early interventions and opportunities for instrument development, as well as inform programmatic changes that meet the unique needs of this population.

Although a precise operational definition of participation has not emerged from the literature, it is widely recognized to encompass varied life domains at the societal level, such as home activities, learning, social interactions (12–14), and productivity (15, 16). The World Health Organization International Classification of Functioning, Disability and Health (ICF) defines participation as "involvement in a life situation" and conceptualizes participation as one of the major components of function and disability in the context of health (17). Although return to effective functioning in the home, work, and social environments is a primary goal of rehabilitation after TBI, long-term improvements in these domains may not always occur (18).

Inability to return to work, attend school, or engage in other valued roles or routines, including those associated with leisure, is common during the years after moderate to severe TBI (11, 19–22). The few studies that include individuals with delayed, or no, recovery of command-following after TBI suggest that impaired participation is a predominant source of long-term societal burden (20). Furthermore, decreased participation across domains is not simply due to reallocating cognitive and psychological resources toward alternative activities (e.g., decreasing leisure to engage in more work activities) (11, 19). While a small number of demographic and injury characteristics have been found to predict participation (e.g., younger age at injury, higher levels of motor function at rehabilitation discharge) (23, 24), personal (e.g., social support) and psychological factors (e.g., psychological resilience) have the strongest influence (25).

Despite improved knowledge of long-term clinical outcomes, participation among individuals who have experienced very severe TBI remains understudied. A more complete understanding of participation over time is necessary to develop or refine participation measures, inform interventions to improve participation, and potentially reduce monetary and emotional burden. This study aims to: (1) characterize the level of participation across the domains of productive, social, and outside activities at 1, 2, and 5 years post injury among persons admitted to acute inpatient rehabilitation without command-following; and (2) compare longitudinal levels of participation between persons who regained and those who did not regain command-following during inpatient rehabilitation. We hypothesized that persons who regained command-following during inpatient rehabilitation would demonstrate higher levels of participation compared to those who did not regain command-following during inpatient rehabilitation. We also explored the relationship between functional recovery and participation to determine whether individuals who regain independence become productive, socially integrated and able to participate in activities outside the home.

MATERIALS AND METHODS

Participants

The sample was drawn from the Traumatic Brain Injury Model Systems (TBIMS) National Database (NDB). The TBIMS NDB is a longitudinal multicenter study which prospectively enrolls and collects data from individuals with moderate to severe TBI hospitalized and later admitted to inpatient rehabilitation facilities in the United States. The TBIMS is currently comprised of 16 regionally and demographically diverse centers. Each center obtains approval to contribute data to the database from their local Institutional Review Board (IRB) and obtains consent from persons with TBI or surrogates as per IRB protocol. A model system must include a Level 1 Trauma Center, acute neurosurgical care, comprehensive inpatient rehabilitation services, and multi-disciplinary rehabilitation and follow-up care. TBI was considered moderate to severe if there was documented evidence of post traumatic amnesia for greater than a day, loss of consciousness >30 min, a Glasgow Coma Scale (GCS) (26) score <13 in the Emergency Department, or intracranial neuroimaging abnormalities. An individual must meet the following criteria to be enrolled in the TBIMS NDB: be at least 16 years old, received care in a TBIMS center within 72 h of injury, and transferred directly from acute care to an affiliated inpatient rehabilitation program. For each participant enrolled in the TBIMS NDB, medical charts were reviewed and an in-person interview, with either the patient or a surrogate, was conducted to collect data on demographics, injury characteristics, and premorbid medical history. Follow-up interviews focusing on recovery of function were conducted at 1, 2, and 5 years post-injury with the participant or surrogate. A data quality review from the TBIMS NDB revealed systematic data entry errors at a single data collection site for variables related to determining command-following and this center was excluded from analysis (37 potential participants excluded). We included all other TBIMS NDB participants whose injury occurred in 2005 or later, who had not regained command-following by the time of their inpatient rehabilitation admission and had subscale scores from the Participation Assessment with Recombined Tools-Objective (PART-O) completed for at least two follow-up visits (at 1, 2, or 5 years post-injury) (**Figure 1**).

The primary analysis divided the sample into those who regained command-following during inpatient rehabilitation [Rehab Command-following (RCF)] vs. those that did not [No Rehab Command-following (nRCF)]. In addition, we conducted a secondary analysis (available in Supplementary Digital Content) that divided the cohort of individuals admitted to inpatient rehabilitation without command-following into those who did and did not regain command-following within 28 days post injury (TFC28, nTFC28, respectively) as this timeframe represents the accepted definition of "prolonged" DoC (6).

Instruments

At the time of participant or proxy consent for TBIMS NDB enrollment, acute care charts were reviewed for demographic and injury characteristics (e.g., age at injury, sex, race, living settings, comorbidities, years of education, time to follow commands, etc.). Additionally, the results of the following assessments were obtained from the TBIMS NDB.

Command-Following

The presence of command-following was determined using two TBIMS variables at the time of rehabilitation admission, consistent with prior TBIMS DoC studies (4, 6). The first variable was the date a participant exhibited command-following on two consecutive assessments within a 24-h period following TBI. This was determined by reviewing acute rehabilitation medical records for documented evidence of command-following on the Glasgow Coma Scale (GCS, command-following is indicated by a motor subscale score of 6) (26). The second variable was the Disability Rating Scale (DRS) motor score (which includes the same items as the GCS motor score, but is inversely scored such that a DRS score of 0 corresponds to command-following) collected at rehabilitation admission (27). Participants were included in the cohort if both variables indicated no evidence of command-following prior to or at the time of inpatient rehabilitation admission.

Participation

The Participation Assessment with Recombined Tools-Objective The PART-O was the main outcome measure of participation. The PART-O is a 17-item self-reported or proxy-reported questionnaire developed specifically for use in persons with TBI. It is administered at every follow-up data collection point for the TBIMS NDB (28, 29). The PART-O provides estimates of participation across three life domains: (1) Productivity—time spent working, at school or on homemaking activities; (2) Social Relations—time spent with friends, giving emotional support, and internet communication; and (3) Out and About—days spent outside the home for leisure, shopping, or other purposes. Items within each domain are averaged to achieve a subscale score that can range from 0 to 5, with higher scores signifying greater levels of participation (29). Subscale scores may be derived when more than 50% of the items are answered. The PART-O has reasonable psychometric properties of person (0.86) and item (0.99) reliability (28). An alternative Rasch-adjusted scoring method was also developed to convert the measure to a unidimensional scale (30). However, because the unidimensionality of participation is not clear (31), and participation may manifest differently for individuals with a DoC (14), the present study utilized scoring based on the three separate subscales.

Functional Status

The FIM is an 18-item standardized measure of self-care, mobility, and cognition, specifically examining level of assistance required in basic activities of daily living (32, 33). It was scored by clinical providers during inpatient rehabilitation and obtained via telephone interview with the participant or proxy in later

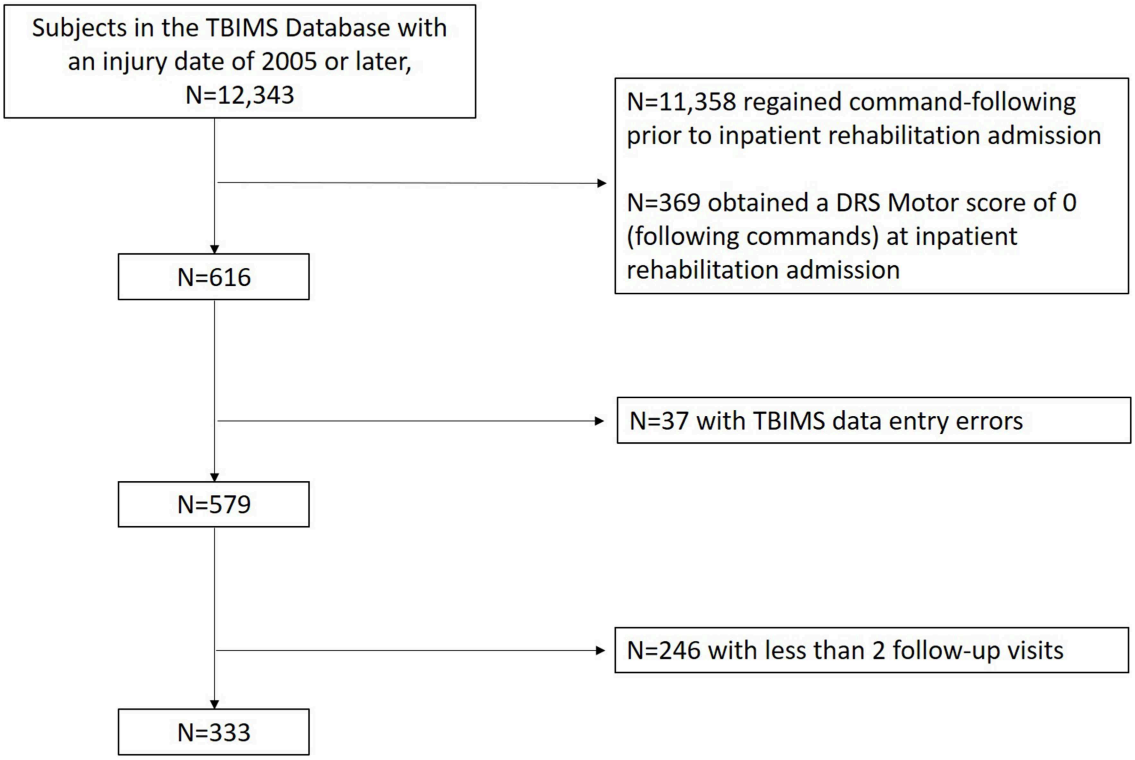

FIGURE 1 | Participant Flow Diagram.

TABLE 1 | Descriptive information for the groups defined by rehab status (Values are quartiles (25th/50th/75th percentiles) or as otherwise Indicated).

	Overall sample	**Rehab command-following**	**No rehab command-following**	***p***
n	333	229	104	
Age (Years)	22/30/46	22/30/46	20.25/28.500/46.750	0.345
Years of Education	11.750/12/15	11/12/15	12/12/15	0.332
Male (%)	74.5	76.9	69.2	0.139
Race (%)				0.807
White	65.2	66.4	62.5	
Black	15.0	15.7	13.5	
Asian/Pacific Islander	2.7	2.6	2.9	
Native American	0.9	0.9	1.0	
Hispanic origin	15.0	13.1	19.2	
Other	1.2	1.3	1.0	
GCS Total at ED Admission	3/6/8	3/6/8	3/5/9	0.931
Days spent in acute	20/27/38	19/25/33	25/36/47.250	<0.001
DRS on Admission to Rehab	21/23/24	21/22/24	21/23/25	<0.05
DRS on Discharge from Rehab	8/11/18	7/10/14.500	11/18.500/22.250	<0.001
FIM Motor at Rehab Admission	13/13/14	13/13/14	13/13/13	0.749
FIM Cognitive at Rehab Admission	5/5/5	5/5/5	5/5/5	0.676
FIM Motor at Rehab Discharge	17/40.500/60	27/49/62	13/16/50	<0.001
FIM Cognitive at Rehab Discharge	7/14/19	10/15/20.500	5/7/14.250	<0.001
Days spent in rehab	30/49/79	30/46/73.500	28.750/51.500/91.500	0.441

p, significance; GCS, Glasgow Coma Scale; ED, Emergency Department; DRS, Disability Rating Scale.

TABLE 2 | Results of cross-sectional analyses for groups defined by recovery of command-following in rehabilitation (Age, FIM Motor, and FIM Cognitive included as covariates in group comparison) x(sd).

Subscale	Year	Overall sample	Rehab command-following	No rehab command-following	Adjusted *p*	Effect size (Cohen's *d*)
Productivity	1	0.445 (0.66)	0.564 (0.720) $n = 201$	0.216 (0.440) $n = 91$	0.835	0.583
	2	0.572 (0.762)	0.707 (0.780) $n = 216$	0.305 (0.650) $n = 94$	0.763	0.560
	5	0.704 (0.858)	0.869 (0.880) $n = 146$	0.320 (0.650) $n = 51$	0.315	0.710
Social Relations	1	1.675 (1.047)	1.908 (0.990) $n = 201$	1.206 (1.020) $n = 91$	0.246	0.698
	2	1.699 (1.047)	1.899 (1.030) $n = 214$	1.259 (0.960) $n = 94$	0.222	0.643
	5	1.705 (1.133)	1.909 (1.120) $n = 146$	1.263 (1.030) $n = 51$	0.467	0.600
Out and About	1	1.112 (0.868)	1.310 (0.800) $n = 201$	0.755 (0.871) $n = 91$	0.608	0.664
	2	1.241 (0.871)	1.399 (0.830) $n = 214$	0.912 (0.860) $n = 94$	0.953	0.576
	5	1.438 (0.903)	1.586 (0.870) $n = 146$	1.116 (0.910) $n = 51$	0.879	0.528

Adjusted p, significance.

follow-ups. Scores are summed into a cognitive subscale (range: 5–35), a motor subscale (range: 13–91), and a total FIM score (range: 18–126), with higher scores representing a greater degree of independence.

Data Analysis

Demographic data for the early and late recovery groups were analyzed separately. A Shapiro-Wilk test revealed that age, years of education, and injury severity measures (i.e., GCS at admission, length of treatment in acute and rehab, and DRS and FIM scores at admission and discharge from rehab) were not normally distributed ($p < 0.001$). Therefore, these variables are reported as medians and interquartile ranges. Continuous demographic data were compared statistically using Mann-Whitney *U* test. Racial and gender compositions were compared using chi-squared tests of association. Cross-sectional analyses comparing the two rehabilitation groups on subscale PART-O scores (i.e., Productivity, Social Relations, Out and About) at each follow-up year were conducted with univariate analysis of covariance with the covariates of age, FIM Motor, and FIM Cognitive scores at time of follow-up. We also explored the relationship of functional status and participation at each follow-up where FIM Motor and Cognitive subscale scores were recoded into ordinal variables with three levels of performance. To better understand the relationship between functional independence and participation, we binned FIM Motor and Cognitive subscale scores into three levels and evaluated median PART-O scores at each FIM bin across subscales and follow-up years. The three FIM bins are based on categories of independence that reflect the underlying individual item rating definitions: Total Assistance Needed (Bin 1, Motor FIM scores = 18–38, Cognitive FIM scores = 5–14), Minimal/Moderate Assistance (Bin 2, Motor FIM scores = 39–77, Cognitive FIM scores = 15–29), and Complete Independence (Bin 3, Motor FIM scores = 78–91, Cognitive FIM scores = 30–35).

Longitudinal analyses were conducted as separate mixed-effects backward elimination models ($p < 0.05$ cutoff) for each of the three PART-O subscales (Productivity, Social Relations, and Out and About) as dependent variables. All three models began with the same fixed predictors and variances/covariances of random terms. Fixed terms consisted of our primary variable of interest, Command-Follow group (command-following recovered during rehabilitation [RCF] vs. command-following not recovered during rehabilitation [nRCF]), as well as year of follow-up (linear and quadratic function), age at injury, gender, length of stay in inpatient rehabilitation, and length of stay in acute care facility. Scores on the FIM Motor and FIM Cognitive subscales were included as time-varying covariates. Two-way interactions of group by year of follow-up, group by age at injury, and age at injury by year of follow-up as well as a three-way interaction of group by age at injury by year of follow-up were also included. The initial random terms were subject intercept, subject's linear term for year of follow-up, and their correlation. If the interaction between a fixed predictor and year of follow-up was significant, that would indicate that the linear trajectory of participation varied with the predictor variable. If a predictor term did not have a significant interaction with year of follow-up, but did have a significant main effect, then that would indicate that the predictor had the same influence on participation regardless of when it was measured, but that it did not predict the trajectory of participation over time. The backward elimination approach was a limited one intended primarily to pretest and remove, if non-significant, higher order interactions, quadratic terms, covariate terms, and random effects. Non-significant terms with the highest *p* value were systematically removed in a stepwise manner until only significant terms remained. By convention, non-significant lower order terms subsumed within significant higher order terms are permitted to remain in the model. Percent of dependent variable variance accounted for by fixed and random predictor terms were computed. Model residuals from fixed and random term predicted values were checked graphically for adherence to assumptions of normality and homoscedasticity, and to assess model fit. Only participants with at least two time points with non-missing dependent variable scores qualified for inclusion in any of the longitudinal analyses.

For the secondary analysis, we repeated the longitudinal analyses with the groups defined by those who did and did not regain command-following within 28 days post injury (TFC28, nTFC28 respectively) rather than those who did and did not regain command-following during inpatient rehabilitation.

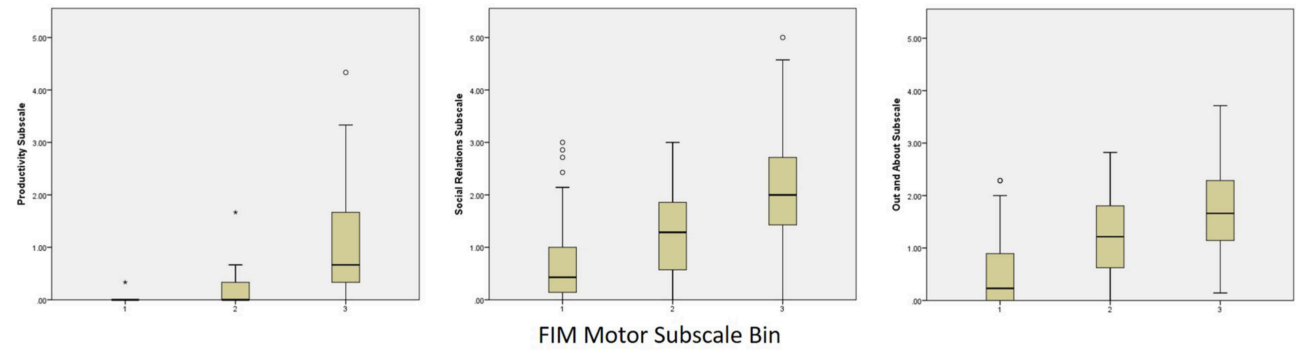

FIGURE 2 | Binned FIM Motor Subscale Performance at Year 5 by PART-O Subscale. FIM bins are as follows: (1) Total Assistance Needed (FIM Motor subscale scores 18–38), (2) Minimal/Moderate Assistance (FIM Motor subscale scores 39–77), (3) Complete Independence (FIM Motor subscale scores 78–91).

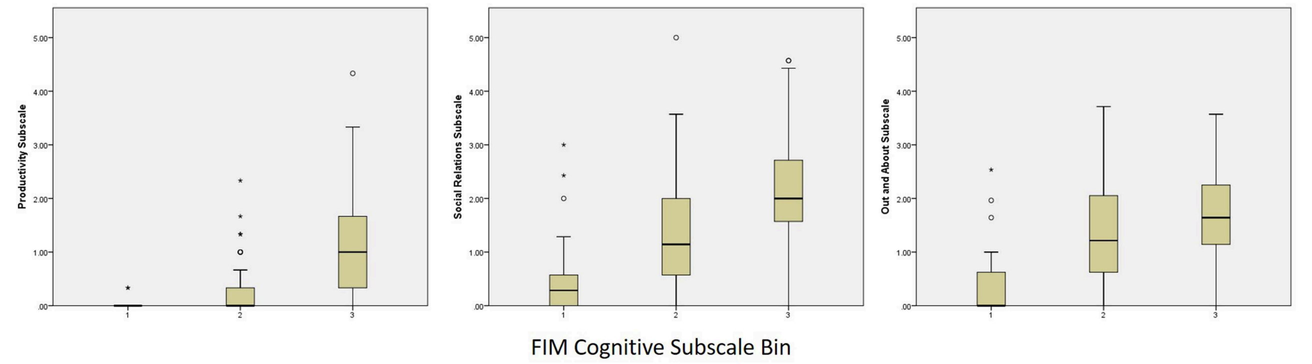

FIGURE 3 | Binned FIM Cognitive Subscale Performance at Year 5 by PART-O Subscale. FIM groups are as follows: (1) Total Assistance Needed (FIM Cognitive subscale scores 5–14), (2) Minimal/Moderate Assistance (FIM Cognitive subscale scores 15–29), (3) Complete Independence (FIM Cognitive subscale scores 30–35).

Analyses were conducted using SAS, version 9.4, and SPSS, version 24.

RESULTS

As the primary measure of this study was introduced into the database in 2007, only subjects with an injury date of 2005 or later were included as they could complete the PART-O measure at the 2nd and 5th year follow-up. Of 12,343 participants with a 2005 injury date or later in the TBIMS-NDB (database as of July 8th, 2019), 11,358 regained command-following before rehabilitation admission and were excluded. After further controlling for DRS motor scores on admission to rehabilitation and number of completed follow-up visits, 333 subjects met inclusion criteria for this study (**Figure 1**). Demographic and injury characteristic data are presented separately for the RCF ($n = 229$) and nRCF ($n = 104$) groups. The RCF group had a shorter length of stay in acute care ($p < 0.001$). In addition, the RCF group was less disabled on rehabilitation admission and discharge, as measured by the DRS (DRS at admission: $p < 0.05$; DRS at discharge: $p < 0.001$), and more independent at time of rehabilitation discharge (FIM Motor: $p < 0.001$; FIM Cognitive: $p < 0.001$), compared to the nRCF group. Demographic and injury characteristics for the groups determined by presence, or not, of command-following at rehabilitation discharge, are presented in **Table 1** and, for the groups defined by days post injury, in **Supplementary Table 1**.

Cross-Sectional PART-O Subscale Performance

Cross-sectional analyses comparing PART-O subscale performance at each year showed that, although descriptively the RCF group had higher levels of participation, there were no significant differences in levels of participation between groups in any subscale at any year despite moderate effect sizes (**Table 2**). Participation scores across subscales and years were notably low with scores ranging from 0.021–1.91 (subscale range: 0–5). Results were similar when groups were assigned based on recovery of command-following within 28 days post-injury (**Supplementary Table 2**).

Categorized performance on the FIM Motor and FIM Cognitive subscales was examined in relation to performance on the PART-O subscales and revealed that participation levels remained low even among subjects who reached ceiling levels of the FIM. In fact, the highest levels of participation across

TABLE 3 | Longitudinal mixed-effects model for PART-O Productivity subscale.

Predictor	Unstandardized partial regression coefficient	95% CI	SE	p
Year	0.035	0.011, 0.058	0.012	0.0036
Age	−0.006	−0.009, −0.003	0.002	0.0003
FIM Motor	0.009	0.006, 0.012	0.002	<0.0001
FIM Cognitive	0.017	0.008, 0.025	0.004	0.0003

CI, confidence interval; SE, standard error; p, significance.

TABLE 4 | Longitudinal mixed-effects model for PART-O Social Relations subscale.

Predictor	Unstandardized partial regression coefficient	95% CI	SE	p
FIM Motor	0.011	0.007, 0.015	0.002	<0.0001
FIM Cognitive	0.029	0.016, 0.041	0.006	<0.0001

CI, confidence interval; SE, standard error; p, significance.

TABLE 5 | Longitudinal mixed-effects model for PART-O Out and About subscale.

Predictor	Unstandardized partial regression coefficient	95% CI	SE	p
Year	0.086	0.029, 0.144	0.029	<0.005
FIM Motor	0.020	0.018, 0.022	0.001	<0.0001
Age	−0.001	−0.005, 0.004	0.002	0.729
Year by Age interaction	−0.002	−0.003, 0.000	0.001	<0.05

CI, confidence interval; SE, standard error; p, significance.

subscales (i.e., scores of 4–5) were attained by fewer than 10 persons across domains and follow-up years. These data were plotted as box and whisker plots in **Figures 2**, **3** for Motor and Cognitive FIM, respectively.

Longitudinal PART-O Subscale Performance

Contrary to our hypothesis, there were no between-group longitudinal differences on any of the participation subscales. The FIM Motor subscale was the only variable independently positively associated with participation across subscales.

In the backward elimination model for the PART-O Productivity subscale, both motor and cognitive FIM scores at follow-up predicted level of productivity ($p < 0.0001$ and $p = 0.0003$ respectively, **Table 3**) with each showing a positive relationship to productivity (estimated partial regression coefficient $= \beta = 0.009$ and 0.017, respectively). In addition, there was a negative main effect of age ($p = 0.0003$, $\beta = -0.006$) with older individuals having less productivity, as well as a positive main effect of year of follow-up ($p = 0.004$, $\beta = 0.035$) indicating that productivity improved over time. The random terms of subject intercept and subject's linear term for year of follow-up were also retained (uncorrelated). All the retained fixed effects in the model accounted for 33% of the variance in PART-O productivity (random and fixed together accounted for 81%).

Follow-up motor and cognitive FIM scores ($p < 0.0001$ for both, **Table 4**) predicted Social Relations participation, with each showing a positive relationship to social participation ($\beta = 0.011$ and 0.02861, respectively). The random terms of subject intercept and year of follow-up were also retained (correlated $r = -0.45$). The percent variance of social participation accounted for by all of the retained fixed effects in the model was 32.189% (random and fixed accounted for 88%).

On the Out and About subscale, higher scores on the follow-up FIM Motor subscale were associated with higher levels of participation ($p < 0.0001$, $\beta = 0.020$, **Table 5**). There was also a main effect of year of follow-up ($p = 0.0034$) and an interaction between age at injury and year of follow-up ($p = 0.041$), whereby the trajectory of increase in follow-up years was sharper for younger participants than for older participants. The random terms of subject intercept and subject's linear term for year of follow-up were also retained (uncorrelated). The percent variance of the PART-O Out and About subscale accounted for by all the retained fixed effects in the model was 42.764% (random and fixed together accounted for 83%).

Similarly, in the secondary analyses (when the groups were defined by recovery of command-following by days post injury rather than command-following before or after rehab discharge) there were no significant effects of interest involving group except for an interaction between group and age for the Out and About subscale and a complex three-way interaction of group, age, and linear time for the Productivity subscale (**Supplementary Tables 3–5**).

For all analyses, residuals from values predicted by the fixed effects as well as from values predicted by the combined fixed and random effects were reasonably normally distributed in accordance with significance test assumptions and indicated good model fit.

DISCUSSION

We found that persons admitted to inpatient rehabilitation without command-following have profoundly impaired levels of participation years later, even when compared to normative participation levels of individuals currently treated in inpatient rehabilitation (29). Although there was a trend, with moderate effect sizes, in the expected direction of greater participation in the group recovering command-following during rehabilitation, this finding did not reach statistical significance. This result was unexpected, as a substantial proportion of persons who recover command-following during inpatient rehabilitation recover functional independence in the 5 years following injury (5). Notably, consistent with the primary analysis, our secondary analysis of groups defined by whether command-following was recovered before 28 days post injury, did not find a clear effect of group on productivity, or interactions between group and time post injury. However, differences in the results of two analyses, such as a complex 3-way interaction between group, time, and age for the Productivity subscale, suggest more work is needed to better understand the implications of applying varying operational definitions to this patient population. In summary, participation among persons admitted to acute inpatient rehabilitation with traumatic DoC is very low up to 5 years post-injury, even in the subgroup of persons who recover functional independence.

Functional independence was the strongest independent contributor to levels of participation. However, even individuals who regained functional independence demonstrated low levels of participation. This is consistent with prior studies showing that although mobility and participation are related, persons who are independent in this domain have low levels of participation (34). Furthermore, in a randomized control trial of patients with severe TBI undergoing a community rehabilitation program, global function and psychological well-being improved in the experimental group, but participation did not (35). One possible explanation for this unexpected result is that the FIM, and other measures of physical and cognitive function, do not comprehensively measure the complex integration of skills, cognitive processes, physical abilities, and behaviors required to participate in societal and work environments. The high degree of variability in levels of participation among the highest functioning subjects suggests that idiosyncratic qualities of the individual and their environment (e.g., social or personal factors) may be meaningful. A closer examination of non-injury factors (e.g., personality characteristics of caregivers, pre- and post-injury levels of spirituality, etc.) which encourage or inhibit participation may be necessary to improve interventions for this population. Alternatively, an examination of the minority of individuals who do have high levels of functioning and relatively high levels of participation may provide valuable information for intervention development. Future studies are needed to fully determine the quality of the relationship between functioning and participation (i.e., mediator vs. moderator) across the spectrum of injury severity.

The current reimbursement model of health care in the United States focuses on independence in mobility and activities of daily living rather than societal engagement. This focus affects what practitioners prioritize as treatment goals, and therefore may result in failure to address the needs of individuals recovering from a traumatic DoC, especially in post-acute stages. The results of our study suggest that regaining functional independence may be a necessary but insufficient milestone for returning to participatory activities. Rehabilitation aimed at improving participation could be more precisely targeted toward individual's current abilities and the goals deemed valuable for the individual with DoC and their caregiver. For example, clinicians may focus on recovery of basic functions and mobility in some situations and on supported community engagement or independent participation in others. In that latter case, providing access to day-programs, specialized transportation, or supportive social internet sites may be appropriate for higher functioning persons with ongoing cognitive impairments (36, 37). Although still well-below the averages of normative samples, the PART-O Social Relations subscale had higher scores than Productivity and Out and About, suggesting that this domain is the most likely to be modifiable in the setting of impaired cognition or physical function. The effectiveness of cognitive and social therapies aimed at improving participation among persons with a DoC requires further investigation. Furthermore, because participation invariabley involves the interaction between individuals and environment, participation, and its conceptualization, may vary across social supports, cultural values, and healthcare models (38). Substantial global variability in rehabilitation service delivery makes it difficult to quantify the role of rehabilitation in recovery of participation (25), especially at the international level.

Although participation does increase in the 5 years post-injury, this increase is not substantial. This finding may be the result of the constraints of the PART-O as a measurement tool for persons with the most severe injuries. Prior studies reporting functional improvement among persons with a DoC have typically employed the FIM, which was developed to monitor the ability to complete basic activities of daily living in inpatient settings (5, 6). However, the PART-O was developed to measure frequency of engaging in activities in a community setting (4). The behavioral profile of persons with severe brain injury may fall below the floor level of measurement for the PART-O, and therefore, small changes in participation may not be reflected in PART-O scores. For example, an individual may be able to comprehend basic information (as measured by the FIM), while not being able to work for money (as assessed by the PART-O). Furthermore, it is possible that the PART-O does not sufficiently capture the variety of ways that low functioning individuals may participate in society, such as participation in a day program as opposed to being competitively employed or studying toward a degree. Similarly, it is possible that individuals may experience residual motor impairment severe enough to compromise participation without impairing FIM-based activities. Granular measures of participation, that account for what persons with severe TBI and caregivers consider meaningful improvement are needed to develop, apply, and evaluate rehabilitation interventions consistent with the ICF guidelines. Although some persons may not achieve complete reintegration into the workforce or social spheres, a tool that evaluates incremental steps toward these goals is needed.

In interpreting and applying the study findings, several limitations are relevant. Only individuals treated at an acute care hospital and transferred directly to acute inpatient rehabilitation for specialized brain injury care were studied. Clinical services may not be provided in a uniform manner, participants may drop out of the study over time, or inpatient rehabilitation may not be offered for some persons who are not following commands. This may lead to a selection bias or confounding in outcome measures and group assignments. Groups differences in demographic characteristics and data on important pre-injury characteristics (e.g., resilience) were lacking, which may have confounded the analysis (39, 40). Therapy services and medical follow-up in the years after rehabilitation discharge may also differ and were not studied. It is possible that changes to the provision of healthcare services occurred in the data collection window, thus introducing temporal effects (i.e., 2005–2017). However, there have been no major, systematic changes to treatment or access to rehabilitation for persons with impaired consciousness over this time period, making it unlikely that our results were affected by the data collection window. Lastly, self-report and surrogate responses were collapsed for the PART-O. Although few persons with TBI provided self-report PART-O responses, self-report responses may systematically differ from surrogate responses, introducing measurement error, though past work has found that surrogate and patient reports are similar (41). Further, while surrogates may accurately report productive activities and activities outside of the home, given their likely involvement in these activities with the participant, they may not be able to as accurately report on social relationships, which can occur in person, over the phone, or online and may not require surrogate support. We examined participation up to 5 years post-injury. It is likely that participation continues to improve over time, and outcomes at 10 years and beyond should be examined as data become available. We analyzed data from the TBIMS, which provides longitudinal outcome measures across the lifespan of individuals admitted to inpatient rehabilitation facilities in the United States. As a result, our findings may not be applicable outside this system of care. However, in a recent exhaustive report on the global burden of TBI, the issues we identified here (e.g., the need for better approaches to assessing participation, rehabilitation approaches that target the specific needs of patients with DoC, etc) appear to be relevant world-wide (42).

In conclusion, participation remains extremely limited among persons who have experienced a traumatic DoC and are admitted to inpatient rehabilitation with persistent impairments in level of consciousness. This is the case even for persons who regain command-following during rehabilitation and for those who recover functional independence. The incongruity between performance on functional and participatory measures suggests that social or psychological factors as well as the complex integration of behavior, cognition and mobility may be meaningful determinants of levels of participation in the years after severe brain injury.

DATA AVAILABILITY STATEMENT

The datasets generated for this study can be found in the Traumatic Brain Injury Model Systems National Data and Statistical Center (https://www.tbindsc.org/Researchers.aspx).

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Partners IRB. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

YB, KE, CM, JW, JG, FH, and RN-R contributed conception and design of the study. CM organized the database. JL performed the longitudinal statistical analyses. CM, YB, KE, and JL wrote the first draft of the manuscript. All authors contributed to manuscript revision, read and approved the submitted version.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2019.01314/full#supplementary-material

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Effect of Cognitive Disability and Ambulation Status on Functioning in Moderate-to-Advanced Parkinson Disease

Chen Yu Wang[1], *Lung Chan*[1,2], *Dean Wu*[1,2], *Wen-Chou Chi*[3,4], *Chia-Feng Yen*[3,5], *Hua-Fang Liao*[3,6], *Chien Tai Hong*[1,2*†] and *Tsan-Hon Liou*[3,7,8,9*†]

[1] Department of Neurology, Shuang Ho Hospital, Taipei Medical University, New Taipei City, Taiwan, [2] Department of Neurology, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan, [3] Taiwan Society of International Classification of Functioning, Disability and Health, TSICF, New Taipei City, Taiwan, [4] Department of Occupational Therapy, Chung Shan Medical University, Taichung, Taiwan, [5] Department of Public Health, Tzu Chi University, Hualien City, Taiwan, [6] School and Graduate Institute of Physical Therapy, College of Medicine, National Taiwan University, Taipei, Taiwan, [7] Department of Physical Medicine and Rehabilitation, Shuang Ho Hospital, Taipei Medical University, New Taipei City, Taiwan, [8] Department of Physical Medicine and Rehabilitation, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan, [9] Graduate Institute of Injury Prevention and Control, College of Public Health, Taipei Medical University, Taipei, Taiwan

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Edited by:
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****Correspondence:***
Chien Tai Hong
ct.hong@tmu.edu.tw
Tsan-Hon Liou
peter_liou@s.tmu.edu.tw

† These authors have contributed equally to this work

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Background: As the disease progresses to moderate to advanced stages, people with Parkinson's disease (PwP) are likely to have various degrees of disability due to the motor and non-motor symptoms, such as ambulatory difficulty and cognitive impairment. The objective of this study was to investigate the impact of cognition and ambulation status on the functioning and disability of PwP using the World Health Orgnaization Disability Assessment Schedule 2.0 (WHODAS 2.0).

Materials and Methods: A group of 10,581 PwP with Hoehn and Yahr Staging 3 and above were collected from a database of disability evaluation and functional assessment using the Taiwan Data Bank of Persons with Disability between July 2012 and October 2018. WHODAS 2.0 was administered and all PwP were grouped based on their ambulatory status, which was assessed by 3-m back and forth walk and cognitive ability, assessed by WHODAS 2.0 first domain with cut-off level at 58.

Results: Non-ambulation and cognitive disability contributed independently to disability in all aspects of WHODAS 2.0 survey, including self-care, getting along with others, performing life activities and participation in society. Compared to ambulation status, cognitive disability had a greater negative impact on functioning in all aspects.

Conclusion: Cognitive disability was associated with greater disability in moderate to advanced PwP than non-ambulatory status. The results of this study may indicate that cognition preservation is essential to ameliorate functional impairment and disability in moderate to advanced PwP.

Keywords: Parkinson's disease, disability, cognition, ambulation, WHODAS 2.0

INTRODUCTION

Parkinson's disease (PD) is the second most common neurodegenerative disease comprising of motor and non-motor features due to dopaminergic and non-dopaminergic deficiencies (1). In industrialized countries, the prevalence of PD is around 0.3% in the general population and 1% in those older than 60 (2). In 2016, 6.1 million individuals were affected by PD, causing 3.2 million Disability-adjusted-life-years. Global burden of this condition is expected to increase as a result of longer life expectancies, longer disease duration, and environmental factors (3).

Disability is defined as "the state of decreased functioning associated with disease, disorder, injury, or other health conditions, which in the context of one's environment is experienced as an impairment, activity limitation, or participation restriction", hence it is fundamental to use a comprehensive assessment tool to examine all aspects that may hinder a person's ability to carry out normal daily activities, whether it may be instrumental activities of daily living, social participation, or environmental contributions (4). The WHO Disability Assessment Schedule 2.0(WHODAS 2.0) is a generic assessment tool developed in accordance to the conceptual framework of the International Classification of Functioning, Disability, and Health and is used to produce standardized disability levels and profiles applicable across different populations and health conditions from various countries including Taiwan with good reliability and validity (5–8). WHODAS 2.0 encompasses six domains of life: cognition (understanding and communicating), mobility (moving and getting around), self-care (hygiene, dressing, eating and staying alone), getting along (interacting with other people), life activities (domestic responsibilities, leisure, work, and school), and participation (joining in community activities). In Taiwan, The Functioning Disability Evaluation Scale Adult Version (FUNDES-Adult) was modified and translated from the WHODAS 2.0 with some minor modifications made to account for the Chinese culture. Domain 7 (environmental attributes) and domain 8 (motor action, capability and capacity scores) were added in order to increase comprehensiveness and to account for perceived environmental barriers (5, 6, 8, 9).

Regarding moderate and advanced PD, disability is traditionally thought to be associated with the core motor features of tremor, rigidity, bradykinesia, and postural instability; out of these features, postural instability is found to be most common in this population and a strong prognostic factor of determining progression to disability (10, 11). However, non-motor aspects of PD can also profoundly impact a person's level of disability, although the extent of their contribution can be oftentimes underestimated or even overlooked (12). Amongst the non-motor symptoms, dementia presents insidiously over the disease course, occurring in up to 40% of people with PD (PwP), which is six times higher than aged matched controls (13, 14). In The Sydney multicenter study of PD, the cumulative prevalence of PD dementia (PDD) is 83% over 20 years and the prevalence increases as age advances (15, 16). Both patients and caregivers frequently report cognitive decline as one of their greatest concerns and a major unmet need despite increasing recognition of PD as much more than a motor disorder (17). It has also been proposed that there are inter-relationships between motor function and cognition based on observations functional mobility is significantly correlated with cognitive impairment and that those with cognitive impairment demonstrate poorer motor function compared to matched PD patients without cognitive impairment (18, 19). Others have found faster rate of cognitive decline in those with postural instability (20). In addition, studies that looked at dual tasking found that even when they are treated optimally, PwP showed deterioration in gait parameters and that the degree of deterioration was correlated with baseline cognitive and mobility status (21). As one of the leading sources of disability globally, it is of utmost importance to understand the association between the major symptoms of PD and the emerging disability in order to provide better care and delay functional limitations. This current study investigated the disability of moderate and advanced PwP at variable cognitive and walking status, which were assessed by WHODAS 2.0 with the objective of identify the associations between ambulation, cognitive status, and disability.

METHODS

Participants and Data Collection

The data from a total of 19,196 moderate and advanced PwP (Hoehn and Yahr, H&Y, stage 3–5) were collected between July 2012 and October 2018 from a registry of disability evaluation and functional assessment established by the Taiwan Data Bank of Persons with Disability. The database was established by the Ministry of Health and Welfare in Taiwan which stipulates that only PwP with modified H&Y stages 3, 4, and 5 are eligible to receive disability certification and corresponding benefits. These may include all persons who are eligible for the first time (first time reaching the disease statue of H&Y stages 3–5) and those who are extending their disability certification. Applicants with PD were selected from the database via the International Classification of Diseases (ICD), Ninth Revision, Clinical Modification (ICD-9-CM) and ICD tenth Revision, Clinical Modification (ICD-10-CM) diagnosis codes ICD-9-CM 332 and ICD-10-CM G20. After excluding those with secondary parkinsonism (ICD-9-CM 332.1), omitted or missing data regarding the patient's ambulatory status, WHODAS 2.0 domains, and those who refused to answer, 10,581 subjects were analyzed (**Figure 1**).

The FUNDES-Adult was administered by multiple certified personnel from different hospitals, including social workers, physical, and occupational therapists from July 2012 and October 2018. For each study participant, basic demographic data including age, gender, residence, employment status, education level, family economic status, urbanization level, modified H&Y stage were collected. Following this, the six WHODAS 2.0 domains of cognition (domain 1), mobility (domain 2), self-care (domain 3), getting along with others (domain 4), household activities component of the life activities domain (domain 5-1, household activities), and participation in society (domain 6) were obtained by asking the participants to rate the extent to

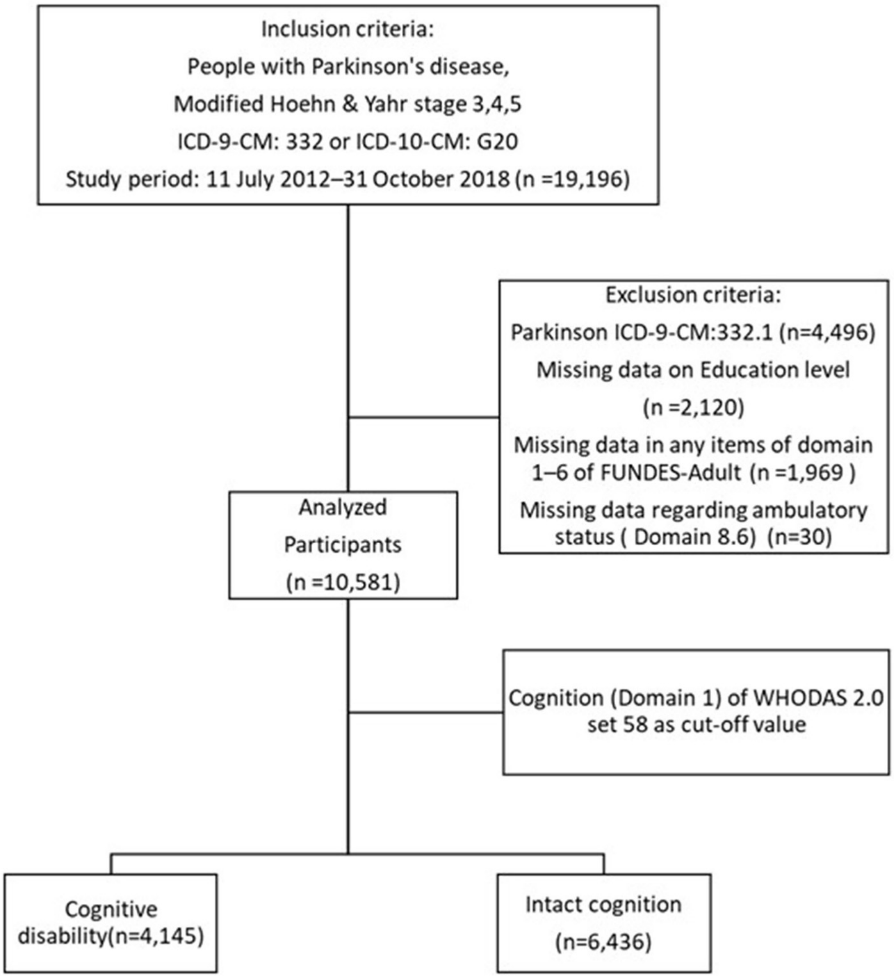

FIGURE 1 | The study participants selection flow chart.

which their disabilities interfered with their lives in the preceding 30 days. Each domain consisted of 4–8 questions and a 5-point scale was used to assess the level of difficulty in the activities in each domain (0 = no difficulty, 1 = mild difficulty, 2 = moderate difficulty, 3 = severe difficulty, 4 = extreme difficulty). For example, domain 1 (cognition) consists of assessments of the following items: concentrating on something for 10 min, remembering to do important things, analyzing, and finding solutions to problems in day-to-day life, learning a new task, understanding what people say and starting and maintaining a conversation. For each item in the cognition domain, a score ranging from 0 to 4 is assigned. The total score is the sum of all the items, which ranges from 0 (best performance) to 20 (worst performance). The absolute score would be transformed to the standardized score for each domain were calculated based on the manual for WHODAS and ranged from 0 to 100, with higher scores indicating greater difficulty. The standardized scores were then summated to form the total score. The questionnaire was administered to the participants or the participants' caregivers if the participants could not answer the questions themselves. Domain 8.6 of the FUNDES-Adult was obtained to determine the patient's walking status, which is assessed by asking the applicant to walk in a straight line for 3 m and then return to the initial location on the spot in front of the interviewer. This aspect of motor capacity was judged with or without assistive technology and personal assistance. Walking statuses were defined as ambulatory/assisted ambulatory (domain 8.6 score from 0 through 3) and non-ambulatory (score of 4) if extreme difficulty is encountered and total assistance is need in an attempt to walk.

Statistical Analysis

The optimal cut-off point on the Receiver Operating Characteristic (ROC) curve was determined using the Youden's index for the highest sensitivity and specificity in predicting cognitive disability in PwP by the ambulatory status based on their score of cognition (WHODAS 2.0 domain 1). The cut-off value was 58 with area under curve was 0.77, with sensitivity and specific of 62 and 79%, respectively (**Figure 2**). Demographic characteristics of age and gender were employed via the χ^2 test

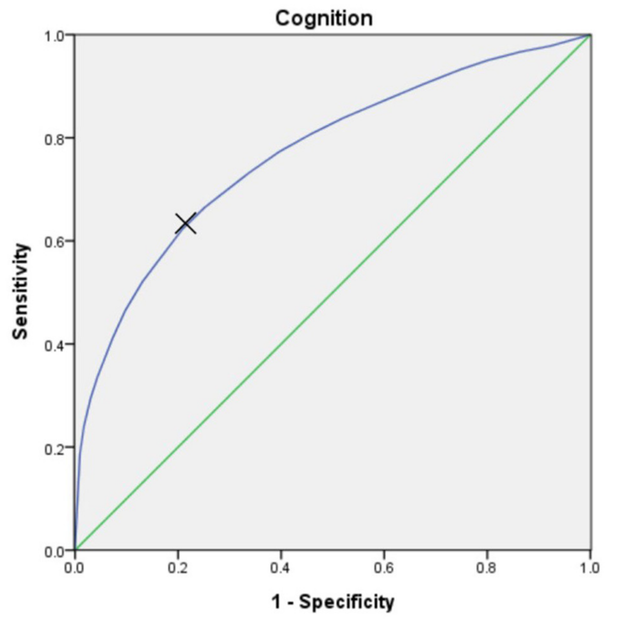

FIGURE 2 | The Receiver Operating Characteristic (ROC) curve, which was utilized to predict the cognitive disability (score of WHODAS 2.0 domain 1) in PwP by ambulatory status. At the cut-off value of 58, the area under the curve was 0.77, with sensitivity and specificity of 62% and 79%, respectively.

and one-way ANOVA test were used for comparisons between groups. Non-parametric regression was applied to compare the impact of cognition and ambulation on different WHODAS 2.0 domains. SAS (version 9.2, SAS institute, Inc., Cary, NC, USA) was utilized to perform the analyses and statistical significance was set at $p < 0.05$.

RESULTS

Of the analyzed 10,581 PwP, 4,145 were categorized as having cognitive disability and the other 6,436 were considered cognitively intact using the cut-off value at 58 score of the cognition domain (domain 1) in WHODAS 2.0. The mean age was 76.4 ± 8.3 years old in the PwP with cognition disability, compared to 71.1 ± 9.9 years old in the cognition intact counterpart. Demographic data of these two groups revealed that the gender distribution was similar; however, significant differences were noted for age, education level, work status residence, severity of disability and modified H&Y stage. All domains of the WHODAS 2.0 were significantly higher in those with cognitive disability than those without, representing higher disability levels in all aspects of daily living (**Table 1**).

TABLE 1 | Demographic data of all the study participants.

	Cognitive disability ($n = 4,145$)	Intact cognition ($n = 6,436$)	*p*-value
Female	2,104 (50.8)	3,205(49.8)	0.33
Age (y/o)	76.4 ± 8.3	71.1 ± 9.9	<0.001
18–64	411 (9.9)	1,690 (26.3)	
Education			<0.001
College or higher	92 (2.2)	131 (2.0)	
Senior high school	305 (7.4)	552 (8.6)	
Junior high school	378 (9.1)	1,125 (17.5)	
Primary school	2,550 (61.5)	4,033 (62.7)	
No education	820 (19.8)	595 (9.3)	
Residence			<0.001
Community dwelling	3,336 (80.5)	6,044 (93.9)	
Institution	809 (19.5)	392 (6.1)	
Urbanization level			<0.001
Rural	567 (13.7)	724 (11.3)	
Suburban	1,505 (36.3)	2,219 (34.5)	
Urban	2,073 (50.0)	3,493 (54.3)	
Work status			<0.001
Employment	13 (0.3)	219 (3.4)	
Unemployment	4,132 (99.7)	6,217 (96.6)	
Family economic status			0.51
General	4,112 (99.2)	6,392 (99.3)	
Middle low and low	33 (0.8)	44 (0.7)	
Modified H&Y Stage			<0.001
Stage 3	879 (21.2)	3,052 (47.4)	
Stage 4	1,658 (40.0)	2,737 (42.5)	
Stage 5	1,608 (38.8)	647 (10.1)	
WHODAS 2.0			
Cognition (domain 1)	81.1 ± 14.2	29.0 ± 17.1	<0.001
Mobility (domain 2)	75.3 ± 22.8	47.8 ± 24.9	<0.001
Self-care (domain 3)	52.6 ± 34.1	30.7 ± 25.2	<0.001
Getting along (domain 4)	83.8 ± 19.7	44.2 ± 27.0	<0.001
Life activities (domain 5-1)	85.2 ± 32.7	60.6 ± 37.9	<0.001
Participation in society (domain 6)	62.1 ± 23.1	40.4 ± 21.1	<0.001
Summary score	72.8 ± 15.2	40.8 ± 16.3	<0.001

PwP, People with Parkinson's disease; H&Y, Modified Hoehn-Yahr Stage; WHODAS, WHO Disability Assessment Scale. Data was presented as number (percentage) or mean ± standard deviation.

Further taking walking status into the analysis for the impact on disability, the overall PwP were grouped according to the combination of two conditions: intact cognition/cognitive disability and ambulatory/non-ambulatory status (**Table 2**). There were 1,231 patients (11.6%) categorized into the cognitive disability/ambulatory or assisted ambulatory group, 4,673 (44.2%) ambulatory or assisted ambulatory/intact cognition, 2,914 (27.5%) in the cognitive disability/non-ambulatory group and 1,763 (16.7%) in the intact cognition/non-ambulatory group. There were statistically significant age differences within the four groups, with non-ambulatory and cognition disability PwP being the oldest (77.6 ± 7.7 years old) and the ambulatory and intact cognition group being the youngest (69.7 ± 10.1 years old, p for trend). We found that the presence of cognitive disability is associated with higher individual domain and total scores in both ambulatory and non-ambulatory groups ($p < 0.05$). Non-ambulatory PwP with cognitive disability had the highest level of disability (76.5 ± 14.4), followed by ambulatory PwP with

TABLE 2 | Subgrouping of all study participants based on ambulation and cognition, *n* = 10,581.

	Ambulatory		**Non-ambulatory**		***p* for trend**
	Cognitive disability (*n* = 1,231)	**Intact cognition (*n* = 4,673)**	**Cognitive disability (*n* = 2,914)**	**Intact cognition (*n* = 1,763)**	
Female	594 (48.3)	2,272 (48.6)	1,510 (51.8)	933 (52.9)	0.46
Age (y/o)	73.6 ± 8.8	69.7 ± 10.1	77.6 ± 7.7	75.0 ± 8.3	<0.001
H&Y Stage					<0.001
Stage 3	533 (43.3)	2,677 (57.3)	346 (11.9)	375 (21.3)	
Stage 4	587 (47.7)	1,815 (38.8)	1,071 (36.8)	922 (52.3)	
Stage 5	111 (9.0)	181 (3.9)	1,497 (51.4)	466 (26.4)	
WHODAS 2.0					
Cognition (domain 1)	73.6 ± 11.5	27.1 ± 17.0	84.2 ± 14.0	34.1 ± 16.4	<0.001
Mobility (domain 2)	61.4 ± 22.4	41.2 ± 21.7	81.2 ± 20.3	65.4 ± 24.1	<0.001
Self-care (domain 3)	42.1 ± 28.9	27.3 ± 22.3	57.1 ± 35.2	39.6 ± 29.9	<0.001
Getting along (domain 4)	74.7 ± 22.1	40.2 ± 25.6	87.7 ± 17.2	54.9 ± 27.8	<0.001
Life activities (domain 5-1)	80.9 ± 33.9	55.7 ± 36.1	87.0 ± 32.0	73.6 ± 39.5	<0.001
Participation in society (domain 6)	55.4 ± 21.7	37.8 ± 20.3	64.9 ± 23.0	47.2 ± 21.6	<0.001

WHODAS, WHO Disability Assessment Scale; H&Y, Hoehn and Yahr Stage. Data was presented as number (percentage) or mean ± standard deviation.

TABLE 3 | Non-parametric regression comparing the effects of cognition and ambulation on WHODAS domains 3–6.

	Self-care (domain 3)			**Getting along (domain 4)**			**Life activities (domain 5-1)**			**Participation in society (domain 6)**		
	β	**SE**	***P*-value**	**β**	**SE**	***P*-value**	**β**	**SE**	***P*-value**	**β**	**SE**	***P*-value**
Cognitive disability (ref = Intact cognition)	14.7	0.7	< 0.001	35	0.5	< 0.001	18.1	0.8	< 0.001	22	0.6	< 0.001
Non-ambulatory (ref= Ambulatory)	10.6	0.7	< 0.001	12	0.6	< 0.001	11.3	0.8	< 0.001	11.3	0.6	< 0.001
Age ≥ 65 (ref = 18–64)	−2.0	0.9	0.02	1.1	0.7	0.12	5.2	1.0	< 0.001	−7.8	0.8	< 0.001
Institution Residence (ref = Community dwelling)	3.3	1.0	< 0.001	2.0	0.8	0.01	2.8	1.1	0.01	0.7	0.9	0.40
Urbanization level												
Suburban (ref = urban)	0.6	0.6	0.36	−0.5	0.5	0.32	−1.0	0.7	0.15	0.2	0.6	0.77
Rural (ref = urban)	−3.0	0.9	0.002	−1.3	0.7	0.07	−2.2	1.1	0.03	−1.7	0.8	0.04
Education ≤6 years (ref ≥ 6 years)	1.6	0.8	0.06	−0.7	0.6	0.26	0.8	0.9	0.36	−1.1	0.7	0.12
Modified H&Y Stage												
Stage 4 (ref = Stage 3)	2.0	0.7	0.003	3.2	0.5	< 0.001	5.8	0.8	< 0.001	3.4	0.6	< 0.001
Stage 5 (ref = Stage 3)	5.0	1.0	< 0.001	9.2	0.8	< 0.001	5.5	1.1	< 0.001	3.5	0.8	< 0.001

cognitive disability (64.2 ± 13.4), non-ambulatory PwP with intact cognition (50.6 ± 15.4) and ambulatory PwP with intact cognition (37.2 ± 15.1). The same trend holds true for each individual domain of the WHODAS 2.0.

In order to further delineate the isolated association between ambulatory status and cognition with the functional disability, a non-parametric regression was conducted. Age, education, and urbanization level, location of residence (whether they are community dwelling or not), modified H&Y were also included in the regression in order to examine their effects (**Table 3**). The results showed that non-ambulatory and cognitive disability were significantly associated with the severity of disability in every aspect. The effect size (β) of cognitive disability was consistently greater than that of ambulatory status in four domains of self-care (14.7 ± 0.7 vs. 10.6 ± 0.7), getting along with others (35 ± 0.5 vs. 12 ± 0.6), life activities (18.1 ± 0.8 vs. 11.3 ± 0.8), and participation (22 ± 0.6 vs. 11.3 ± 0.6). Similarly, disease stage (modified H&Y stage) also showed a statistically significant effect in all four domains, though the effect sizes were still smaller compared to either that of cognition and ambulation status. Institutional residents, age, and level of urbanization also appears to have impact on some domains whereas education level does not.

DISCUSSION

The findings from the present study revealed that non-ambulatory status and cognitive disability were both independently associated with the severity of disability, and the contribution of cognition was greater than ambulation. Unlike the PD-specific *Unified Parkinson's Disease Rating Scale* (UPDRS) (22), the present study utilized WHODAs 2.0 to evaluate the multiple aspects of disability, which can be assessed by qualified medical personnel who do not necessarily have to be physicians, is less time-consuming and enables the evaluation of disability under the ICF framework. Using WHODAS 2.0, the present study showed that the disability in moderate to advanced PwP is not merely limited to motor-related life activities, but affects one's ability to understand and communicate, getting along with people and participation in society and such difficulties become more prominent as cognition levels deteriorate and as independent or assisted ambulation is lost. Out of the four study groups, non-ambulatory PwP with cognitive disability have the most severe disabilities in all domains of daily functioning. These findings are consistent with previous findings, indicating that functional decline in PD results from motor impairment and is likely aggravated by concomitant cognitive impairment (23–25). Furthermore, based on the results of our non-parametric analysis, we hypothesize that as a determinant of functional disability, cognition is likely to be more important than ambulation status in later stages of PD.

It has been demonstrated that axial impairment (postural instability and gait difficulty) is strongly associated with the disability, functional dependence, and poor quality of life in non-demented mild to moderate PwP whereas there is relatively little impact of cognitive performance on functional outcome. (26) The loss of functional dependency tends to occur at the transition between H&Y stages 2–3 which characterizes the emergence of postural instability and possibly loss of independent ambulation (27, 28). It is thought that gait impairment portends the loss of many gait-dependent activities and thus, the effect of early manifesting gait disturbance such as freezing and postural instability can become especially prominent. The cognition is more likely to be spared or mild impairment when the affected persons are still in their early stages of PD. In contrast to the findings in early disease, we observed that ambulatory PwP with cognitive disability had higher overall disability compared to those who were cognitively intact but non-ambulatory, suggesting that cognitive function contributes more to disability than mobility and ambulation status. This illustrates the important concept of disparity between mobility and "functional mobility" in PD (29): despite that the ambulatory/cognition disability group had preserved physiological ability of moving independently or with assistance, they still experienced more difficulties in performing life activities and in maintaining an active and social life.

The findings of the present study may indicate the necessity of cognitive interventions, such medical therapy or cognitive training to prevent the disability of PwP. So far, there is evidence to support the efficacy and safety of acetylcholinesterase inhibitors such as rivastigmine with regarding slowing the cognitive impairment in PDD (30, 31). It will be worthwhile to investigate whether this benefit can translate into improvements in functional ability. Non-pharmacological options, on the other hand, may be preferable in those who are already burdened by polypharmacy or in cases who are already suffering from drug side effects (32). Compelling evidence from randomized controlled trials have found that cognitive training can improve cognitive domains known to be impaired in PD, such as working memory, processing speed, and executive function (33, 34). Cognitive training can also reduce motor complications such as freezing of gait (35, 36). Another study found that cognitive rehabilitation of a 3-month duration can lead to improved cognition and reduced functional disability measured by WHODAS. Moreover, these improvements were sustained after a period of 18 months (37). The targeted effects of aerobic exercise on motor and cognitive circuitry is also promising, with observed reduction in motor symptom severity and non-motor symptoms of fatigue, depression, and executive function (38). Since the aforementioned studies included mild to moderate PD or exclude patients with dementia, whether the same benefits can be replicated in more severely affected patients should be further investigated. The impact magnitude of physical exercise on cognitive function and real-world activities needs to be further clarified.

As a cross-sectional study, the limitations of this study include its sampling population, which consists of moderate to advanced PwP, restricting the applicability of the aforementioned findings to people with early stage or mild disease and precludes inferences about causality. Secondly, due to the retrospective nature of the study, the group with cognition disability was defined using the more generic cognition domain score on the FUNDES-Adult instead of tests such as the Mini Mental State exam or the Montreal Cognitive Assessment and definitions of the Movement Disorder Society criteria for PDD (39); cognition while those in this group may not strictly fulfill the diagnosis of "dementia" and may even include those with non-demented cognitive impairment, this method may have wider applicability in the primary care setting, providing an easier assessment of cognitive status for Physical Medicine and Rehabilitation physicians, physical therapists, or clinicians less familiar PDD diagnosis or when formal comprehensive neuropsychological testing cannot be conducted. Similarly, ambulation and walking status was evaluated by asking the patient to walk back and fro 3 m (domain 8.6 of FUNDES-Adult) instead of tests such as the Timed up and Go test. The 3-m walking course has been found to be a valid form of assessment of walking status compared to longer course lengths and is employed on a national level by the Taiwanese government after being tested for its validity and reliability (5, 8, 40). Thirdly, we cannot gather information on disease duration, treatment status, comorbidities in our cohort, for instance, co-existing cerebrovascular disease, amyloid pathology, and mood disorders, the impact of which can potentially confound our analysis but due to the advantage of having a large sample size, the evidence nonetheless still supports our hypothesis. Finally, the ambulation assessment by to and fro 3-m walk is episodic and the PwP may in their off status, which may result in miss categorization.

CONCLUSION

In mid-to-late stages of disease, PwP may experience significant functional disability resulting from dependent ambulation and cognitive impairment. This study identified that cognitive status has a greater impact on functional disability compared to ambulation status in those who are modified H-Y stages 3 and above. Future research must determine whether methods for secondary prevention of cognitive decline in this population can delay or mitigate functional dependency and reduce the social and economic burden brought about by this neurodegenerative disease.

DATA AVAILABILITY STATEMENT

The datasets generated for this study are available on request to the corresponding author.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Joint Institutional Review Board of Taipei Medical University (N201805048). Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

AUTHOR CONTRIBUTIONS

CW: data analysis and manuscript writing. LC: study design and manuscript revision. DW: data collection. W-CC, C-FY, and H-FL: study design and data collection. CH: study design, data analysis, and manuscript revision. T-HL: study design, data collection, data analysis, and manuscript revision.

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Changes in Activity Participation Among Older Adults With Subjective Cognitive Decline or Objective Cognitive Deficits

Shlomit Rotenberg[1]*, Adina Maeir[2] and Deirdre R. Dawson[1,3]

[1] Dawson Lab, Rotman Research Institute, Baycrest, Toronto, ON, Canada, [2] Cog-Fun Lab, School of Occupational Therapy, Hebrew University, Jerusalem, Israel, [3] Department of Occupational Science & Occupational Therapy, University of Toronto, Toronto, ON, Canada

Participation in daily activities is crucial for healthy aging. There is limited research on participation of older adults with subjective cognitive decline (SCD), defined as the experience of cognitive deficits with no evidence of objective cognitive deficits. Therefore, this study examined perceived changes in participation in this population, and compared it to perceived changes reported by individuals with objective cognitive deficits. The study aimed to: (1) examine the reported changes in activity participation of older with SCD; (2) investigate differences in the reported changes in participation between individuals with SCD and those with mild or severe objective cognitive deficits; (3) examine the relationship between activity participation, subjective memory, and objective cognitive status; and (4) explore whether subjective memory explains additional variance in activity participation after accounting for age and objective cognitive deficits. Participants were 115 older adults (60+), divided into three groups based on their Montreal Cognitive Assessment (MoCA) scores: (1) SCD (MoCA$\geq$26; $n = 66$); (2) mild objective cognitive deficits (MoCA = 20–25; $n = 34$); and (3) severe objective cognitive deficits (MoCA$\leq$19; $n = 15$). The Activity Card Sort was used to measure participation in instrumental activities of daily living, social, and leisure activities. The Multifactorial Memory Questionnaire—Ability subscale was used to assess subjective memory. We found that individuals with SCD, mild cognitive deficits and severe cognitive deficits reported participation withdrawal to a level of 80, 70, and 58% of their past participation, respectively. A significant between group difference was found on participation [$\chi^2(2) = 16.44, p < 0.01$], with the SCD group reporting higher participation than the other two groups. Participation significantly correlated with both cognitive status ($r = 0.40$, $p < 0.01$) and subjective memory ($r = 0.45$, $p < 0.05$). A regression analysis revealed that subjective memory contributed significantly to the explained variance in participation, beyond that accounted for by objective cognitive deficits and age. Our findings demonstrate the important role of subjective memory problems in activity participation of older adults, even in the absence of objective cognitive deficits.

Keywords: metamemory, daily functioning, activity participation, aging, subjective cognitive decline

Edited by:
Lisa Tabor Connor,
Washington University in St. Louis,
United States

Reviewed by:
Mary Carolyn Baum,
Washington University in St. Louis,
United States
Federica Piras,
Santa Lucia Foundation (IRCCS), Italy

***Correspondence:**
Shlomit Rotenberg
srotenberg@research.baycrest.org

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INTRODUCTION

Many older adults experience cognitive problems. The reported prevalence of subjective cognitive problems in older adults varies widely, from 22 to 80% (1–3). The prevalence of objective impairments is significantly lower, with an estimated 6–26% of older adults diagnosed with mild cognitive impairment (4, 5), and 4–15% with dementia (5, 6). The subjective experience of cognitive decline without objective evidence of cognitive deficits is referred to as subjective cognitive decline (SCD) (7). SCD is increasingly understood to be a risk factor for future cognitive decline (8, 9) and considered by some to be prodromal for dementia (10).

The relationship between objective and subjective cognitive functioning in older adults is not fully understood. A systematic review and meta-analysis of 50 studies showed a small but significant relationship between subjective and objective cognitive functioning in older adults (11). Additionally, subjective memory, measures by the reported frequency of memory related mistakes in daily functioning, was associated with objective cognitive abilities in older adults with mild cognitive impairment (MCI), but not in older adults with SCD (12).

Participation in daily activities of older adults with SCD is not often studied. This is important because preserving functional abilities despite age related health changes is crucial for healthy aging as defined by the World Health Organization (WHO) (13). Moreover, the International Classification of Functioning, Disability and Health (ICF) (14), that describes the broad consequences of health conditions, highlights the important role of participation in daily activities for the well-being of individuals with any health condition. The ICF model describes reciprocal interactions between body functions, such as objective cognitive abilities, contextual personal factors such as subjective perceptions of memory and participation in everyday life activities (14). Despite the importance of activity participation in aging and the theoretical basis, provided by the ICF, for interactions between participation, cognition status and subjective memory, this relationship has not been widely studied among older adults with SCD.

The few studies that explored whether older adults with SCD report difficulties with everyday functioning have focused predominantly on basic and instrumental activities of daily living (BADL and IADL). A population based study in Germany found that only 3.4% of older adults with SCD reported impaired IADL (15), suggesting that people with preserved cognitive abilities are fairly independent in IADL. Furthermore, older adults with SCD reported better IADL functioning compared to older adults with MCI and dementia (16). However, older adults with SCD are more likely to develop BADL and IADL difficulties over a 1 year period compared to healthy older adults with no SCD (17). Additionally, conversion rates from SCD to dementia are higher in people with SCD who also have impaired IADL (15).

The ICF definition of participation as "involvement in a life situation" [(14), p. 10], covers a wide range of domains, including IADL, community, social, recreational, leisure, and religious activities. In line with the ICF model, this study aimed to expand on the body of knowledge regarding activity participation in older adults, and examined their participation not only in IADL activities, but also in a wide range of social and leisure activities. This is important because participation in social and leisure activities is associated with decreased risk for future cognitive decline in older adults (18, 19). Due to the limited research on activity participation of older adults with SCD, this study aimed to understand participation in this population by examining perceived changes in participation over 5–10 years, and comparing it to changes reported by people with objective cognitive deficits. We also aimed to understand the relationship between subjective memory, objective cognitive status, and activity participation. The specific study objectives were to: (1) examine perceived changes in participation of older adults with SCD and those with objective cognitive deficits in relation to their own participation 5–10 years before; (2) investigate differences in participation withdrawal between older adults with SCD and those with objective cognitive deficits; (3) examine the correlations between participation, subjective memory, and objective cognitive status; and (4) explore whether the severity of subjective memory problems explains variance in participation, over and above that explained by age and objective cognitive deficits.

MATERIALS AND METHODS

Study Design and Procedure

This study was a secondary data analysis of data collected for two studies: (1) a pilot intervention study for older adults with SCD (pre-training data only), performed in Canada (20); and (2) a cross-sectional study comparing older adults who reported memory problems at a geriatric clinic to age matched older adults who did not seek medical help for their perceived memory problems, performed in Israel (21). In study 1, participants were recruited from a research subject pool and a community psycho-education program, and in study 2 through a geriatric clinic and convenience sampling in the community. The use of the data for this secondary analysis was approved by the Baycrest Research Ethics Board (study 1), the Helsinki Committee of Maccabi Healthcare Services and the Hebrew University Institutional Review Board (study 2).

Participants

Participants were 115 community dwelling older adults, age 60, or greater. Participants from both studies had self-reported memory and/or cognitive problems. Participants were allocated to one of three groups based on their cognitive status, as measured by the Montreal Cognitive Assessment (MoCA) (22), using cut-off scores suggested by Horton et al. (23): (1) SCD, with MoCA scores ≥ 26 ($n = 66$); (2): mild objective cognitive deficits (mild-CD), with MoCA scores = 20–25 ($n = 34$); and (3): severe cognitive deficits (severe-CD), with MoCA scores ≤ 19 ($n = 15$). According to Horton et al. (23) the mild-CD and severe-CD groups may be perceived as equivalent to MCI and dementia, respectively, however, the available data were not sufficient to inform such diagnoses.

Measures

Cognitive status was measured using the MoCA (22), a widely used short cognitive screening test that covers a wide range of cognitive domains. The MoCA scores range from 0 to 30, with higher scores reflecting better cognitive performance. The MoCA demonstrated good internal consistency (Cronbach's $\alpha = 0.83$) and adequate known-group validity, with high diagnostic value in older adults with MCI and dementia (24).

The Activity Card Sort (ACS) (25) is a self-report measure that examines current activity participation compared to an individual's past participation. The ACS examines participation in four domains: (1) IADL (e.g., laundry, paying bills); (2) leisure with low physical demands (e.g., hand crafts, watching television, attending concerts); (3) leisure with high physical demands (e.g., sports, camping); and (4) social activities (e.g., entertaining, volunteer work). The ACS is comprised of pictures representing a wide range of activities, each scored on involvement in the past (rated as "performed" or "didn't performed") and in the present (rated as "doing now," "doing less than in the past," or "not doing/have given up"). Each activity performed in the past is given a score of one point, and a total score of past participation is calculated as the sum of those activities. Current activities are allocated one point if currently performed, 0.5 points if performed less than in the past, and zero points for activities that are not currently performed. These scores are summed to produce a current participation score. Changes in participation are than calculated as the proportion of the activities currently performed relative to those performed in the past, by dividing the total current participation score by the total past participation score. The ACS provides a total change score, and four sub-scores for four activity domains. Scores range from 0 to 100%, with lower percentages scores representing less preserved activity participation and more withdrawal from previous participation. The original ACS version, with 80 pictures, was used in study 1, and the Hebrew version (26), with 88 pictures, was used in study 2. Participants were asked to consider "past participation" as their participation five (study 1) or 10 (study 2) years earlier. The ACS presents good known group validity, and was able to discriminate between healthy adults, healthy older adults, and individuals with neurological disabilities (26, 27).

The Multifactorial Memory Questionnaire (MMQ)—Ability subscale (28) was used to assess subjective memory. The MMQ-Ability is a self report questionnaire that measures the frequency of memory related mistakes in daily life (e.g., forget to pay a bill, difficulty recalling a word). It consists of 20 items, scored on a five point Likert scale. The total score ranges from 0 to 80, with higher scores indicating better subjective memory ability. The MMQ-Ability has good internal consistency (Cronbach's $\alpha = 0.93$) and excellent content validity (83–100% agreement between raters) in clinical and non-clinical older adult populations (29). Construct validity of the MMQ-Ability was moderate to strong ($r = 0.43$–0.89) with other subjective memory questionnaires (29). Data on the MMQ were available for participants in study 2 only ($n = 91$).

Each of the two studies in this secondary data analysis used a different measure of mood. Study 1 used the Center for Epidemiological studies Depression scale (CES-D) (30), a 20 item questionaire of depression symptomology, scored on a four point scale. Study 2 ($n = 91$) used the Patient Health Questionnaire (PHQ-9) (31), a nine item questionnaire scored on a four point scale. For both measures, higher scores reflect more depressive symptomology. We classified participants as having depressive symptomology based on the accepted cutoff score of 16 for the CES-D (30) and 10 for the PHQ-9 (31).

Statistical Analysis

Descriptive statistics were used to describe the demographic variables and changes in participation as rated on the ACS. The Kruskal-Wallis H test was used to compare between the three cognitive groups on demographic data and the level of maintained participation as measured by the ACS. A non-parametric test of between group differences was chosen because four of the five ACS scores were not distributed normally. Where statistically significant differences were found in the Kruskal-Wallis H test, we performed a Dunn's *post-hoc* test with Bonferroni correction, to compare each of the three cognitive groups to the others. A chi-square test was used to compare between the cognitive groups on nominal variables (gender and presence of depressive symptoms). Effect sizes were calculated using epsilon square (ε^2) (32), and interrupted as follows: $\varepsilon^2 = 0.00<0.01$-negligible; $0.01<0.04$-weak; $0.04<0.16$-moderate; $0.16<0.36$-relatively strong; $0.36<0.64$-strong; $0.64<1.00$-very strong (33). A partial correlation was computed between participation, objective cognitive status and subjective memory, controlling for age. An exploratory hierarchical linear regression model was used to assess the impact of subjective memory on participation, beyond age and objective cognitive functioning. Age and MoCA scores were entered into blocks one and two, and the MMQ-Ability score was added into the third block. The reported p values are the result of two-sided tests, with an alpha level of 5%. All analyses were performed using SPSS 24.0 for Windows (SPSS Inc., Chicago, IL).

RESULTS

The demographic characteristics of the full sample and by cognitive groups are presented in **Table 1**. Significant group effects were found for age, education and depression. *Post-hoc* tests revealed that the SCD group was significantly younger and more educated than the two groups with objective cognitive deficits, but no significant differences were found between the mild-CD and severe-CD groups on age and education. The severe-CD group significantly more depressed than the other two groups.

To examine perceived changes in participation (study objective 1) we calculated the proportion of self-reported current participation in relation to individuals past participation. Individuals with SCD, mild-CD and severe-CD all reported reduced levels of participation of 79, 70, and 58%, respectively (see **Table 1**). We found similar trends of reduced participation in all four ACS subscales, with the SCD group reporting highest rates, and the severe-CD group reporting lowest rates of retained participation.

To address objective 2, we examined between group differences in the reported changes in participation using a

TABLE 1 | Participant characteristics and between group comparison.

	Total Sample ($n = 115$) *n* (%)	SCD ($n = 66$)	Mild-CD ($n = 34$) *n* (%)	Severe-CD ($n = 15$)	$\chi^2(2)$[a], *p*
Gender-Female	74 (65.2)	47 (71.2)	20 (58.8)	8 (53.3)	2.59 (0.274)
Depressive symptoms[b]	14 (12.2)	4 (6.1)	3 (8.8)	8 (53.3)	19.36 (0.000)
	Mean ± SD		**Mean ± SD**		**$\chi^2(2)$[c]**
Age (years)	77.88 ± 7.15	75.86 ± 7.49	80.00 ± 7.56	81.93 ± 6.50	12.41 (0.002)
Education (years)	15.20 ± 3.99	15.96 ± 3.65	14.28 ± 4.36	14.00 ± 4.16	7.66 (0.020)
MMQ-Ability[d]	43.18 ± 13.20	46.80 ± 12.89	41.53 ± 12.24	36.07 ± 13.30	9.65 (0.008)
ACS					
Total Score	73.37 ± 16.79	78.57 ± 13.74	70.05 ± 15.99	57.99 ± 20.22	16.44 (0.000)
IADL	79.40 ± 19.03	84.28 ± 13.99	77.16 ± 21.42	63.07 ± 23.39	10.94 (0.004)
Leisure, low physical demands	80.20 ± 15.97	82.83 ± 13.50	79.41 ± 17.37	70.43 ± 19.53	5.76 (0.056)
Leisure, high physical demands	53.15 ± 29.37	61.68 ± 26.42	46.43 ± 27.21	30.86 ± 32.47	14.16 (0.001)
Social	71.65 ± 20.08	77.11 ± 17.91	67.14 ± 17.87	57.86 ± 25.41	12.39 (0.002)

SCD, subjective cognitive decline; CD, cognitive deficits; MMQ, Multifactorial Memory Questionnaire; ACS, Activity Card Sort.

[a] *Chi-square test.*

[b] *Presence of depressive symptoms was determined by the cut-off scores of 16 for the Center for Epidemiological studies Depression scale (CES-D) for participants in study 1, and 10 on the Patient Health Questionnaire (PHQ-9) for participants in study 2.*

[c] *Kruskal-Wallis Test.*

[d] *MMQ scores available for 91 participants only.*

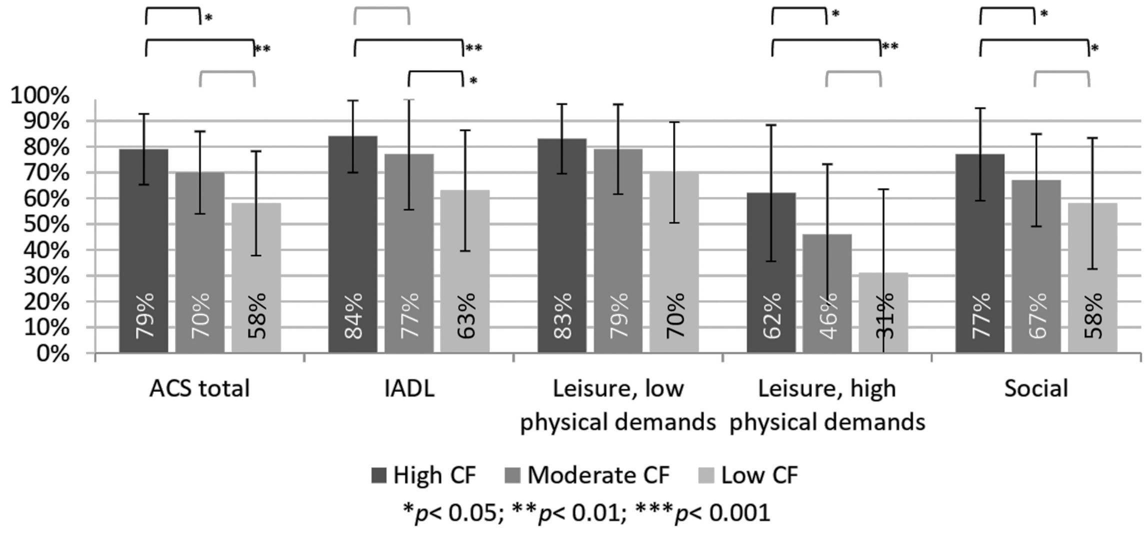

FIGURE 1 | Between group differences on participation: *post-hoc* Dunn's test on ACS scales.

Kruskal-Wallis test. The results, presented in **Table 1**, show a significant group effect on participation reported on the ACS-total scores and three of the four ACS sub-scores. A *post-hoc* Dunn's test showed that the SCD group reported significantly higher retained participation compared to both other groups on the ACS-total, as well as the subscales of social activities and leisure activities with high physical demands (see **Figure 1**). The SCD group reported significantly higher retained participation in IADL compared to the severe-CD group, but not to the mild-CD group. The mild-CD group reported significantly higher retained participation compared to the severe-CD group on the IADL subscale. The between group effect size on the ACS-total score was moderate ($\varepsilon^2 = 0.07$) between the SCD and mild-CD groups, and relatively strong ($\varepsilon^2 = 0.17$) between the SCD and severe-CD groups.

For objective 3, associations of the ACS scores to objective cognitive status (measured by the MoCA) and subjective memory (MMQ-Ability) were examined using a partial correlation analysis. Age was defined as a covariant because the SCD group was significantly younger than the other two groups. Following application of the Bonferroni correction, we found significant positive moderate correlations between the ACS total score and

TABLE 2 | Associations of participation to objective cognition and subjective memory.

	MoCA ***n* = 115, r[a] (*p*)**	**MMQ—Ability[a]** ***n* = 91, r (*p*)[b]**
ACS—Total score	0.40 (0.000)	0.45 (0.000)
ACS—IADL	0.39 (0.000)	0.34 (0.001)
ACS—Leisure, low physical demands	0.27 (0.010)	0.35 (0.001)
ACS—Leisure, high physical demands	0.29 (0.006)	0.42 (0.000)
ACS—Social	0.27 (0.012)	0.36 (0.000)

MoCA, Montreal Cognitive Assessment; MMQ, Multifactorial Memory Questionnaire; ACS, Activity Card Sort; IADL, instrumental activities of daily living.

[a] MMQ scores available for 91 participants only.

[b] Correlations were calculated with age as a covariate to control for age differences.

TABLE 3 | Exploratory hierarchical regression for participation (*n* = 91).

	B	**SE B**	**Beta (*p*)**	**R^2**	**R^2 change**	**F (*p*)**
Block 1						
Age	−1.11	0.23	−0.45 (0.000)	0.21	0.21	23.11 (0.000)
Block 2						
Age	−0.86	0.22	−0.35 (0.000)	0.33	0.13	16.65 (0.000)
MoCA	1.84	0.45	0.37 (0.000)			
Block 3						
Age	−0.94	0.21	−0.38 (0.000)	0.42	0.09	13.61 (0.000)
MoCA	1.33	0.44	0.27 (0.004)			
MMQ-Ability	0.43	0.12	0.32 (0.000)			

MoCA, Montreal Cognitive Assessment; MMQ, Multifactorial Memory Questionnaire; ACS, Activity Card Sort.

both MoCA scores and MMQ-Ability scores, when controlling for age (see **Table 2**). The results suggest that more preserved participation is associated with better objective cognitive status and lower frequency of memory problems in daily life (reflected by a higher MMQ-Ability score).

We used an exploratory hierarchical linear regression model to examine whether the severity of subjective memory problems explains additional variance in participation over and above that explained by age and objective cognitive (objective 4). Age was entered in block one, the MoCA was added in block two and the MMQ-Ability was added into the third block. The regression results (see **Table 3**) show that age and MoCA scores explained a significant proportion of the variance (33.2%) of participation. After controlling for age and cognitive status, subjective memory significantly explained another 9% of the variance in participation. The overall model explained 42.3% of the variance in participation among older adults.

DISCUSSION

This study examined perceived changes in participation in IADL, leisure, and social activities among older adults with SCD and those with objective cognitive deficits. We found that older adults with SCD reported reduced activity participation, to ∼79% of their total participation 5–10 years prior. Although they reported significantly less withdrawal from participation compared to both the mild-CD (70%) and the severe-CD (58%) groups, the reported withdrawal from their own level of participation warrant attention. We also examined the relationship of perceived changes in participation to subjective memory and objective cognition, and found significant moderate to strong correlations. The severity of subjective memory problems explained an additional 9% of the variance in participation, beyond the 33% explained by objective cognitive deficits.

Participation in Older Adults With SCD

Participants with SCD reported withdrawal from social activities (77%) and leisure activities with high physical demands (62%), and to a lesser extent also from IADL (84%) and leisure activities with low physical demands (83%). While there are no normative data available for the ACS, these findings are concerning as we know that engagement in social and leisure activities is important for delaying and preventing cognitive decline as people age (18). The reported decline in leisure activities with high physical demands are specifically disturbing given the association between aerobic activity and preserved cognitive functioning in older adults (34).

Although the reported withdrawal from participation in those with SCD was less severe than in the two groups with objective cognitive deficits, the results suggest that healthcare professionals should assess participation in IADL, social, and leisure activities among older adults reporting memory problems, even in the absence of objective cognitive deficits. Identifying withdrawal from participation in people with SCD is important, since activity participation is a modifiable factor, that was shown to improve through intervention (35, 36). Preventing participation withdrawal in older adults with subjective memory problems is key to supporting their quality of life (21). Also, given the higher rates of conversion from SCD to dementia in people who also report impaired IADL (15) it is possible that identifying these impairments and providing interventions that improve IADL functioning in people with SCD may delay their future cognitive deterioration.

The reported withdrawal from social and leisure activities in the SCD group to a level of 62–82% of previous participation is important to highlight because most studies on this population focus on ADL and/or IADL and not much is known about changes their social and leisure participation. The reported reduction in social and leisure activities, especially leisure activities with high physical demands, is disturbing because involvement in social activities and other activities in the community were shown to be associated with lower risk of cognitive decline over a 3–4 year period (18, 19).

Participation and Objective Cognition

The moderate and significant correlations between participation and objective cognitive status in our sample of older adults who report subjective memory problems (with or without objective cognitive deficits), suggests that objective cognition plays a role in their everyday functioning. This is supported by the finding that those with no objective cognitive deficits reported significantly less occupational withdrawal than both other groups.

Examination of the four ACS subscales revealed a consistent pattern over the three cognitive groups, where the most withdrawal is reported from leisure activities with high physical demands, followed by social activities. The SCD group reported significantly less withdrawal from participation in both these areas compared to the other two groups. The mild-CD and severe-CD groups did not differ significantly on participation in leisure activities with high physical demands and social activities. This could be explained by the high cognitive demands inherent in social activities and leisure activities with high physical demands. On the ACS, both sub-scales include non-routine activities that require planning and problem solving, and therefore may be more susceptible to decline in people with cognitive deficits. However, it is also possible that physical ability contributed to these scores as many of the activities in these two subscales are performed outside the home. As the SCD group is significantly younger than the other two groups, it is possible that they are more mobile. Leisure activities with low physical demands were reported to be relatively preserved in all three groups. It is possible that these activities are more preserved not only due to their low physical demands, but also do to their low cognitive demands, because many of the activity in this sub-scale of the ACS are non-complex leisure activities, such as watching movies and television or doing hand crafts. We would suggest that future studies document physical ability to help elucidate this issue, and provide insight as to the underlying physical and/or cognitive mechanisms behind the reported withdrawal from participation.

The severe-CD group reported significantly more withdrawal in IADL compared to the other two groups, yet there was no statistically significant difference between the SCD and mild-CD groups. These findings support the definition of "major neurocognitive disorder" (previously dementia), as involving interference in everyday functioning and independence (37). There are two ways to explain the relatively preserved IADL participation in the mild-CD group. One is that many of the IADL activities in the ACS are routine activities (e.g., doing dishes, laundry) that don't require high cognitive reserves. Another possible explanation is that IADL activities, more than social and leisure activities, are fundamental in preserving independence. Therefore, when everyday functioning requires greater effort due to reduced cognitive abilities (38), it is possible that these efforts are channeled toward IADL activities at the expense of social and leisure activities.

Participation and Subjective Memory

An important finding from this study is that subjective memory explained 9% of the variance in participation in everyday activity, in addition to that explained by age and objective cognition. Identifying difficulties in everyday functioning in people with subjective memory problems, even in the absence of objective cognitive decline (i.e., people with SCD) is important, both as a risk factor for future cognitive decline (15) and as a factor that may influence their current quality of life (21, 39). Healthcare professionals should assess participation from a broad perspective, and inquire about changes in social and leisure participation, even in people with no objective cognitive deficits.

We found that subjective memory was moderately and significantly correlated with participation in daily activities, when controlling for age. The more memory related mistakes older adults reported in their everyday life, the more withdrawal they reported from participation daily activities. Similar findings have been reported in qualitative studies of older adults who experience cognitive problems including declines in daily activities, changes in life roles and loss of independence (40, 41). Similar to Montejo et al. (42), we found a significant relationship between subjective memory and IADL functioning. Our results expand this body of knowledge and show significant associations between subjective memory and social and leisure activities, areas of daily activities sparsely studied in this population.

CONCLUSION

SCD is not known to be associated with decline in daily functioning (15), but this study suggests that although people with SCD are independent in BADL and IADL they experience withdrawal from social and leisure activities. The results highlight the importance of asking people with SCD about change in their participation, to indentify withdrawal from participation early on in the potential trajectory of cognitive decline, and provide intervention to promote ongoing participation.

STUDY LIMITATIONS

This study had a number of limitations. First, we were unable to control for depression in the regression analysis as there were too few people over the cut-off score for depression to do a sub-group analysis. This may have affected the results, as depression is known to interact with cognition in this population (11). While it has been argued that understanding the day-to-day difficulties experienced by people with subjective cognitive problems is clinically important regardless of the etiology (11), we think this warrants further study. We also did not have a measure of apathy, another factor that may have had a mediating effect on participation. A second limitation is that participants' cognitive status was determined based only on the MoCA test, which is not a comprehensive diagnostic tool (22). Although we used cut-off scores suggested by Horton et al. (23), we did not have the necessary recourses to make conclusive diagnoses of SCD, MCI or dementia in our study participants. Thus, the division of our groups may not be a completely accurate representation of these three diagnoses. Our use of the MMQ-Ability subscale as the measure of subjective cognition also may have provided a limited representation of broader concept of SCD. In future studies, we suggest using other measures of subjective cognition and adding a control sample of healthy older adults who report no subjective cognitive changes, in order to compare changes in activity participation related to normal aging with those that we observed in individuals with SCD and objective cognitive changes. A third limitation of the study is that the analysis was unable to account for the different recruitment methods in the two parent studies. The relationship between subjective and objective cognition may differ in older adults recruited through community sources compared to those recruited in a clinical context (43). Finally, several methodological issues make us cautious about generalizing the results. The use of convenience sampling in both studies means that the samples may not be representative of the larger population; the self-report nature of the MMQ and ACS means these data are subject to recall bias; and finally, we had MMQ scores on only 91 of the participants.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this manuscript will be made available by the authors, without undue reservation, to any qualified researcher.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Baycrest Research Ethics Board; the Helsinki Committee of Maccabi Healthcare Services; and the Hebrew University Institutional Review Board. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

SR, AM, and DD contributed to the conception and design of the study. SR organized the database, performed the data analysis, and wrote the manuscript. AM and DD contributed to data analysis and interpretation. DD revised the manuscript. All authors contributed to manuscript revision, read and approved the submitted version.

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Characterization of Upper Limb Impairments at Body Function, Activity, and Participation in Persons With Multiple Sclerosis by Behavioral and EMG Assessment: A Cross-Sectional Study

Nicola Valè [1†], **Marialuisa Gandolfi** [1,2*†], **Stefano Mazzoleni** [3], **Elena Battini** [3], **Eleonora Kirilova Dimitrova** [1], **Alberto Gajofatto** [1,4], **Francesco Ferraro** [5], **Matteo Castelli** [6], **Maruo Camin** [6], **Mirko Filippetti** [7], **Carola De Paoli** [7], **Alessandro Picelli** [1,2], **Jessica Corradi** [1], **Elena Chemello** [7], **Andreas Waldner** [8], **Leopold Saltuari** [9,10] and **Nicola Smania** [1,2]

[1] Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy, [2] UOC Neurorehabilitation, AOUI Verona, Verona, Italy, [3] The BioRobotics Institute, Scuola Superiore Sant' Anna, Pontedera, Italy, [4] UOC Neurologia dU, Azienda Ospedaliera Universitaria Integrata, Verona, Italy, [5] Section of Neuromotor Rehabilitation, Department of Neuroscience, ASST Carlo Poma, Mantova, Italy, [6] Centro di Riabilitazione Franca Martini–ATSM ONLUS, Trento, Italy, [7] School of Specialization in Physical Medicine and Rehabilitation, University of Verona, Verona, Italy, [8] Department of Neurological Rehabilitation, Private Hospital Villa Melitta, Bolzano, Italy, [9] Research Department for Neurorehabilitation South Tyrol, Bolzano, Italy, [10] Department of Neurology, Hochzirl Hospital, Zirl, Austria

Background: Multiple sclerosis (MS) is a chronic inflammatory demyelinating and disabling disease which primarily affects individuals in their early life between 20 and 40 years of age. MS is a complex condition, which may lead to a variety of upper limb (UL) dysfunctions and functional deficits.

Objective: To explore upper limb impairments at body function, activity, and participation in persons with MS (PwMS) and severe hand dexterity impairment by behavioral and surface electromyography (sEMG) assessments.

Methods: This observational cross-sectional study involved 41 PwMS with severe hand dexterity impairment stratified according to the Expanded Disability Status Scale (EDSS) into mild–moderate ($n = 17$; EDSS, 1–5.5), severe ambulant ($n = 15$; EDSS, 6–6.5), and severe nonambulant ($n = 9$; EDSS, 7–9.5). Behavioral outcome measures exploring body function, activity, and participation were administered. The sEMG activity of six upper limb muscles of the most affected side was measured during a reaching task.

Results: The most severe group was significantly older and more affected by secondary progressive MS than the other two groups. Positive significant associations between UL deterioration and impairments at different International Classification of Functioning, Disability, and Health domains were noted in the most severe group. The progressive decline in manual dexterity was moderately to strongly associated with the deterioration of the overall UL activity ($\rho = 0.72$; $p < 0.001$) and disuse (amount of use $\rho = 0.71$; $p < 0.001$; quality of movement $\rho = 0.77$; $p < 0.001$). There was a low correlation

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Washington University in St. Louis,
United States

Reviewed by:
Nathan P. Wages,
Ohio University, United States
Pietro Caliandro,
Agostino Gemelli University
Polyclinic, Italy

***Correspondence:**
Marialuisa Gandolfi
marialuisa.gandolfi@univr.it

† These authors have contributed equally to this work

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between manual dexterity and UL function ($\rho = 0.33$; $p = 0.03$). The muscle activation pattern investigated by sEMG was characterized by a decrease in modularity and timing delay in the wrist extensor muscles activation in the severe ambulant patients (EDSS, 6–6.5). Similar impairments were observed in the proximal muscles (anterior deltoid) in the more advanced stages (EDSS ≥ 7).

Conclusion: Behavioral assessment, together with measures of muscle activation patterns, allows investigating the pathophysiology of UL impairments in PwMS across progressive neurological disability severity to implement task-specific rehabilitation interventions.

Keywords: upper limb abnormalities, quality of life, participation, electromyography, multiple sclerosis

INTRODUCTION

Multiple sclerosis (MS) is the most common non-traumatic cause of neurological disability in young adults between 20 and 40 years old, affecting about 2–3 million people globally (1, 2). A greater understanding of the underlying genetic and environmental factors involved in the MS pathophysiology has been reached, followed by early accurate diagnosis and extensive therapeutic management toward more personalized medicine (2). However, MS continues to be a challenging condition both in the treatment and prevention of the disabling progression of the disease, especially in the progressive forms (2).

Rehabilitation plays an integral part in the management of people with multiple sclerosis (PwMS). In the last decade, special attention has been paid on gait and balance disturbances, as they have been considered to be one of the key determinants of mobility limitations and disability (3). However, up to 66% of these patients suffer from upper limb (UL) dysfunctions (4). Since MS typically affects multiple functional systems, a variety of symptoms significantly impact on the patient's ability to perform activities of daily living and quality of life (QoL) (4). Common manifestations include muscle weakness, tremor, sensory deficits, and impaired motor control (2). Fatigue and pain further impair motor and functional outcomes (2).

The pathophysiology of UL impairments in PwMS is complex and only partially known. The bulk of the literature on this topic suggests that sensorimotor dysfunctions are not the only mechanism to explain UL disability (5). For instance, cognitive impairments (i.e., attentional and memory deficits) and UL disuse might further affect UL function with negative consequences on activity and participation (6–11).

Two issues need to be addressed to improve knowledge on the pathophysiology of UL impairments. First, specific UL assessment protocols should be shared among clinicians and researchers. Second, technology-aided assessments should be integrated into the UL assessment to explore function from a qualitative and quantitative point of view. An accurate UL assessment is challenging due to the inherent variability of UL movements and the multifaceted manifestation of UL dysfunctions in PwMS. Of note, the standard neurological disability assessment using the Expanded Disability Status Scale (EDSS) is mainly focused on mobility and walking ability (8). As highlighted in the recent overview by Lamers et al. (8), UL dysfunction in PwMS should be investigated within the International Classification of Functioning, Disability, and Health (ICF) framework including outcome measures referring to body structure and function, activity, and participation (8). A consensus of diagnostic hand dexterity impairment criteria using the Nine-Hole Peg Test (NHPT) has been reached. These criteria should improve the accuracy of epidemiological studies and allow to monitor sensorimotor function in PwMS (3, 12, 13). Of note, a specific altered pattern of hand movement can reflect brain maladaptation (14). However, the relationship between different levels of UL impairments deserves further investigation (5, 12, 15).

The literature on the instrumental assessment of UL dysfunctions in PwMS is scant. Constraints in the use of such technology are the costs to acquire the technological devices, the need for specific expertise to acquire and analyze data, and the time requested to set up the instrumental paradigm. Strengths are the possibility to use it during functional tasks and activity. Scattered evidence in PwMS suggests that surface electromyography (sEMG) has many advantages over other neurophysiological investigations to study muscle activation pattern including non-invasive assessment, the possibility to describe muscle activation during a controlled and repeatable functional task, and the affordable costs in the rehabilitation setting. Preliminary studies on small samples have reported lower modulation in sEMG activity of distal UL muscles in patients with moderate impairment during reaching to grasp task (16). A more recent study by Pellegrino et al. (17) suggested that both kinematic and electromyographic parameters might represent biomarkers to help clinicians in differentiating patients with different levels of UL motor impairment from healthy subjects (17). Noteworthy, no patients with severe UL impairments have been investigated, and no correlation between clinical outcome and sEMG data was performed.

To accomplish this goal, we explored UL impairments at different levels of ICF by behavioral and sEMG assessment in a cohort of PwMS affected by severe hand dexterity impairment and different levels of neurological disability.

Knowledge gained from this study will provide new insights into the progressive deterioration of UL function and activity across the different disease stages, as a thorough investigation of the UL impairments at different ICF domains would show that manual dexterity deficit may be associated with multiple UL dysfunctions depending on the neurological disability. Preliminary analysis of UL muscle activation may suggest changing in the modularity and timing of UL muscle activation during a reaching task as sEMG correlates of the UL decline in PwMS (16). Our preliminary results would be a reference for prospective longitudinal studies on a large cohort of patients to study behavioral and muscle activation pattern deterioration in the different stages of the illness identified by the EDSS.

METHODS

In this observational cross-sectional study, we used data provided by a database created for a randomized controlled trial on hand dexterity robot-assisted rehabilitation by Gandolfi et al. (18). A total of 113 patients were screened at the UOC Neurorehabilitation Unit (AOUI Verona) and the Multiple Sclerosis Center, U.O. Neurologia dU (AUOI Verona) from March 2014 to March 2017. Inclusion criteria were the following: confirmed diagnosis of MS (19); age between 18 and 65 years, EDSS score $1.5 < x < 8$ (19); Mini-Mental State Evaluation $\geq$ 24/30 (20); Modified Ashworth Scale score evaluated at the elbow, wrist, and fingers ≤ 2 (21); and NHPT score between 30 and 300 s (13). Exclusion criteria were the absence of relapses or relapse-related treatments in the 3 months before the study, and other neurological or orthopedic diseases interfering with UL function. After being informed about the experimental nature of the study, patients gave their informed written consent. The study was carried out following the Helsinki Declaration, approved by the local Ethics Committee (prog no. 230 CESC), and registered at a clinical trial. Eligible patients were categorized into three disability groups according to the EDSS: group 1, mild–moderate (1.5–5.5); group 2, severe ambulant (6–6.5); and group 3, severe non-ambulant (5). The EDSS was used to categorize the different disease stage severity, as it is the worldwide measure of neurological impairment in PwMS already used in the literature (5).

ASSESSMENTS

A neurologist determined demographic and clinical data such as gender, age, hand dominance determined by the Edinburg Handedness Inventory (EHI) (22), disease duration (years), type of MS, and the EDSS. According to the ICF, clinical and instrumental assessments were administered by a research therapist to explore body function, activity, and participation. The ICF is the WHO framework for measuring health and disability at the individual and population levels, taking into account environmental and personal factors (23). The body function domain refers to the physiological function of the body system, including psychological functions. The activity domain refers to the execution of a task or action by the individual. The participation level describes the personal involvement in real-life situations (23). Clinical assessments were carried out by blinded assessors about the EDSS score cut points defining the different study groups. A physiotherapist with experience in the sEMG acquisition acquired instrumental assessments. Data processing was carried out by external research collaborators not involved in the data collection to limit possible performance and detection bias.

Upper Limb Functions and Structures

The Fugl–Meyer–UL section (FM) was used as a measure of UL function. FM includes evaluation of reflex activity, volitional movement, and coordination of the UL (range of score, 0–66; higher = better performance) (24). The Motricity Index measured muscle strength at the shoulder, elbow, and pinch grip (range of score, 0–100; higher = better performance) (25). The Modified Ashworth Scale (MAS) measured resistance during passive stretching of shoulder adductors, elbow, and wrist flexors (range of score, 0–5; higher = worse performance) (21). A total UL MAS score was also computed as the sum of shoulder abductors, elbow, and wrist flexors single scores (21). Tremor Severity Scales assessed the UL tremor across four domains: rest tremor, postural tremor, kinetic tremor, and intention tremor (range of score for each domain, 0–10; higher = more severe tremor) (26). Numeric Rating Scale assessed fatigue. Patients answered the question "Do you perceive fatigue during UL activity?" (range of score, 0–10; higher = worse symptoms) (27).

Upper Limb Activity

The NHPT was used to evaluate manual dexterity by computing the pegs *per second* (peg/s) rate. The NHPT has been reported to be responsive to UL activity level worsening (12, 13, 28). A previous study by Lamers et al. (15) suggested that the scores below 0.27 pegs/s indicate a severe hand dexterity deficit (15). The action research arm test (ARAT) measured functional arm skills with 19 items categorized in four sections (grasp, grip, pinch, and gross) (range of score, 0–57; higher = better performance) (29). The motor activity log (MAL) assessed changes in the amount and the quality of the arm use in accomplishing 30 daily activities (range of score, 0–168; higher = better performance) (30).

Participation Level

The Multiple Sclerosis Quality of Life-54 with the physical health and mental health domains measured generic and MS-specific domains of health-related QoL (range of score, 0–100; higher = better performance) (31). The patient's satisfaction with daily activities or social roles was assessed using the Life Habits Assessment–general short form (32).

Instrumental Assessment

The patients underwent one session (three trials/session) of sEMG acquisition as follows. The sEMG amplitude domain from six upper limb muscles of the more affected side (deltoid scapular, deltoid clavicular, triceps brachii, biceps brachii, flexor carpi radialis, and extensor carpi radialis) was measured using pairs of self-adhesive surface electrodes. The sEMG signals from trapezius inferior and pectoralis major along with data from the inertial sensor fixed to the subjects' hand were not considered because of the low quality of the signals acquired. Disposable

Ag–AgCl electrodes were placed according to the Surface Electromyography for the Non-invasive Assessment of Muscles guidelines with an interelectrode spacing of 0.02 m. Before electrode placement, the skin was shaved with a disposable, single-use razor and cleaned with alcohol (33). Raw sEMG signals were collected using BTS FREEEMG 300 wireless sEMG sensors (BTS spa, Milan, Italy) at a sampling rate of 1,000 Hz. Raw sEMG signals were processed with a customized routine developed in MATLAB environment (MathWorks, USA). The raw sEMG signal was bandpass filtered at 20–450 Hz and then smoothed using a 20-ms root mean square algorithm to obtain the envelope. Signals were recorded during a functional task of reaching while grasping an object (ARAT grasp section; **Figure 1**). Patients sat upright in a standard chair with a firm back without armrests according to the ARAT standard procedures (34). Patients were asked to keep the trunk in contact with the back of the chair during testing. The UL was positioned in pronated position on the table. The task consisted of grasping and placing a 7.5-cm wooden cube on a shelf of standardized height (37 cm) corresponding to the grasp item of the ARAT testing. The task was divided into three phases by identifying four temporal events (start, grasping the cube, placing the cube on the shelf, returning to initial position). The task was repeated three times with a resting time of 2 min between trials, and the signals were averaged and time normalized. Normative data were collected on a convenient sample involving 10 healthy age-matched controls undergoing one session (three trials/session) of the same sEMG acquisition protocol. The sEMG paradigm is illustrated in **Figure 1**.

DATA ANALYSIS

Results about the most affected UL were reported. Descriptive statistics included median and first through third quartiles (Q1; Q3) to describe the magnitude of UL impairments on the different ICF domains in the whole group and the different EDSS subgroups. Since the data were not normally distributed (Shapiro–Wilk test), non-parametric tests were used for inferential statistics. The Kruskal–Wallis H test ("one-way ANOVA on ranks") was used to determine statistically significant differences between the three groups of the independent variables. *Post hoc* between-group comparisons were performed using the Mann–Whitney *U* test (corrected for multiple comparisons using Tukey's multiple comparisons test).

As manual dexterity was previously showed to play a key role in the UL overall impairment, linear correlations between the NHPT and other outcome measures were computed using Spearman's correlation in the all sample to explore the strength of the relationship among outcome measures. Data distribution did not allow to perform a linear regression model, and the correlation strength was defined as very high ($\rho > 0.9$), high ($\rho =$ 0.7–0.89), moderate ($\rho =$ 0.5–0.69), low ($\rho =$ 0.3–0.49), or very low ($\rho < 0.29$) (35).

The sEMG data were qualitatively and quantitatively analyzed. The normalized mean sEMG envelope for healthy subjects and each patients' subgroup was used to display the muscle activation patterns during the movement and reported in figures. Moreover, the timing of maximal muscle activation for each phase was calculated as a percentage of the relative movement phase (1–100%) for each group. One-way ANOVA was used to determine statistically significant differences among groups. *Post hoc* between-group comparisons were performed using the Mann–Whitney *U*-test. According to the functional involvement of the six muscles during the reaching task, muscles were coupled as follows: (1) deltoid clavicular and biceps brachii, as shoulder flexors; (2) biceps and triceps brachii, as agonist and antagonist actors during the elbow flexion; and (3) flexor and extensor carpi radialis because involved in maintaining the wrist in neutral position during the wooden cube displacement. The mean difference between the timing of maximal muscle activation for each couple of muscles in each subgroup of PwMS patients was computed. No frequency domain data analysis was performed. Statistical analysis was carried out with SPSS 20.0 (IBM SPSS Statistics for Windows, Version 20.0, Armonk, NY, USA) and Stata/IC 15.1 for MAC (StataCorp, TX, USA).

RESULTS

Forty-one patients have been included and allocated to mild–moderate ($n = 17$), severe ambulant ($n = 15$), and severe non-ambulant ($n = 9$) groups. All patients were assisted by family members and were living in their home. No patients were institutionalized or community-dwelling PwMS. Significant between-group differences in age ($p = 0.05$) and the type of MS among groups were measured. The most severe group was older than the other two groups. Moreover, the majority of patients in the most severe group were affected by secondary progressive MS. **Table 1** reports demographic and clinical characteristics of the sample.

Body Functions and Structures Level

A statistically significant difference was found in UL function (FM scale), and muscle tone (MAS), and the fatigue perceived were measured (**Table 2**) among groups. *Post hoc* comparisons showed that participant in the severe non-ambulant group (group 3) experienced significantly higher UL muscle tone than the mild–moderate group (group 1) ($p = 0.002$). Fatigue was significantly higher in the severe ambulant group (group 2) than the mild–moderate group (group 1) ($p = 0.008$) and significantly lower in the severe nonambulant group (group 3) than the severe ambulant ($p = 0.004$).

Activity Level

Manual dexterity assessed with the NHPT differed significantly among groups (**Table 2**). PwMS showed a progressive decrease of peg/second rate and a progressive reduction in UL use according to the neurological disability (**Table 2**). The severe non-ambulant participants (group 3) experienced significantly higher impairments than the mild–moderate group (group 1) in the NHPT ($p = 0.015$) and MAL ($p < 0.001$). The NHPT score was strongly correlated to ARAT ($\rho = 0.721$, $p < 0.001$), MAL-AOM ($\rho = 0.712$, $p < 0.001$), and MAL-QOM ($\rho = 0.769$, $p < 0.001$). Conversely, there was a low correlation between FM and NHPT score. Within the ICF framework, outcome measures belonging to the activity domain were moderate to very strongly correlated with each other. The MAL score in the severe

FIGURE 1 | The reaching task (ARAT grasp subscale). The movement was divided into three phases, as shown.

TABLE 1 | Demographic and clinical characteristic of the sample.

		MS subgroups			***p*-value**
		Group 1	**Group 2**	**Group 3**	
	Total (*n* = 41)	**Mild–moderate EDSS (1–5.5) (*n* = 17)**	**Severe ambulant EDSS (6–6.5) (*n* = 15)**	**Severe NA EDSS (7–9.5) (*n* = 9)**	
Gender (F/M)	25/16	12/5	7/8	6/3	0.35
Age (years)	50.88 ± 10.9	45.88 ± 11.98	54.07 ± 9.16	55 ± 8.35	0.05*
EDSS	6 (4.25–6.5)	4 (3.5–5.25)	6 (6–6.5)	7.5 (7-8)	<0.001*
EDSS sensory	2 (0.5–2)	1 (0–2)	2 (2)	1.5 (0.5–2)	
Hand dominance (R/L/A)	36/5/0	13/4/0	14/1/0	9/0/0	0.16
Disease duration (years)	14.20 ± 8.76	12.12 ± 9.5	14.60 ± 8.52	17.44 ± 6.23	0.29
Type of MS (PP/RP/RR/SP)	2/2/22/15	0/1/13/3	1/1/8/5	1/0/1/7/9	0.05*
Visual impairment (yes/no)	2/39	0/17	1/14	1/8	0.70

Data are presented as frequency mean ± SD or median (25th/75th percentiles).

F, female; M, male; EDSS, Expanded Disability Status Scale; NA, nonambulant; R, right; L, left; A, ambidextrous; MS, Multiple sclerosis; RR, relapsing remitting; SP, secondary progressive; PP, primary progressive.

[*] *Significant p-value.*

ambulant participants (group 2) differed significantly from the severe non-ambulant group (group 3) ($p = 0.001$). No significant differences in the ARAT total score were measured. However, the grip subsection score was statistically different among groups ($p = 0.01$). *Post hoc* comparisons showed that the severe non-ambulant group (group 3) performance was worse than the mild–moderate group (group 1) (**Table 2**, **Figure 2**).

Participation Level

The patient's satisfaction with daily activities or social roles assessed by the Life Habits Assessment–general short form differed significantly among groups (**Table 2**). Participants in the mild–moderate group (group 1) reported significantly higher satisfaction than the severe ambulant (group 2) ($p = 0.001$) and severe non-ambulant (group 3) group ($p < 0.001$). *Post hoc* comparisons are shown in **Figure 2**.

Instrumental Assessment Results

The mean sEMG envelope in healthy controls showed a relevant activation of deltoid anterior between phases 2 and 3, corresponding to the deltoid's typical recruitment during the shoulder flexion. The triceps brachii activity was almost absent during the entire movement, while a slight activation of the biceps brachii was recorded during phases 2 and 3. Although the overall activation value for flexor carpi muscles was <0.02 mV, a modulation in its activity, associated with the activity of higher intensity of extensor carpi activation, was found at about 30% and 70–80% of the movement. This coupled activation was consistent with forearm muscles' function of wrist stabilization during a grasping task. In PwMS, a progressive decrease in the modularity of muscle activation was reported in association with increasing in neurological disability. This loss of modularity was especially evident in the flexor and extensor carpi muscles, where the most severe patients showed a constant (but low) muscle activation (**Figure 3**).

The between-group analysis of the timing of maximal muscle activation showed statistically significant differences in the anterior deltoid in phase 3 ($p = 0.034$), which was during the eccentric contraction of the muscle, and in the extensor carpi muscles during phase 2 ($p = 0.020$), while subjects were holding the cube (**Table 3**). The *post hoc* analysis showed that severe non-ambulant patients reported a delayed maximal activation of the deltoid anterior compared to other groups in the last movement phase ($p = 0.027$; adjusted for multiple comparisons). Similarly,

TABLE 2 | Median scores (25th /75th percentiles) of clinical variables and p values comparing the three groups.

		MS subgroups			
		Group 1	**Group 2**	**Group 3**	
	Total ($n = 41$)	**Mild–moderate EDSS (1–5.5) ($n = 17$)**	**Severe ambulant EDSS (6–6.5) ($n = 15$)**	**Severe NA EDSS (7–9.5) ($n = 9$)**	**p value**
Body function and structures					
Fugl–Meyer (0–66)	60 (43–64.5)	63 (56.5–65)	56 (42–64)	48 (36.5–61)	0.037*
Motricity Index (0–100)	85 (73–93)	92 (74–93.75)	83 (71–94.75)	73 (64.5–90.5)	0.179
- Pinch grip (0–33)	26 (22–33)	26 (26–33)	26 (24–29.5)	22 (22–26)	0.169
- Elbow flexor (0–33)	25 (25–33)	33 (25–33)	25 (22–33)	25 (25–33)	0.579
- Shoulder abductors (0–33)	25 (25–33)	33 (25–33)	25 (25–33)	25 (19–33)	0.125
Modified Ashworth Scale (0–15)	0 (0–1)	0 (0–0.5)	0 (0–2)	2 (0.5–3)	0.008*
- Elbow flexors (0–5)	0 (0–1)	0 (0–0)	0 (0–0.5)	1 (0–1)	0.004*
- Wrist flexors (0–5)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0.5)	0.056
- Finger flexors (0–5)	0 (0–0)	0 (0–0)	0 (0–0.5)	0 (0–1)	0.395
Tremor Severity scale (0–5)	0 (0–2)	0 (0–2)	0 (0–3)	0 (0–2.5)	0.689
Numeric Rating Scale fatigue	6 (5–8)	6 (5–7.5)	8 (7–9)	5 (5–7.5)	0.005*
Activity level					
NHPT (pegs/sec)	0.23 (0.14–0.27)	0.26 (0.23–0.28)	0.18 (0.15–0.26)	0.07 (0.04–0.20)	0.027*
ARAT (0–57)	49 (39.59–53)	52 (48–53)	47 (34–52)	40 (16.5–52.5)	0.145
- Grasp (0–18)	18 (12–18)	18 (18)	15.5 (11.75–18)	13 (6–18)	0.054
- Grip (0–12)	10 (8–12)	12 (11–12)	10 (7.75–12)	8 (6–10.25)	0.01*
- Pinch (0–18)	13 (12–17.5)	15 (12.25–15.75)	13 (9.75–18)	12 (2–13)	0.660
- Gross (0–9)	9 (7–9)	9 (9)	9 (5.75–9)	8 (4–9)	0.052
MAL AoU	113.5 (76.25–132.75)	131 (115.5–147.5)	113 (92–132)	69.5 (27.25–82.75)	0.005*
MAL QoM	108.75 (86.125–126.75)	123 (110.5–130.5)	108.5 (100–119)	69 (24–80.5)	0.001*
Participation level					
LifeH	11.85 (9.97–12.91)	12.7 (12.1–14.53)	11.56 (8.95–12.1)	10.4 (8.72–10.66)	< 0.001*
MSQOL-54	102.17 (60.8–129.84)	127.93 (60.22–146.15)	65.64 (51.2–110.49)	103 (78.57–121.32)	0.160

Data are presented as median (25th/75th percentiles).

EDSS, Expanded Disability Status Scale; MS, multiple sclerosis; NA, non-ambulant; NHPT, Nine-Hole Peg Test; ARAT, action research arm test; MAL, motor activity log; MSQoL-54, Multiple Sclerosis Quality of Life-54; LifeH, Life Habits assessment–general short form.

**Significant p-value.*

extensor carpi muscles were activated with a significant delay in the severe group compared with the mild–moderate patients in phase 2 ($p = 0.043$; adjusted for multiple comparisons). Interestingly, the difference of the maximal activation of extensor carpi muscles between patients and healthy subjects during the holding-cube phase was found to be significantly correlated to the performance at the NHPT ($\rho = -0.44$; $p = 0.038$).

The comparison between the difference in the timing of maximal activation between functionally coupled muscles did not show any significant difference between groups. However, during phase 2, the maximum of proximal muscles activation (biceps brachii and deltoid anterior) occurred almost simultaneously in healthy controls and moderate and severe ambulant patients (groups 1 and 2). Conversely, severe non-ambulant patients (group 3) showed a remarkable decrease in the modularity of biceps brachii, which resulted in a different sequence in the timing of activation. Similarly, the difference in temporal activation of the biceps and triceps brachii showed an opposite behavior between the severe non-ambulant group and the other two groups. More in detail, patients of group 3 activated the triceps brachii more than other patients, and the lack of modularity of biceps activity prevents the calculation of the maximum of the envelope. Concerning the forearm muscles, the differences between the timing of maximal activation between the flexors and extensor muscles, both in phases 2 and 3, were remarkably higher in all groups as compared to the healthy controls (**Figure 4**).

DISCUSSION

The results of this observational cross-sectional study suggest that manual dexterity might be already impaired in the mild–moderate stages when the overall neurological disability is low. Strong to moderate significant associations between UL deterioration and impairments at different ICF levels were noted in the most severe group. The progressive decline in manual dexterity, as measured by the NHPT, was associated with the deterioration of the overall UL activity (measured by ARAT) and disuse. Weakness, sensory loss, and tremor seemed not to be significant determinants of UL deterioration in our cohort.

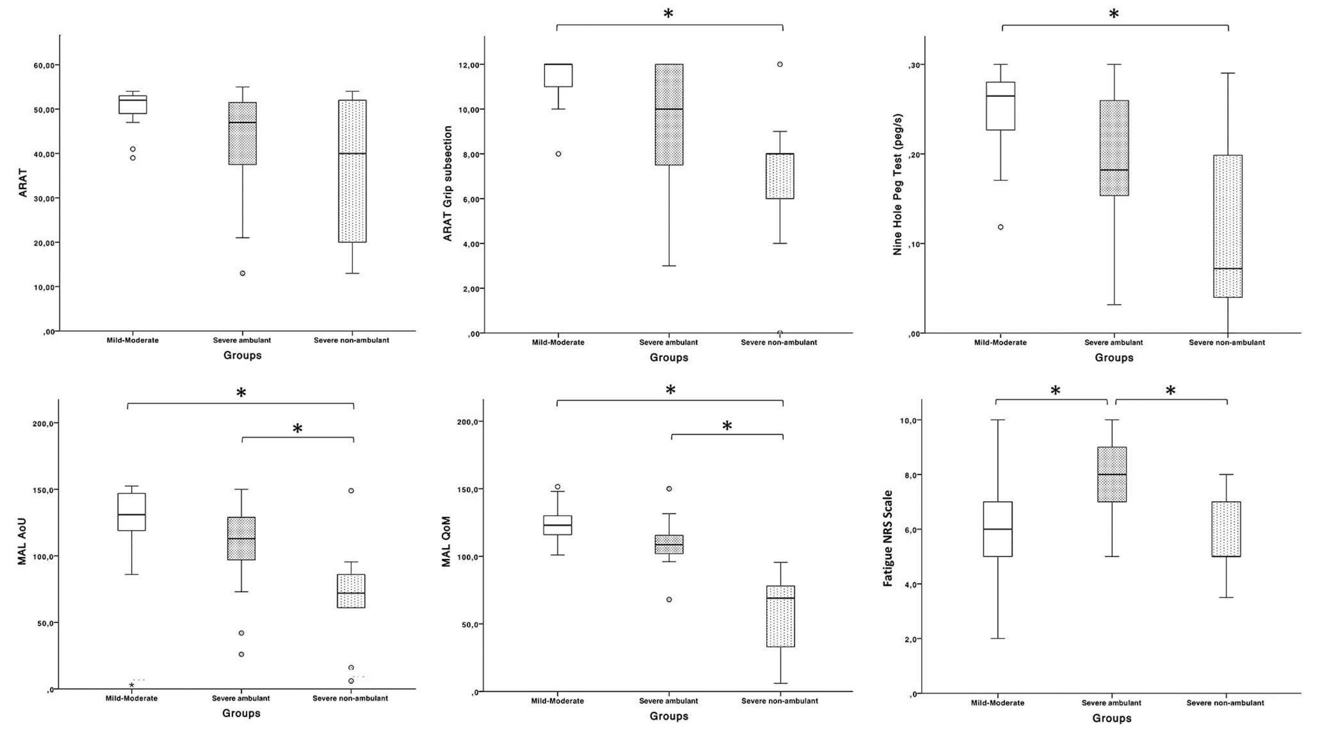

FIGURE 2 | Median scores of clinical variables comparing the three subgroups. *Significant *p*-value.

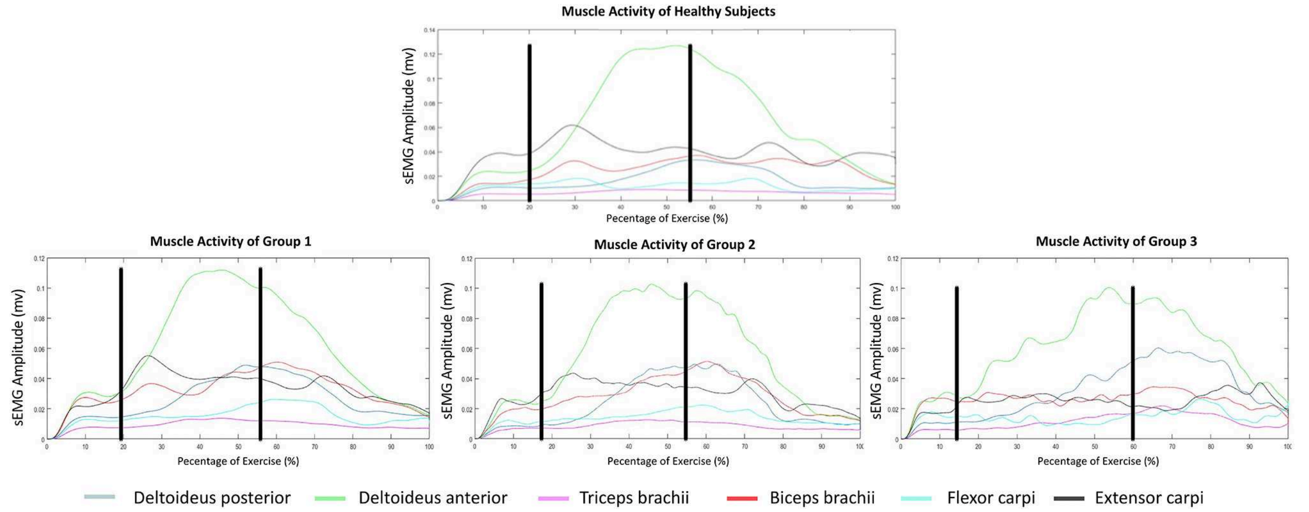

FIGURE 3 | Mean surface sEMG envelope of healthy subjects **(Top)** and patients **(Bottom)**.

The sEMG assessment showed impairments in both modularity and timing of activation of distal (extensor carpi) muscles in the severe ambulant patients, while impairments in the timing of activation in the proximal muscles (anterior deltoid) were found in the more advanced stages (EDSS $\geq$ 7).

To the best of our knowledge, this study is the first one exploring objectively and subjectively UL dysfunction at different ICF levels using clinical and instrumental assessments. Strength in the methodology includes the fact that all patients suffered from severe manual dexterity impairment and that clinical and instrumental assessments were combined to explore the multifaceted nature of UL dysfunction. Limitations are the small sample of patients with severe neurological impairments and the lack of prospective longitudinal assessments. Concerning

TABLE 3 | Mean (standard deviation) of timing maximal muscle activation.

	Movement phase	**Healthy subjects**	**MS subgroups**			***p*-value**
			Group 1	**Group 2**	**Group 3**	
			Mild–moderate	**Severe ambulant**	**Severe NA**	
			EDSS (1–5.5)	**EDSS (6–6.5)**	**EDSS (7–9.5)**	
Anterior deltoid	1	72.5 (25.6)	71.3 (23.4)	84.6 (15.2)	65.5 (24.3)	0.58
	2	81.4 (15.0)	66.5 (17.9)	78.6 (18.7)	82.8 (6.9)	0.14
	3	2.7 (3.8)	6.2 (7.2)	5.8 (11.6)	23.5 (27.4)	0.034*
Biceps brachii	1	65.1 (22.5)	57.2 (22.6)	59.4 (25.4)	64.5 (24.0)	0.86
	2	67.5 (31.2)	56.17 (38.0)	67.8 (29.9)	59.3 (28.9)	0.84
	3	42.9 (29.5)	32.8 (22.6)	39.6 (20.2)	30.0 (32.7)	0.75
Triceps brachii	1	67.1 (17.3)	73.4 (20.0)	68.0 (21.9)	54.0 (30.2)	0.47
	2	68.5 (9.5)	68.6 (26.5)	48.8 (35.2)	84.8 (15.6)	0.14
	3	15.1 (13.3)	18.7 (26.6)	27.2 (32.8)	25.0 (25.7)	0.77
Flexor carpi	1	82.7 (15.8)	74.5 (21.4)	60.8 (24.7)	63.8 (16.0)	0.16
	2	34.4 (34.9)	70.6 (37.3)	47.0 (43.7)	50.0 (38.5)	0.19
	3	22.0 (13.3)	32.2 (31.7)	59.2 (45.3)	64.0 (45.6)	0.07
Extensor carpi	1	81.1 (21.6)	73.6 (29.3)	52.0 (23.0)	65.0 (23.6)	0.18
	2	27.2 (15.3)	26.3 (24.6)	65.4 (34.8)	54.5 (43.2)	0.020*
	3	41.5 (31.9)	29.0 (28.0)	15.4 (15.3)	50.3 (30.2)	0.19

Data are reported as movement phase percentage.
**Significant p-value.*

previous literature, our data confirm positive associations between manual dexterity and UL function and activity level and further explore new associations for discussion.

According to the literature, manual dexterity impairment is one of the major determinants of disability in PwMS since the first stages of the illness (5, 15). Hand dexterity plays a crucial role in everyday life activities and social participation, as it has been reported to be associated with independence in activities of daily living and UL use (36). The NHPT is recommended as a gold standard to measure hand dexterity for its excellent psychometric properties. However, caution should be taken when assessing PwMS with low ($EDSS < 3$) or high disability ($EDSS > 6$) for its floor and ceiling effects, respectively (37). We reported an overall mean score of NHPT of 0.19 pegs/s ranging between 0.23 pegs/s of the mild–moderate group to 0.12 pegs/s of the severe non-ambulant group, which is below the cutoff values previously suggested (0.27 pegs/s) (15). The comprehensive UL assessment allowed to explore UL dysfunction across neurological disability stages further. In the mild–moderate disability group, with EDSS below six, manual dexterity impairments were not associated with multiple UL dysfunctions as shown by high performances in UL function, overall UL activity, and use. Similarly, the sEMG mean level of activation was similar between patients and healthy subjects, and no significant differences were reported in the sEMG timing of activation.

Of note, sEMG alterations but not clinical dysfunctions were evident in patients with EDSS between 6 and 6.5 (severe ambulant group). The sEMG analysis suggested a progressive reduction in the modularity of muscular activation pattern according to increasing neurological disability. Modularity in muscular activation is defined as the difference between the maximum and minimum values of muscular activation (16). This dysfunction could account for the differences in the timing of maximal activation of the forearm muscles measured between the severe and the mild–moderate patients during phase 2 of the movement. In this part of the movement, patients were holding the cube and moving it to the shelf. Therefore, extensor carpi muscles were supposed to act as wrist stabilizers counterbalancing the activation of flexor muscles. The impairment of this activation timing could contribute to developing dysfunctional grasping and, as a consequence, manual dexterity deterioration. This hypothesis is supported by the significant inverse correlation measured between the NHPT and patients' abnormalities in extensor carpi timing of maximal activation compared to controls. Even in these severely impaired patients, the sEMG mean level of activation was similar to healthy subjects. Hence, sEMG data on the amplitude domain suggested that abnormalities in the timing of activation of distal UL muscles rather than the magnitude of UL muscle activation could be crucial in dexterity deterioration. This impairment could occur as a consequence of different pathophysiological mechanisms such as reduction in central drive, reduction in motoneuron excitability in the spinal cord, or reduction in sarcoplasmic reticulum calcium uptake in the skeletal muscle. Noteworthy, the only significant clinical symptom in this group was fatigue.

In the most advanced stages, with EDSS above 6.5, no further sEMG parameters deterioration were noted in distal segments. However, proximal shoulder muscles showed a delay in the

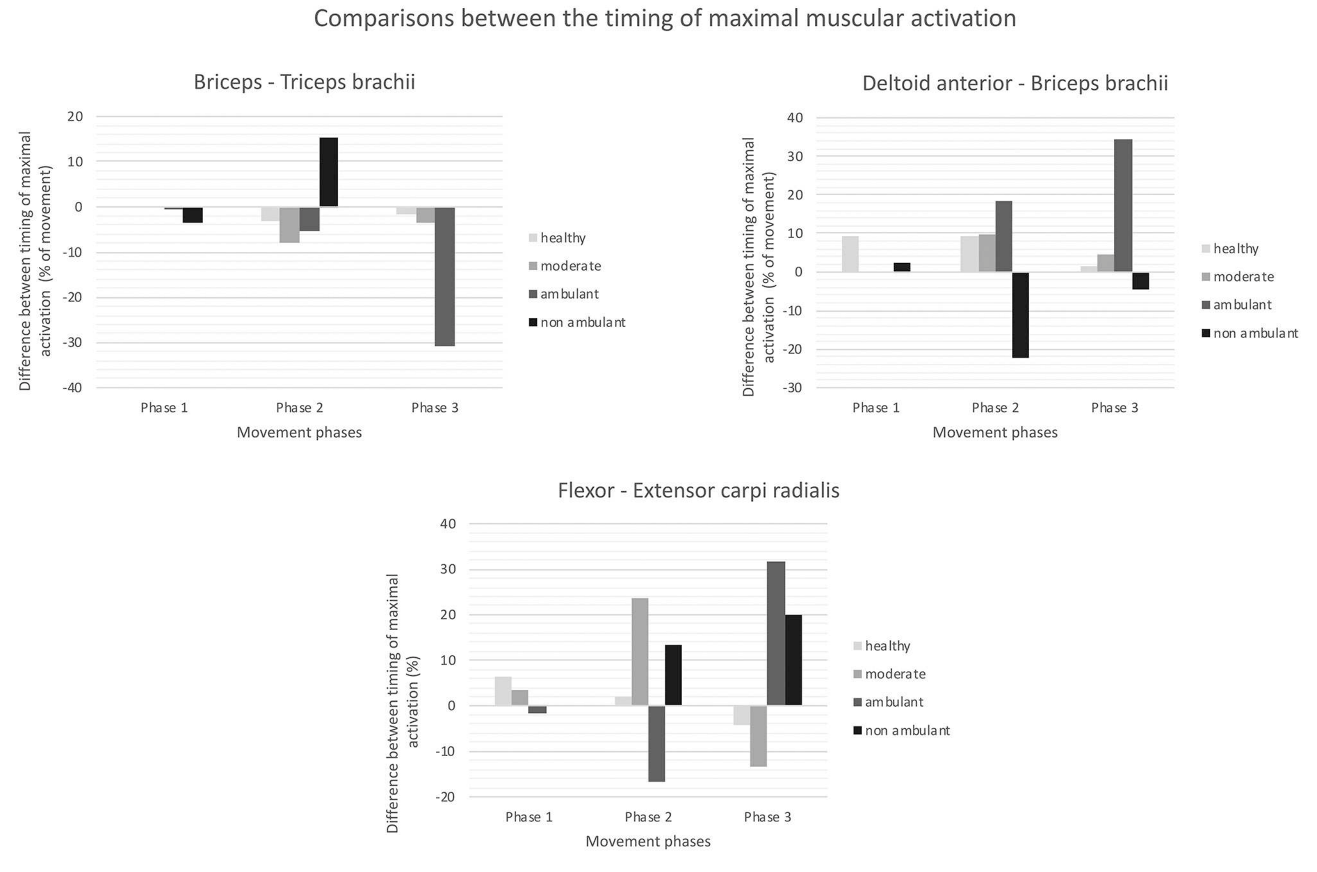

FIGURE 4 | Difference between the timing of maximal activation for functionally coupled muscles.

maximal muscle activation in the eccentric anterior deltoid contraction during phase 3. These findings were associated with a UL disuse, impairment in grip task, and an overall decrease in UL function. Interestingly, the significant increase in fatigue observed in the previous stage (group 2) was followed by a significant decrease in the symptom's severity. A possible explanation is that the UL disuse was likely to account for lower perceived fatigue. Fatigue is considered one of the most disabling symptoms affecting PwMS, leading to the limitation in UL activities and social participation (37). Both peripheral and central mechanisms have been described in MS-related fatigue (38). In the present study, fatigue was assessed using a Numeric Rating Scale by which patients reported their overall perceived fatigue during the day while using the UL. This finding might be influenced by the nature of the assessment used and should be confirmed using more specific outcome measures of muscle endurance (i.e., handgrip or static fatigue elbow extension) (15).

So far, positive associations between manual dexterity and UL deteriorations have been reported by two clinical cross-sectional studies and one clinical instrumental observational study (5, 15, 17). The cross-sectional study by Bertoni et al. (5) explored for the first time UL dysfunctions at different ICF levels in 105 patients (5). These authors found that patients with moderate neurological disability (EDSS < 4) showed limitation in manipulating small objects, while severely affected subjects with severe hand dexterity impairment showed proximal UL muscles strength deficit. Lamers et al. (15) found that different levels of hand dexterity ability based on NHPT accounted for different associations among outcome measures (15). In particular, muscle strength and active wrist mobility seemed to be more relevant in patients with severe manual dexterity impairment. Authors concluded that quantitative analysis of other factors that may contribute to UL impairment like sensorimotor function, force control, and fatigue are needed (15). A more recent study by Pellegrino et al. (17) investigated UL muscle activation pattern and coordination in different mechanical environments in 11 patients (17). The sEMG analysis showed modifications of the muscle activation pattern in PwMS compared to healthy controls during planar reaching movements in PwMS with mild–moderate UL impairment in Pellegrino et al. (17). In their study, patients were asked to perform reaching movement while grasping the handle of a robotic manipulandum. In contrast with previous findings on stroke patients (39), Pellegrino et al. (17) found no difference in the number of synergies involved in the task between patients and healthy controls. However, proximal muscles like anterior deltoid and biceps brachii showed different activation pattern compared to controls. In particular, the authors reported that shoulder muscles had different amplitude modulations and increased activity during the return phase, moving the manipulandum toward their body while flexing the elbow. Moreover, during the elbow extension, PwMS coactivated biceps and triceps brachii. Their findings suggested that the analysis of muscle activation pattern could improve the understanding of UL impairment in PwMS representing biomarkers that help in discriminating MS patients and healthy subjects.

Literature findings are partially consistent with ours. We did not find a significant association between the NHPT and Motricity Index, tremor, and sensory loss. One explanation could be the low level of tremor symptoms and a mild decrease in sensory loss present in our sample. Interestingly, a positive association was found between NHPT and UL disuse, suggesting that behavioral factors could account for severity hand dexterity impairment of PwMS. In this regard, despite the severe hand dexterity, the ARAT total score indicates a notable UL capacity in groups 1 and 2 and limited UL capacity only in group 3. UL disuse was never explored in the previous cross-sectional studies. The concept of UL disuse was derived from primary research with monkeys (6) and then extensively studied in stroke patients (7). Briefly, injury in the central nervous system (CNS) leads to sensorimotor deficits and depressed CNS. As a consequence, the patients experience fewer movements, unsuccessful motor attempts, and compensatory behavior patterns. PwMS reported 50% less use of both arms as healthy control and overall lower quality of the movement (8–11). Noteworthy, a reduction in UL use is closely related to disability and can sustain maladaptive brain reorganization (1). Specific interventions to overcome the UL disuse, however, is still under debate in PwMS (40). In the pilot randomized controlled trial by Mark et al. (40), 20 adults with hemiparetic MS were randomized to receive 35 h of either constraint-induced movement therapy or program of complementary and alternative medicine over 10 consecutive weekdays (40). Changes in the MAL was the primary outcome measure. Results suggested that constraint-induced movement therapy might increase real-world use of the more-affected arm in PwMS, and these effects might last up to 1 year. Interestingly, the training effects paralleled white matter changes.

Our findings support the use of sEMG parameters in the assessment of PwMS. Accordingly, previous work by Pellegrino et al. (16) concluded that both kinematic and electromyographic parameters might represent biomarkers that help clinicians in differentiating patients with different levels of UL motor impairment from healthy subjects (16). Surface EMG was reported to help investigate motor dysfunction as force control and fatigue in PwMS (17, 18). Results are strengthened by the sEMG protocol used during a task of reaching while grasping an object. The sEMG assessment has considerable advantages over other neurophysiological evaluation in the rehabilitation setting being portable and readily operable with different tasks (41). Considering the biology-function continuum for assessment tools in patients with CNS lesions, clinical scales inform of clinical status, providing mainly functional insight (41). Conversely, sEMG can provide an aspect of biology insight (17). Our preliminary analysis was focused on identifying changes in the modulation and timing of activation to explore the muscle coordination in functionally coupled muscles like anterior deltoid and biceps brachii, biceps and triceps brachii, flexors, and extensors carpi.

The main limitation of our study is the cross-sectional design that did not allow to track the time course of the UL deterioration and to follow the real impact of the disease on the ICF domains. Further prospective longitudinal studies should consider these limits and introduce the evaluation of all the clinical and neurophysiological data in a longitudinal prospective manner along different disease stages. In addition, the small sample allowed only a preliminary exploration of data using nonparametric tests for inferential statistic and did not allow to explore potential gender differences among groups. Cognitive assessments (i.e., attention, memory, and executive functions deficits, and mood disorders) and fatigue investigation to distinguish between central and peripheral components of the disturbance should be explored in future studies. The strengths of this study are the use of specific study population and the attempt to use a multidimensional approach to characterize UL impairments.

To conclude, the analysis of sEMG data on the amplitude domain and the association between impairments in body structure, function, activity, and participation provided new insight into the understanding of UL disability progression in PwMS. Manual dexterity should represent a primary target in PwMS rehabilitation to prevent the development of secondary UL impairment. The sEMG analysis suggests that impairments in the forearm muscle activation were associated with increasing neurological disability and UL deficits at the different ICF levels.

DATA AVAILABILITY STATEMENT

The datasets generated for this study are available on request to the corresponding author.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by CESC prog.n.230. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

MG and NS have made substantial contributions to conception and design. AG, MCas, MCam, EC, and AP participated in the enrollment phase. JC and CD carried out the clinical assessment. NV, MF, and ED carried out instrumental assessments. SM and EB designed the algorithm for sEMG data analysis. MG and NV participated in the statistical analysis and drafted the manuscripts. NV, FF, AW, and LS participated in the manuscript revision process and gave the final approval of the version.

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Implementing a Standardized Language Evaluation in the Acute Phases of Aphasia: Linking Evidence-Based Practice and Practice-Based Evidence

Megan E. Schliep [1,2]*, ***Laura Kasparian*** [3], ***Olga Kaminski*** [3], ***Carla Tierney-Hendricks*** [1,2], ***Esther Ayuk*** [2], ***Lynne Brady Wagner*** [2], ***Semra Koymen*** [3] **and** ***Sofia Vallila-Rohter*** [1,3]*

[1] MGH Institute of Health Professions, Boston, MA, United States, [2] Speech-Language Pathology Department, Spaulding Rehabilitation Hospital, Boston, MA, United States, [3] Speech-Language and Swallow Department, Brigham and Women's Hospital, Boston, MA, United States

Edited by:
Lisa Tabor Connor,
Washington University in St. Louis,
United States

Reviewed by:
Evy Visch-brink,
Erasmus University Medical Center
Rotterdam, Rotterdam, Netherlands
Robert Peter Fucetola,
Washington University in St. Louis,
United States

***Correspondence:**
Megan E. Schliep
mschliep@mghihp.edu
Sofia Vallila-Rohter
svallilarohter@mghihp.edu

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The research to practice gap is a significant problem across all disciplines of healthcare. A major challenge associated with the adoption of evidence into routine clinical care is the disconnect between findings that are identified in a controlled research setting, and the needs and challenges of a real-world clinical practice setting. Implementation Science, which is the study of methods to promote research into clinical practice, provides frameworks to promote the translation of findings into practice. To begin to bridge the research-practice gap in assessing recovery in individuals with aphasia in the acute phases of recovery following stroke, clinicians in an acute care hospital and an inpatient rehabilitation hospital followed an implementation science framework to select and implement a standardized language assessment to evaluate early changes in language performance across multiple timepoints. Using a secure online database to track patient data and language metrics, clinically-accessible information was examined to identify predictors of recovery in the acute phases of stroke. We report on the feasibility of implementing such standardized assessments into routine clinical care via measures of adherence. We also report on initial analyses of the data within the database that provide insights into the opportunities to track change. This initiative highlights the feasibility of collecting clinical data using a standardized assessment measure across acute and inpatient rehabilitation care settings. Practice-based evidence may inform future research by contributing pilot data and systematic observations that may lead to the development of empirical studies, which can then feed back into clinical practice.

Keywords: implementation science, aphasia, standardized assessment, acute care, rehabilitation, stroke recovery

INTRODUCTION

Two million people in the United States are living with aphasia—an impairment in language comprehension and production. Speech-language pathologists play a central role in the assessment and diagnosis of individuals with language deficits following stroke, and current clinical practice for the assessment of language skills following stroke is variable across and within clinical practice settings (1). Lack of consistency places limitations on the understanding of early stroke recovery, and limits care continuity between settings and clinicians. Further, there is a disconnect between what occurs within clinical practice and advancements being made in research to inform recovery predictions.

The research to practice gap, defined as the discrepancy between evidenced-based interventions and what takes place in practice, has been well-documented (2–6). Studies have suggested that it takes 17 years for 14% of healthcare research to be adopted into routine clinical practice (7). This slow translation of research to the clinic is one of the disconnects that confines healthcare and clinicians' abilities to optimize care for patients. The limited uptake of research has been attributed to a variety of factors, including the level of relevance of research findings to practice, organizational constraints that impact the adoption of findings into practice, and the degree of benefit to the target population to sustain the practice (4, 6, 8).

Evidence-based medicine calls for the integration of the best available evidence from systematic research in the care and clinical decision-making process for individual patients (9). The goal of EBP involves the integration of (1) external scientific evidence, (2) clinical expertise, and (3) client, patient, and caregiver values and perspectives (9–11). A major challenge associated with the adoption of EBP, however, is the disconnect between the findings identified in a controlled lab setting and those that are ultimately implemented in a real-world clinical practice setting (3, 12–16). The scientific pipeline has generally prioritized scientific control for internal validity; while categorically important, the focus on internal validity may come at the expense of external validity, or generalizability across setting and time (3). By bringing research closer to the actual practice setting and creating practice-based evidence, results may be more relevant, tailored, and actionable to patients and clinicians (3, 17–19).

Important for any attempts to bring research close to the practice setting is Implementation Science. Implementation Science is the study of methods that promote systematic uptake of research into routine clinical practice (8, 20–22), offering frameworks and structure to help guide successful implementation [e.g., (22–24)]. Additionally, practice-based evidence, the concept that clinicians can structure practice and measure outcomes in the real-world care setting, offers an opportunity to inform research needs and speed the research to practice transfer (3, 17–20, 25).

Prior work has demonstrated that, with the guidance of implementation science frameworks, a standardized process for the evaluation of language was feasible in acute care and improved diagnosis and reporting of aphasia [see (26)]. The current manuscript describes a follow-up study that reports on the long-term adherence to the implemented measure, and on the extension to an inpatient rehabilitation facility. Clinicians in acute care and inpatient rehabilitation hospitals, both within the same healthcare network, have been working together with the long-term goal of populating a database with consistent measures of language performance across the early stages of aphasia diagnosis to begin to inform early language recovery patterns. Stroke-related information, including lesion size and lesion location, have been identified as key factors in predicting language outcomes, and initial aphasia severity has been acknowledged as the most robust factor in predicting language recovery (27–33). The extent to which clinicians make recovery predictions, however, and share these with their patients is limited. One of the reasons research knowledge about recovery has not translated to the clinic is that current predictive information is not fine-grained enough to capture clinically-observable skills at the individual level, or they require high-level analyses that are more consistent with the research setting. Standardizing clinical practice to gather data may help shed light on the types of data that are feasible to capture clinically and could be informative to outcomes.

Thus, to begin to bridge the research-practice gap in predicting language abilities in individuals with aphasia in the acute phases of recovery following stroke, this manuscript reports on (1) the feasibility of adhering to a standardized language assessment protocol in acute care over a 2-year period, (2) the iterative implementation process utilized in an inpatient rehabilitation care facility following an implementation science framework, and (3) a pilot evaluation of data collected through standardized assessments to begin to evaluate predictive models of language recovery after stroke.

Part I—The Feasibility of Adhering to a Standardized Language Assessment Protocol in Acute Care

Between October of 2016 and June of 2017, an iterative process of implementation was carried out at Brigham and Women's Hospital (BWH) to standardize the process of language evaluation. BWH is a 777-bed acute-care teaching hospital of Harvard Medical School within the Partners HealthCare Network. The hospital transitioned from paper medical records to electronic medical records in 2015, which created an opportunity for clinicians to assess clinical practices and consider how to most effectively integrate clinical expertise within the new documentation structure. The goal of this implementation project was to identify a clinical process to improve the evaluation and diagnosis of aphasia within the constraints of the acute care setting and to maximize efficiency and clarity of information within the electronic medical record. In brief review [see (26) for full report], a team of researchers and clinicians formed an implementation team and carried out the implementation process using the fourteen-step, four phase, Quality Implementation Framework (QIF) proposed by Meyers et al. [(22), see **Figure 1**].

QIF Phase 1 (considerations of the host setting), readiness for change was facilitated by the transition to the electronic record. During QIF Phase 2 (creating a structure for implementation), a literature review was performed by the implementation team to select an assessment that was feasible to administer in acute care that addressed implementation goals of improved diagnosis [the Western Aphasia Battery-Bedside Version (WAB-Bedside)], and software was selected to support data collection and entry into the medical record [REDCap, a secure online database supported

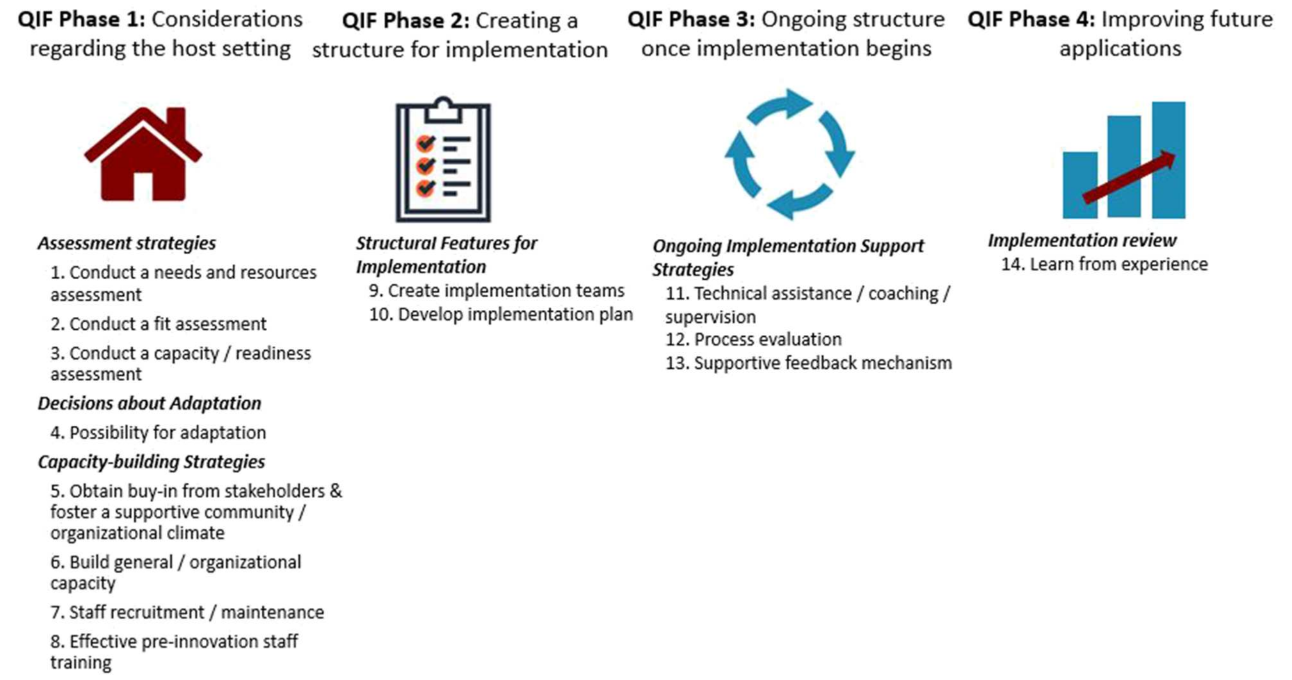

FIGURE 1 | Fourteen critical steps of quality implementation according to the Quality Implementation Framework (QIF) established by Meyers et al. (22).

by Partners HealthCare (34)]. In QIF Phase 3 (maintenance of the structure once implementation begins), a screening tool was developed to assess patient ability to participate in assessment given that certain patients seen in acute care were not sufficiently alert and oriented to attempt purposeful responses [see (26) for additional details regarding the screener], training sessions were held to educate staff about the measure, and surveys were collected to gather data about evolving practice patterns and needs. QIF Phase 4 (improving future applications) involved evaluation of the implementation to improve future practice. Evaluation of the implementation, carried out through medical record review of 50 (25 post-implementation and 25 pre-implementation) records demonstrated improved consistency of reporting on language domains of repetition ability, naming ability, yes-no question response accuracy, and awareness of errors, as well as a significant increase in the reporting of specific aphasia diagnosis (26). In addition to quantifiable improvements, the team felt that administering a standardized measure helped improve handoff communication and streamlined practice. Therefore, in July of 2017 training sessions were held to expand the standardized measure to the entire BWH clinical team. In this follow-up study, we aimed to determine adherence to the standardized protocol over the two-year period since expansion to the clinical team.

METHODS

Based on processes established via the implementation referenced above, since 2017, when a consult was placed requesting a language evaluation at BWH, patients were screened to determine if they were sufficiently alert to complete the standardized assessment. If passed, participants were given the spoken and auditory comprehension portions of the WAB-Bedside (35), and data were entered directly into an online database supported by REDCap. The onboarding of new staff involved training on the administration of the standardized assessment and on the data entry process in REDCap by supervisors and senior staff. Once new clinicians were ready to administer the measure in their clinical practice, they were observed by a senior clinician who provided feedback on administration. Clinicians were accompanied by a senior clinical team member until they were judged to adhere to the standardized protocol. Standardized evaluation procedures were reinforced quarterly through staff meetings.

Retrospective medical record review was conducted to evaluate adherence to the standardized evaluation process in acute care. This retrospective medical record review was approved by the Institutional Review Board of Partners HealthCare. Partners HealthCare has a Research Patient Data Registry (RPDR), that allows data to be queried based on the International Classification of Diseases (ICD-10) diagnosis codes. Using the RPDR, we identified patients older than 18 who were admitted to BWH from July 2017 to August 2019 with diagnosis codes that contained the search terms: speech and language deficits (following cerebrovascular disease, cerebral infarction, hemorrhage etc.), aphasia, cognitive deficits, cognitive impairment, cognitive functions, and brain neoplasm (see **Data Sheet 1** for a full list of query items). Billing data from these queries were searched for Current Procedural Terminology (CPT) billing codes 92523 (Evaluation of speech

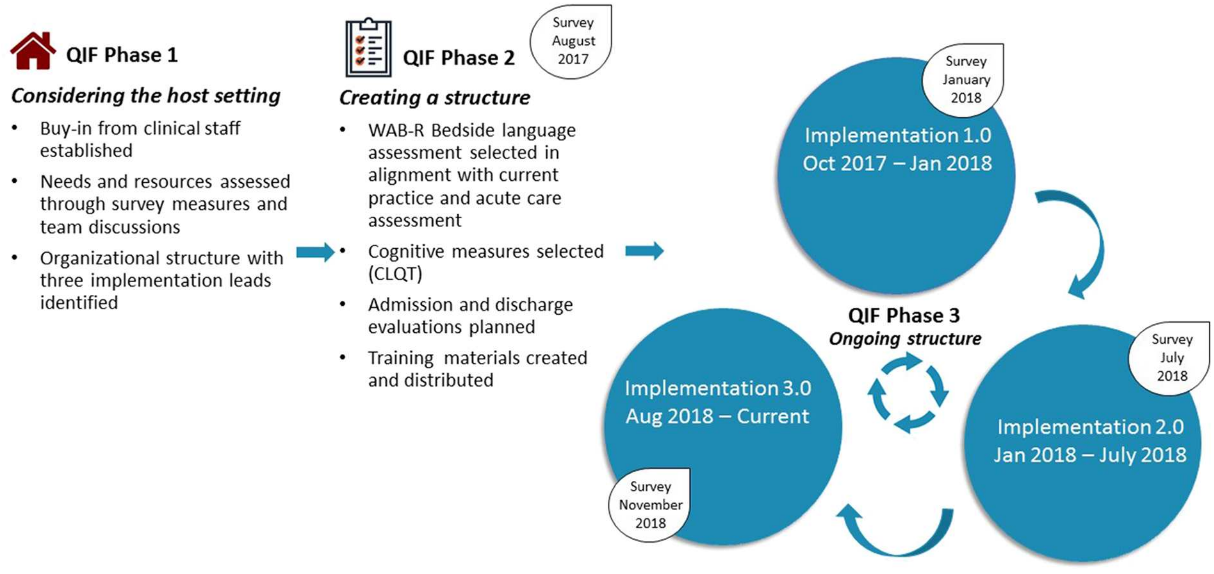

FIGURE 2 | Summary of QIF Process at Spaulding Rehabilitation Hospital. **Implementation 1.0** included the WAB Bedside, as well as four subtests from the CLQT (Clock Drawing, Symbol Cancellation, Design Memory, Design Generation). Assessment of reading and writing skills was formalized to improve consistency of administration. The assessment measure was administered to all patients with CVA admitted to the Stroke Program. **Implementation 2.0** included the addition of a screening tool, administration of the full WAB (rather than WAB Bedside) upon admission for individuals with L MCA stroke, and re-evaluation via the WAB Bedside at 10–14 days post admission. **Implementation 3.0** included training and expansion for assessment administration by all clinicians, including full-time employees and per diem weekend staff, as well as expansion to CVA admissions hospital-wide (rather than just those admitted to the Stroke Program).

sound production; with evaluation of language comprehension and expression and 96105 (Assessment of aphasia and cognitive performance testing), the two billing codes used at BWH for language evaluations. In this manner, medical record numbers for patients admitted to BWH who received language evaluations were identified. Duplicate entries were removed and billing data was compared to language evaluation data in the REDCap database to determine the percentage of language evaluations that were performed using the standardized process over the 2-year period.

RESULTS

The RPDR data pull resulted in 371 entries corresponding to patients who were billed for receiving a language evaluation in the period from June 2017 until August 2019. These patients represented primary diagnoses that included cerebral infarction, non-traumatic hemorrhage, and malignant neoplasm. An examination of adherence demonstrates that of the 371 entries, 260 individuals (70.1%) received the standardized assessment protocol.

Part II—The Iterative Implementation Process Utilized in an Inpatient Rehabilitation Care Facility Following an Implementation Science Framework

In early 2016, clinicians at Spaulding Rehabilitation Hospital (SRH), an acute rehabilitation hospital within the Partners HealthCare Network, recognized the need for standardization and began trialing a standardized language assessment tool with all patients admitted to the Stroke Rehabilitation Program, where all admitted patients carry a diagnosis of stroke. The standardization process followed an informal procedure until 2017, when a collaboration was formed with Brigham and Women's Hospital.

METHODS

In June of 2017, based on prior work, teams worked together to initiate an iterative implementation based on the four phases of the quality improvement framework (QIF) for implementation proposed by [Meyers et al. (22)] with the goal of aligning procedures and resources across the two facilities. Three phases of QIF have been implemented, with key considerations and/or changes identified in **Figure 2**. Survey measures were administered to clinical staff at each phase of implementation to gather feedback and evaluate for potential improvements.

QIF Phase 1: Initial Considerations Regarding the Host Setting

Initial considerations of the host setting demonstrated that buy-in from stakeholders was already established, as the SRH clinical team had recognized the need for standardization 1 year prior. SRH was using the WAB-bedside assessment, which aligned with the measure implemented at BWH, making alignment of measures readily feasible. An organizational structure was implemented, with three members of the clinical team identified as implementation leads. A survey was distributed to clinicians to identify aspects of current practice that were effective and those that might be improved upon (see **Data Sheet 2**). Implementation leads held meetings with BWH researcher-clinicians to gather insights about the process at BWH and establish a plan for SRH.

QIF Phase 2: Creating a Structure for Implementation

In addition to the WAB-bedside language evaluation, data on cognitive measures was important for SRH clinicians to gather, therefore, four subtests of the Cognitive Linguistic Quick Test [CLQT (36)] were added to the standardized process. In addition, it was determined that re-evaluation prior to discharge would be meaningful to evaluate change, and re-administration of the WAB-bedside and CLQT subtests was targeted to occur within 48 h of planned discharge. While at BWH, WAB-bedside data were entered directly into a REDCap database, the CLQT is not as seamlessly administered on a computer and SRH clinicians felt paper administration was more conducive to the rehabilitation environment, therefore a decision was made to use traditional paper and pencil formats for both assessments. It was decided that the standardized implementation would first be carried out only by full time clinicians within the Stroke Program of SRH. Staff training occurred through meetings and printed materials distributed throughout the Stroke Program. This plan was put into place in October of 2017 and maintained until January 2018 and was referred to as Implementation 1.0.

QIF Phase 3: Ongoing Structure Once Implementation Begins

At the end of implementation 1.0, a survey was distributed to full-time clinical staff. Survey responses and observations from implementation leads revealed that clinicians felt that the WAB-bedside was not sufficient, in many cases, to evaluate language abilities for individuals having experienced left middle cerebral artery (MCA) or anterior cerebral artery (ACA) cerebrovascular accidents, who are those who most consistently present with aphasia. A more comprehensive evaluation was requested. In addition, re-administering measures was difficult to do 48-h prior to discharge in the setting of shifting discharge plans and caseloads. In response to these observations, the standardized process was modified to (1) include different language assessments for patients experiencing left hemisphere strokes (Full WAB-R) vs. those affecting the right hemisphere and/or cerebellum (WAB-Bedside) (see **Supplementary Figure 1**), and (2) schedule re-testing to take place 10–14 days after initial assessment so that calendar alerts could be programmed and re-testing scheduled. This structure (Implementation 2.0) was carried out until July 2018, when another survey was administered. Survey data and implementation guided observation led to Implementation 3.0 characterized by the creation of templates to guide write-ups of evaluations and expansion of the measure to include per diem staff for improved consistency. Educational materials about the standardized process were distributed to all staff and full time clinicians were identified as point-people for per diem clinicians. To establish a process for evaluating data, research staff also joined the project, and, on a weekly basis, a research assistant at the MGH Institute of Health Professions pulled standardized language evaluation data from the Spaulding electronic medical record into the REDCap database. Implementation 3.0 was carried out on the Stroke Program from August 2018 until December 2018. This period is referred to as Implementation 3.0-Stroke Program. In January 2019, educational meetings were held and the standardized process was expanded to include clinicians on other services within SRH also involved in language evaluations. The period from January 2019 to August 2019 is referred to as Implementation 3.0-Hospital.

Evaluation of Adherence

Adherence to the implementation measure was evaluated over Implementation 3.0-Stroke Program and Implementation 3.0-Hospital. To do so, Spaulding Rehabilitation Hospital admission data were retrieved for all patients admitted with diagnosis classifications of stroke rehabilitation, physical medicine and rehabilitation (PMR) stroke, Acute neurology stroke, PMR neurology, neurology and brain injury. For the period from August 2018 to December 2018, data were filtered to only consider patients admitted to the Stroke Program. From January 2018 to August 2019 all stroke admissions data were included (Implementation 3.0-Hospital). Admissions data were then compared with REDCap data to determine whether patients received the standardized protocol or another assessment procedure.

RESULTS

From August 2018 to December 2018, there were a total of 169 admissions to the Stroke Program comprising 79 with L MCA/ACA strokes and 90 with other stroke locations. Eighty-three percent of these patients were evaluated using a standardized assessment for language. Examining specific adherence to the administration of the Full WAB for L MCA/ACA CVA patients, however, demonstrated 33% adherence, with the remaining 50% receiving the WAB bedside. See **Table 1** for additional adherence rates.

For Implementation 3.0 Hospital (January 2019–August 2019) there were a total of 402 stroke admissions hospital-wide with 170 and 232 admissions for L MCA/ACA strokes and other stroke locations, respectively. Sixty-four percent of these patients were evaluated using a standardized assessment for language. Examining specific adherence to the administration of the Full WAB for L MCA/ACA CVA patients, however, demonstrated 27% adherence, with the remaining 37% receiving the WAB bedside.

Part III—Pilot Evaluation of Data Collected Through Standardized Assessments to Begin to Evaluate Predictive Models of Language Recovery After Stroke

One of the long-term goals of the collaborative standardization of evaluations is to contribute to a language database that can be used to inform recovery predictions of language in the

TABLE 1 | Adherence to Spaulding Rehabilitation Assessment Protocol (percentages).

			Stroke program administration August 2018–December 2018	Hospital-wide administration January 2019–August 2019		
			Stroke program admissions	Stroke program admissions	Other rehabilitation program admissions	TOTAL hospital admissions*
L MCA/ACA CVA	Admission	**Adherence to protocol**				
		Language measure (WAB-R)	33%	31%	2%	27%
		Cognitive-linguistic measure (CLQT)	68%	61%	35%	52%
		Rate of administration of alternative measures				
		Language measure (WAB-bedside)	50%	40%	31%	37%
	Re-evaluation	**Adherence to protocol**				
		Language measure (WAB-bedside)	38%	22%	5%	16%
		Cognitive-linguistic measure (CLQT)	25%	14%	35%	52%
		Rate of administration of alternative measures				
		Language measure (WAB-R)	9%	8%	2%	6%
Other CVA Location	Admission	**Adherence to protocol**				
		Language measure (WAB-bedside)	51%	53%	28%	43%
		Cognitive-linguistic measures (CLQT)	63%	67%	31%	52%
		Rate of administration of alternative measures				
		Language measure (WAB-R)	1%	2%	0%	1%
	Re-evaluation	**Adherence to protocol**				
		Language measure (WAB-bedside)	20%	8%	0%	4%
		Cognitive-linguistic measure (CLQT)	28%	13%	5%	9%
		Rate of administration of alternative measures				
		Language measure (WAB-R)	2%	1%	0%	<1%

**TOTAL Hospital Admissions includes Stroke and Rehabilitation Program Admissions.*

acute phase of recovery. In order to begin to evaluate data, we conducted pilot analyses over cases with at least two time points of evaluation.

METHODS

Participants

Records from standardized language evaluations completed at BWH and SRH per clinical protocol were retrieved for patients who were evaluated at a minimum of two timepoints between June 2017 and July 2019. To be included in pilot analyses, patients had to be native English speakers, 18 years of age or older, and have sustained a left MCA stroke that could have extended into anterior cerebral artery (ACA) and posterior cerebral artery (PCA) territory within the same hemisphere. Patients with prior history of stroke or comorbidities including developmental delay or other significant neurologic history (e.g., neurodegenerative disorder) were excluded. See **Table 2** for demographic and stroke-related information, including WAB Aphasia Quotient (AQ) and Aphasia Classification information across timepoints.

Of the 796 database entries, 37 patients met inclusion criteria and were evaluated at two or more timepoints. Of these 37 patients, 9 were evaluated at BWH admission, then again at SRH admission, while another 7 were evaluated at all three timepoints: BWH admission, SRH admission, and SRH re-evaluation. The remaining 21 patients received evaluation at the two SRH timepoints, SRH admission and SRH re-evaluation. In addition to language evaluation data, patient age, sex, NIH Stroke Scale NIHSS) score, receipt of Tissue Plasminogen activator (tPA), date of stroke, and date of hospital admission were retrieved from the database.

Radiology Scan Information

Radiology reports and clinical scans (MRI) were retrieved from the Partners HealthCare Research Patient Data Registry (RPDR) for all patients whose acute care hospitalization was within the Partners HealthCare Network. Clinical scans were retrieved with the intent of completing lesion masking (outlining the lesion) and calculating lesion volume and location based on regions of interest. The fact that these were clinical scans, however, presented several challenges for lesion masking and normalization. Motion artifacts were present in many samples and structural scans varied in their alignment, slice resolution, and whole-brain coverage, with many of the higher resolution scans only including partial brains. It was determined that

TABLE 2 | Demographic and stroke-related information for eligible cases.

				BWH evaluation				SRH ADMISSION evaluation				SRH re-evaluation			
Case #	**Age range**	**NIHSS**	**Lesion location**	**Days: stroke to eval**	**WAB type**	**WAB AQ**	**WAB aphasia classification**	**Days: stroke to eval**	**WAB type**	**WAB AQ**	**WAB aphasia classification**	**Days: stroke to eval**	**WAB type**	**WAB AQ**	**WAB aphasia classification**
1	70–74	1	Posterior	4	B	85	Anomic	7	F	98.4	No Aphasia				
2	85–89	29	Both	1	B	80	Anomic	5	F	94.6	Anomic				
3	90–94	20	Posterior	3	B	40.8	Conduction	6	F	55.5	Conduction				
4	55–59	4	Both	1	B	38.3	Broca's	8	F	79.4	TCM				
5	65–69	15	Both	2	B	36.7	Broca's	3	F	37.5	Broca's				
6	80–84	4	Both	1	B	31.7	Wernicke's	6	F	45.2	Wernicke's				
7	80–84	4	Both	0	B	24.2	Wernicke's	5	B	**	Fluent				
8	40–44	6	Both	1	B	20	Broca's	5	B	**	Broca's				
9	80–84	11	Both	3	B	19.2	Broca's	4	F	11.9	Broca's				
10	70–74	5	Anterior	2	B	55.8	TCM	5	F	78	Anomic	14	B	90.8	Anomic
11	80–84	19	Both	4	B	48.3	Broca's	10	F	68.5	TCM	37	B	96.7	No Aphasia
12	80–84	–	Posterior	1	B	41.7	Wernicke's	4	B	40	Wernicke's	23	B	26.7	Wernicke's
13	65–69	–	Both	14	B	39.2	Broca's	16	F	34.4	Broca's	37	F	43.8	Broca's
14	85–89	16	Anterior	6	B	19.2	Broca's	14	F	18.6	Broca's	33	F	**	Broca's
15	70–74	22	Both	14	B	10	Global	16	F	7.2	Broca's	30	B	15	Broca's
16	55–59	29	Both	7	B	*	Global	16	F	11.3	Global	29	B	34.2	Broca's
17	75–79	8	Anterior					5	F	80.8	Anomic	15	B	91.7	Anomic
18	50–54	13	*L BG*					6	F	79.5	TCM	17	F	94.3	Anomic
19	50–54	18	Anterior					4	B	78.3	Anomic	22	B	97.5	Anomic
20	45–49	17	*L IVH*					19	B	75.8	TCS	34	B	76.7	Conduction
21	50–54	7	Anterior					14	B	67.5	Anomic	31	B	85	Anomic
22	70–74	3	Anterior					14	B	61.7	Anomic	27	B	80.8	Anomic
23	85–89	7	*L MCA*					12	F	61.2	Broca's	28	B	86.7	Anomic
24	65–69	9	*Posterior*					11	F	59.1	TCS	34	B	91.7	Anomic
25	65–69	–	*L MCA*					22	F	58.9	TCM	41	F	77.6	Anomic
26	80–84	–	Both					6	F	56.6	Wernicke's	18	F	70.3	TCS
27	40–44	10	Anterior					20	F	48.9	TCM	28	B	53.3	Broca's
28	60–64	6	*L MCA/PCA*					34	F	32.4	Wernicke's	57	F	35.1	Wernicke's
29	75–79	2	Anterior					5	F	27.2	Broca's	17	B	57.5	Broca's
30	25–29	22	*L MCA/PCA*					17	B	25	Broca's	35	B	53.3	Broca's
31	80–84	8	Both					8	B	23.3	Wernicke's	20	B	24.2	Wernicke's
32	55–59	22	Both					8	F	22	Global	20	F	35.1	TC-Mixed
33	55–59	18	*Both*					16	F	12.1	Global	50	F	18	Global
34	90–94	–	*L MCA*					10	F	9.7	Broca's	24	B	20	Broca's
35	45–49	–	*L MCA*					9	F	7.5	Global	19	B	32.5	Broca's
36	75–79	18	*L MCA*					5	F	0	Global	25	F	34.7	Global
37	40–44	25	*L MCA*					17	F	**	Global	30	B	38.3	Broca's

*Age range rather than specific age is reported and sex is omitted from this table for confidentiality purposes. Lesion Location information is reported based on the radiology report from the medical record; in cases where the radiology report was not available, location was obtained from the clinical note and is reported in italics—this information is included for information purposes only and is not included in statistical analyses. Severity ratings for Aphasia Quotient (AQ) are as follows: 0–25 Severe-Profound; 26–50 Severe, 51–75 Moderate; 76+ Mild. "B" denotes WAB Bedside version; "F" denotes WAB Full version. *Denotes participant was unable to pass screener to yield AQ; **Denotes missing subdomain scores, impacting calculation of AQ.*

reliable lesion volumes would not be obtainable from these non-standardized scans, therefore based on the lesion information outlined in radiology reports, as well as clinical scan data, lesions were classified at anterior lesions, posterior lesions, or both anterior/posterior lesions. Classifications were reviewed by two study staff. For patients admitted to SRH from a hospital outside the Partners HealthCare Network for whom radiology reports were not available, lesion data was retrieved from clinical notes within the medical record for informational purposes only and this lesion data was not included in statistical analyses, with the exception of two patients for whom complete radiology report information was available.

Data Analysis

Statistical analyses were preformed using R Software for Statistical Computing (37). The first set of analyses examined the dependent variable, SRH Admission AQ. Data on this dependent measure were available from 34 patients, as three of the patients in our sample were missing a WAB subdomain score, impacting calculation of an AQ. Regression analyses were run in a forward selection manner to evaluate the relationship between independent and dependent variables, and strength of potential models, entering up to three variables due to our sample size. Variables were entered into the model based on their hypothesized predictability as reported in the literature and on correlation strength with the dependent variable. The first regression evaluated aphasia severity (AQ) accounting for days post-onset of evaluation. Then, additional models were evaluated in a step-up manner, adding lesion location, coded as anterior/posterior only or both, and NIHSS. We then ran a second set of analyses using a different outcome variable: aphasia severity (AQ) at SRH re-evaluation.

In addition to pilot regression analyses, we were interested in examining the proportion of maximal recovery made by each patient. Given that patients varied in their initial severity, a proportional maximal recovery was computed for each patient to account for the differences in potential change. This was calculated as the observed change, or difference between scores, divided by the maximum potential change (T2 severity – T1 severity)/(severity score maximum - T1 severity) (28, 38). An important limitation to address here is a lack of consistency over whether the WAB-Bedside or Full WAB was entered into this comparison. Both tests yield an Aphasia Quotient and according to the WAB Testing manual, interpretation of the WAB-Bedside sections and tasks are consistent with the full test (35), suggesting that a comparison is possible, but should be interpreted with caution.

RESULTS

Correlation across continuous variables of interest was assessed (**Table 3**). A very strong negative correlation was observed between time (number of days from stroke until rehabilitation admission evaluation) and aphasia severity (AQ) at all three timepoints. A strong correlation was observed between time and NIHSS, and a minimal to moderate correlation was observed between time and age. NIHSS was moderate-strongly negatively correlated with initial BWH acute care severity, however, the correlation was observed to be less strong by the time of SRH re-evaluation. Predictor variables were not highly correlated with each other.

TABLE 3 | Correlation matrix between continuous variables of interest.

	Age	NIHSS	BWH AQ	Days to SRH eval 1	SRH eval 1 AQ	SRH eval 2 AQ
Age	1	0.46	−0.27	0.43	−0.27	−0.34
NIHSS		1	−0.69	0.87	−0.66	−0.46
BWH AQ			1	−0.96	1	0.94
Days to SRH Eval 1				1	−0.95	−0.84
SRH Eval 1 AQ					1	0.96
SRH Eval 2 AQ						1

Shading reflects the relative strength of correlations, with darker shading indicating a stronger correlation.

Predictors of SRH Admission AQ and SRH Re-Evaluation AQ

Regression analysis with days post-onset of evaluation as the predictor and SRH Admission AQ as the outcome variable only accounted for 3% of the variance, and was not statistically significant ($p = 0.321$). Consistent with prior studies, when lesion was included in the model as a predictor, the model was statistically significant, accounting for 26.0% of the variance in SRH Admission AQ [$F_{(2,22)} = 3.871$, $p = 0.03$]. NIHSS, which was the next most highly correlated variable was added to the model and contributed to an R-squared change of 5.4%. Though this model accounted for a larger percentage of the variance, the model was not significant [$\mathrm{F}_{(3,18)} = 2.75$, $p = 0.07$].

Regression analysis with days post-onset of evaluation as the predictor, and SRH Re-Evaluation AQ as the outcome variable, was not statistically significant ($p = 0.285$) and only accounted for 4.4% of the variance in the model. Including lesion in the model as a predictor explained an additional 14.3% of the variance in SRH Re-Evaluation AQ, but was again not statistically significant [$F_{(2,15)} = 1.728$, $p = 0.21$]. Similarly, the addition of NIHSS explained an additional 9.6% of the variance, but the model was not statistically significant.

Language Severity Change

Given the focus of this project on the implementation of standardized language assessment measures in acute care and inpatient rehabilitation, we were interested in examining the proportion of maximal recovery made by individual patients. Comparisons of aphasia severity at SRH Admission and SRH re-evaluation showed a wide variety of proportion change ranging from 1% proportion maximal recovery to 89% proportion maximal recovery. The correlation between time between evaluations (as measured in days) and change was not significant, $r_{(27)} = 0.01$, $p = 0.95$ (see **Figure 3**). The correlation of proportion maximum recovery and aphasia severity at initial evaluation was significant $r_{(27)} = 0.62$, $p < 0.001$ (see **Figure 4**). Individuals with lower aphasia severity scores corresponding to more severe language impairment showed more limited proportion recovery over this limited timeframe.

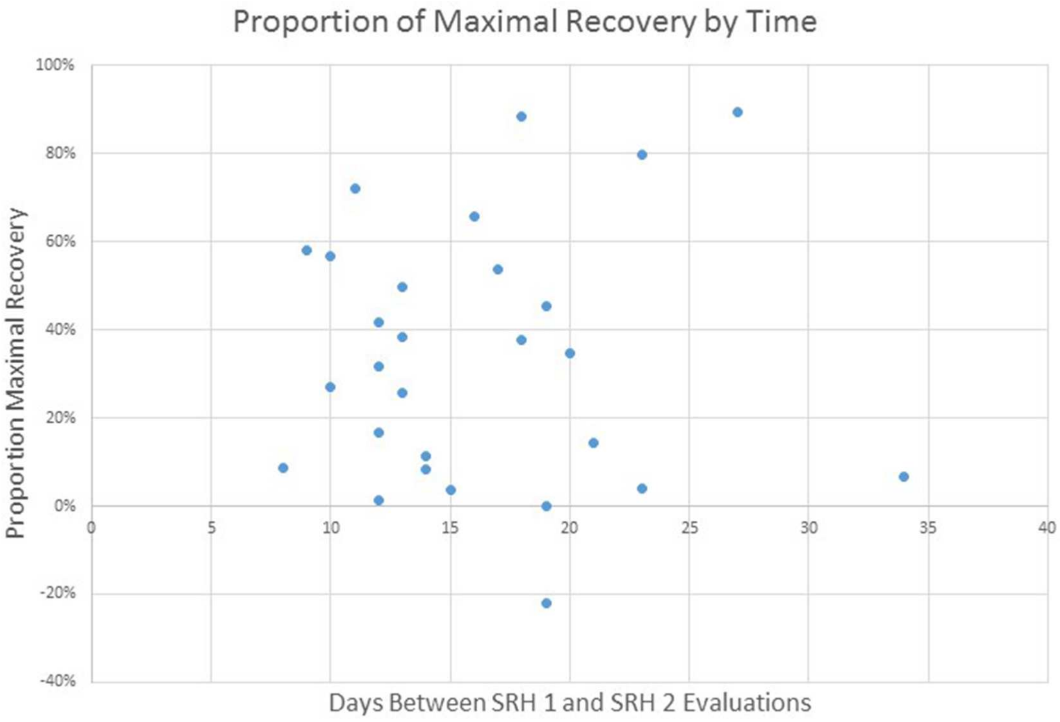

FIGURE 3 | WAB AQ proportion of maximal recovery from SRH initial evaluation to re-evaluation as a function of time (days) between evaluations.

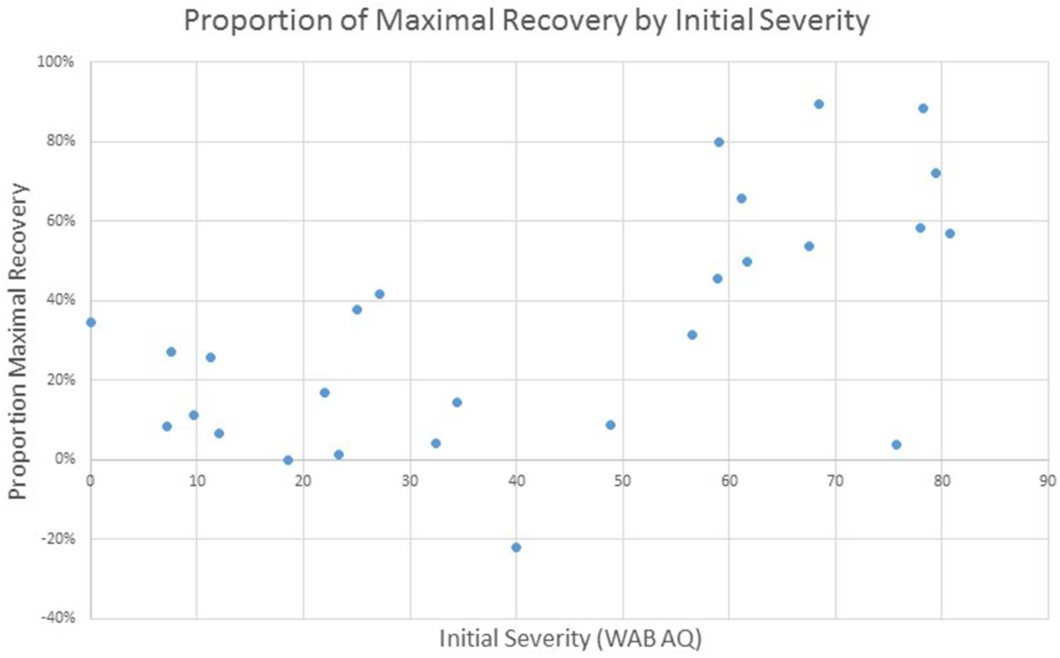

FIGURE 4 | WAB AQ proportion of maximal recovery from SRH initial evaluation to re-evaluation as a function of severity at initial assessment.

DISCUSSION

Results from the current study demonstrate that implementing standardized processes for the evaluation of language is feasible in acute care and inpatient rehabilitation settings, though an ideal process has yet to be identified, particularly for the inpatient rehabilitation setting. For the acute care setting, adherence rates to a standardized protocol over a 2-year period demonstrated

70% adherence. In a survey regarding practice patterns, 70.1% of clinicians reported completing informal assessment measures and 51.1% reported using individualized assessments developed by clinicians or the institution (1) in the acute stages post-stroke, thus 70% adherence over a two-year period with limited reinforcement measures is encouraging. Follow-up conversations with clinicians have revealed that in some cases, computers were not available in rooms, sessions were interrupted by other caregivers or exclusionary conditions, such as evaluating non-English speaking patients prevented the complete administration of the bedside WAB. Clinicians continue to express satisfaction with the measure, stating that the administration is efficient and informative and that using a standardized vocabulary across caregivers is helpful for patient hand-off. In this acute practice setting, the primary needs are to determine the presence or absence of aphasia, administer a diagnosis, initiate therapy and determine the next level of recommended care, conditions satisfied by the measure. Importantly, clinicians continue to supplement the standardized protocol, evaluating additional cognitive-linguistic domains based on their clinical judgment.

Within the inpatient rehabilitation setting, the QIF framework, and collaborative approach, has led to multiple iterations of implementation. Overall results of this initiative demonstrated that administering a standardized assessment in inpatient rehabilitation is feasible, with standardized language or cognitive assessment being completed upon admission for between 52 and 71% of patients in the Stroke Program. Clinician adherence is consistent with rates reported in studies that examine standardized assessment practices within other rehabilitation disciplines, such as physical therapy [48–66% adherence (39, 40)], and those specifically examining post-stroke standardized assessment practice patterns [52–88% adherence (41, 42)]. Incorporating measurable outcomes into clinical practice has been recognized as important for evaluating the effect of interventions, quality of care, advancing knowledge and policy (43–45). While standardization initiatives represented changes in practice, changes were feasible and adhered to over time in acute care.

The iterative process of implementation, however, revealed challenges identifying a suitable language measure for all patients. Initially, the WAB-Bedside was judged to be too abbreviated for L MCA CVA patients in the inpatient rehabilitation setting, yet closer examination once the Full WAB was recommended revealed low rates of administration. This indicates a need to revisit assessment procedures to improve adherence in a way that supports clinical data collection and decision-making. The inpatient rehabilitation setting offers more time for evaluation relative to acute care, but these evaluations establish foundations for goals targeted over a longer period of time than in acute care and that must ready the patient, in many cases, for discharge home. Language interventions are often characterized as being either impairment-based, focusing on stimulating impaired subdomains of speaking, listening, reading, or writing; or communication-based, focused on building functional communication through a variety of methods (46). The WAB is an impairment-based measure, which may not capture the range of deficits and abilities important to evaluate when selecting a combination of impairment-based and communication-based interventions, particularly for patients returning home or to work and resuming activities of daily life [e.g., work demands, finances, group and/or social activities, routine home activities see (47)]. While clinicians expressed an interested in utilizing the full WAB, it may be that on a case-by-base basis the more abbreviated bedside WAB, which provides an overall evaluation of language ability, accompanied by more comprehensive impairment-based testing of specific domains and/or evaluations of communication functioning was better suited than the full WAB. In the acute rehabilitation setting, language evaluations are used to plan interventions that must stimulate the language system and also provide access to functional communication sufficient for the home, work or next level of care. The inclusion of functional measures should be considered in future iterations of implementation as they may more appropriately capture patient performance and level of functioning, important for guiding planning for participation at the next level of care.

Interestingly, clinician adherence to the standardized protocol was higher for the CLQT than for language assessment in both the stroke program and the hospital. This may reflect the fact that there are fewer alternate assessments of cognitive abilities that are suitable for stroke and individuals with language deficits. This may also reflect the importance of insights gained from the assessment of cognitive domains on intervention goals at this level of care. Clinicians are tasked with making initial recommendations regarding discharge planning early in each patient's rehabilitation stay. Discharge recommendations (e.g., discharge home independently, 24-h supervision, or skilled nursing services) go beyond considerations of language ability to consider level of cognitive functioning and safety, making cognitive evaluations meaningful.

Based on the data obtained through standardized assessment of language skills across settings, initial model evaluations over pilot data support previous studies that have found that lesion location and size are predictive of outcomes (31, 33, 48–50). Though limited in power, models that incorporated lesion location accounted for the largest degree of variance. Initial evaluation of proportion maximal recovery demonstrated greater proportion of recovery for individuals with lower severities of aphasia at initial assessment, consistent with prior studies which have shown that patients with more severe levels of impairment show more limited improvement (28, 51).

The current evaluation of predictors of outcomes was only preliminary given the small sample size. Furthermore, the assessment measures incorporated in the current implementation were impairment-based measures that present potential limitations. We propose that an improved understanding of the predictors of recovery will come through consideration of both impairment-based and functional outcome measures. Next steps in evaluating appropriate outcome measures should also examine practice patterns to better understand how outcome measures are utilized to guide intervention planning, as information obtained in assessments needs to be deemed meaningful to clinical practice. Clinical-decision making tools, such as algorithms have been shown to reduce variability in clinical care practices and improve patient outcomes (52). Guidelines that help align outcome measurement with treatment selection, however, are not readily available to guide aphasia assessment and intervention practices.

Additionally, future work will involve exploring metrics obtained by other disciplines, including physical and occupational therapy, through interdisciplinary partnerships to identify what measures are meaningful and clinically-feasible. Adoption into routine clinical practice offers the potential to contribute data that can then be evaluated via new predictive models of improvement. While analyses of data collected in a clinical context may not advance knowledge in the same manner as highly-controlled empirical studies, enlisting clinicians, and creating practice-based evidence may inform the research trajectory and contribute pilot data or systematic observations that can lead to the development of well-controlled empirical studies, which can then feed back into clinical practice. A pattern of practice, evaluation, analysis, and knowledge transfer has the potential to result in research findings that more readily translate into clinical practice, strengthening the bridge that links research and practice.

DATA AVAILABILITY STATEMENT

The datasets generated for this study are available on request to the corresponding author.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Partners IRB. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

AUTHOR CONTRIBUTIONS

MS, SV-R, and CT-H organized the database. MS performed statistical analyses and wrote the first draft of the manuscript. SV-R and CT-H wrote sections of the manuscript. All authors contributed to the conception and design of the study and contributed to the manuscript review and revision.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2020.00412/full#supplementary-material

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Self-Perception of Physical Function Contributes to Participation in Cognitively- and Physically-Demanding Activities After Stroke

Marjorie L. Nicholas[1], *Kari Burch*[2], *Julianne R. Mitchell*[3], *Annie B. Fox*[4], *Carolyn M. Baum*[5] *and Lisa Tabor Connor*[2,3]*

[1] *Department of Communication Sciences & Disorders, MGH Institute of Health Professions, Boston, MA, United States,* [2] *Program in Occupational Therapy and Department of Neurology, Washington University School of Medicine, St. Louis, MO, United States,* [3] *Department of Occupational Therapy, MGH Institute of Health Professions, Boston, MA, United States,* [4] *Center for Interprofessional Studies and Innovation, MGH Institute of Health Professions, Boston, MA, United States,* [5] *Program in Occupational Therapy and Departments of Neurology & Social Work, Washington University in St. Louis, St. Louis, MO, United States*

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***Correspondence:**
Lisa Tabor Connor
lconnor@wustl.edu

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Background: Persons with and without aphasia experience decreased participation in meaningful activities post-stroke that result in reduced autonomy and poorer quality of life. Physical, cognitive, and/or communication deficits are prevalent post-stroke and many activities given up are purported to require high levels of communicative, cognitive, or physical skill. However, the relationship between deficits after stroke and participation in life activities that appear to require high skill levels in these three areas has not been investigated fully.

Objectives: The objectives of this study are to: (1) determine differences in reported participation in communicatively-, cognitively-, or physically-demanding activities in persons after stroke with and without aphasia living in the community, and to (2) investigate whether performance on commonly used self-perception assessments of these three areas predicts reported participation in activities requiring higher levels of skill in these domains.

Methods: In a cross-sectional design, 82 individuals at least 6 months post-stroke with ($N = 34$) and without aphasia ($N = 48$) were administered a battery of neuropsychological and participation-based assessments. Supported communication techniques maximized inclusion of individuals with aphasia. A series of regression analyses investigated the relationship between self-perceived communicative, cognitive, and physical functioning and reported participation in activities post-stroke that required high amounts of skilled function in these areas.

Results: People with and without aphasia did not differ in terms of the percentage retained in communicatively-, cognitively-, or physically-demanding activities. All individuals retained higher levels of participation in communicatively- and cognitively-demanding activities (at least 60% retained), compared to participation in physically-demanding activities (about 50% retained). The strongest predictor for retaining participation in two of the three domains of activities was self-perception of physical function, though much of the variance remained unexplained. Self-perception of communication was not related to participation retention in any of the three domains.

Significance of Impact: Rehabilitation professionals should be aware of the impact that a variety of communicative, cognitive, and physical factors may have on participation post-stroke. Self-perceptions of impairments in communication and cognition may not directly predict participation in activities requiring high levels of communicative and/or cognitive skill, at least for those with mild impairment, even though activities requiring those skills are given up or done less after stroke.

Keywords: stroke, activity participation, patient-reported outcome assessment, community reintegration, aphasia, cognition, physical function and mobility

INTRODUCTION

Stroke is the fifth leading cause of death in the US, with an annual prevalence of 795,000 (1). Aphasia, characterized by difficulty in producing and understanding spoken language, reading, and writing, occurs in 25–40% of stroke cases, and is estimated to currently affect ∼2 million Americans (2). After stroke, both persons with aphasia (PWA) and without aphasia (PWOA) experience diminished participation in everyday life and in their meaningful daily activities and role functioning [e.g., Foley et al. (3)]. Understanding the factors that enhance or inhibit participation post-stroke is imperative to enable PWA and PWOA to live satisfying, meaningful lives. Although many persons who have had a stroke experience diminished participation in everyday life activities, the extent to which community-dwelling PWA are able to resume pre-stroke roles and participate in meaningful activities after stroke has received considerably less attention in the literature (4–8) than studies examining PWOA because PWA are largely excluded from research due to their communication deficits (9).

Participation is a complex construct defined broadly in the World Health Organizations's International Classification of Functioning and Disability as "involvement in a life situation," arising from an interaction among body structures and body functions, environmental factors, personal factors, and activity demands (10, 11). After a stroke, participation has been measured by using assessments of retention of previous activities, reintegration in the home and community, and perceived recovery from the stroke (12–14). Participation restrictions post-stroke often result in reduced autonomy and poorer quality of life [e.g., Hartman-Maeir et al. (15)], consistent with an occupational perspective that participation in everyday activities is required to improve and maintain health and well-being (16, 17).

In addition to chronic physical impairments, persistent communicative and cognitive stroke sequelae affect more than 50% of the community-dwelling stroke population and result in diminished activity engagement; the majority of individuals report lacking even one important and meaningful activity to do each day (14, 15, 18). Even 6 months or more after mild stroke, individuals report decreased participation in meaningful activities, including work, volunteering, travel, and socialization (3, 19, 20).

PWA may be increasingly susceptible to reductions in participation, as activity engagement may be associated with aphasia severity (21–23). Several studies have identified that the majority of these individuals have difficulty with instrumental activities of daily living (IADL) after stroke (14, 15, 24, 25). Common examples of difficult post-stroke activities that are characterized as "complex" IADLs include household tasks such as meal preparation, housekeeping, laundry, driving, and socializing (14, 15). These activities vary with respect to how communicatively- and/or cognitively-demanding they are. Some activities like doing laundry may have fewer demands in these areas, while others like socializing with friends and family or conducting transactions such as shopping or banking, clearly have higher communicative and cognitive demands.

The ability to perform IADLs post-stroke, as well as return to community activities, is associated with improved life satisfaction as well as health-related quality of life (HRQOL), a construct encompassing physical, non-physical (communicative and cognitive), social, and role functioning as well as subjective experiences of health and well-being (14, 15, 26, 27). Further, participation is a significant predictor of life satisfaction after stroke, beyond that which is accounted for by variables such as depression (15). On the negative side, long-term dissatisfaction, and decreased quality of life are associated with decreased activity engagement and participation after stroke (15).

Many of the activities found to be difficult post-stroke and which exert a powerful influence on HRQOL are frequently described as "complex" or "higher order" IADL, implying that the activities require higher levels of communicative and/or cognitive functioning (14, 15, 28). Aphasia, as an impairment of language affecting communication, may be considered as one of many areas that falls under the larger umbrella of cognitive impairments. Moreover, PWA may have concomitant deficits in executive functions, memory, attention, and visuospatial functions. Impairments in these areas seen in PWA may be chronic and to some extent under-treated because physical impairment is often the main focus in intervention post-stroke (15, 29–34).

An additional challenge that needs to be addressed is measuring the construct of participation, particularly in PWA who have difficulty with either verbal expression or comprehension of language. The Activity Card Sort (ACS) (35) is one measure that is ideally suited for people with impaired communication because it does not require overt language expression and can be easily adapted to require minimal language comprehension. The ACS consists of 89 photographs of activities, grouped into four categories: Instrumental, High Demand Leisure, Low Demand Leisure, and Social Activities. The ACS includes activities that represent common and likely-to-be valued activities that encompass a range of life pursuits. Individuals group the photographs into piles to indicate whether they have ever done the activity prior and whether they continue to do it now, among other types of sorts. Clinicians and researchers can determine which activities have been given up or retained post-stroke and can calculate percentage retained of the activities in each of the four activity domains. Several published studies have used the ACS to assess the extent to which people with various health conditions have retained their participation in activities (19, 36–43).

To understand better the nature of the demands of activities themselves and how those demands influence participation, an unpublished study was completed in our laboratory using the ACS. Forty-three healthy adult raters judged the extent to which nine dimensions of activity were needed to be able to participate in each of the 89 activities. The nine dimensions that each activity was rated on were: physical exertion, a partner to do the activity with, mobility, expressive communication, language comprehension, cognitive skills, fine motor skills, financial resources, and need for transportation.

To further understand factors affecting post-stroke participation in meaningful life activities, the current study used a subset of these dimensional scores obtained for the ACS activities to examine the question: What is the relationship between self-perception ratings of communication, cognition, and physical functioning post-stroke to participation in PWA and PWOA? We hypothesize that self-perception ratings of communicative and cognitive impairments will predict retention scores for items rated as requiring high levels of skill in these areas. For example, people with self-perceptions of greater communication impairment may show less retention of activities that are high in communication and/or cognitive demands; and conversely people who perceive themselves as having relatively preserved communication and cognitive skills may show greater retention of cognitively and communicatively-demanding activities (21). Both groups of participants are expected to show a decrease in retention of activities that are physically demanding if they perceive themselves as physically limited by the sequelae of their stroke. Conversely, some activities may be deemed more important to quality of life than others by participants so that they return to them despite having difficulty with multiple dimensions required to perform the activity. Thus, although we expect our general hypothesis to be supported, it is also possible that nuances will emerge across activities where this is not the case.

There are several different types of measures of impairment post-stroke, including (1) measures known as "patient-reported" or self-perception measures, commonly using various scales, questionnaires, or survey approaches; and (2) objective measures such as those often administered by clinicians to assess behavior that can be compared to group norms. Both means of assessment are undoubtedly important to obtaining a full and well-rounded assessment of contructs of interest. In this paper we focus on measures of self-perception of impairments as they relate to participation; a subsequent study will address a similar question using only objective measures.

MATERIALS AND METHODS

Study Population

Participants were 34 people with aphasia and 48 people without aphasia who received medical services for a stroke at Barnes Jewish Hospital in St. Louis, Missouri, who lived in the community, and consented to have their data included in the Washington University Cognitive Rehabilitation Research Group's Stroke Registry or who participated in the research study at the MGH Institute of Health Professions in Boston, Massachusetts. Both sites received approval from their respective Institutional Review Boards and informed consent procedures were followed. Inclusion criteria for this study included: (1) six months or greater post-stroke, (2) ability to withstand two hours of testing, and (3) ability to commute to testing site by car or taxicab. Exclusion criteria included: (1) history of multiple strokes, (2) traumatic brain injury, (3) seizure disorder, (4) pre-stroke disability as evaluated by modified Rankin Scale (score of ≥ 2), (5) pre-existing neurological condition that could interfere with evaluation (e.g., MS, dementia, PD, ALS), or (6) severe medical or psychiatric illness. Written consent was obtained at testing.

People With Aphasia (PWA)

Inclusion criteria included: presence of aphasia by National Institute of Health Stroke Scale (NIHSS) aphasia item with a score > 0 at the acute hospital stay ($N = 28$) or who had received diagnostic confirmation of aphasia within the past 6 months ($N = 6$, all recruited from MGH Institute of Health Professions); and the capacity to give reliable yes/no responses.

Participants were screened over the phone to confirm that they were eligible to participate in this study. The aim was to include all who could provide a reliable yes/no response. The screening involved reading a story consisting of 3 brief sentences two times. Comprehension questions requiring yes/no responses were read. Candidates could indicate their yes/no response by any means they chose (e.g., a tap for "yes"). Those who answered 3 of 4 questions qualified for the study. If there was any doubt about eligibility, PWA were invited to the study and further evaluation was done with a consent comprehension assessment conducted with supported communication techniques [as described in Tucker et al. (44)]. Only if the participant was then unable to indicate comprehension of key elements of consent was that individual excluded from participating in the study. Two people

TABLE 1 | Participant characteristics with means (M) and standard deviations (SD) in parentheses.

	All ($n = 82$)	PWA ($n = 34$)	PWOA ($n = 48$)
	M(SD)/n(%)	M(SD)/n(%)	M(SD)/n(%)
Age, mean (SD)	60 (12)	62 (12)	59 (12)
GENDER AND EDUCATION			
Men	28 (34)	14 (41)	14 (29)
Women	54 (66)	20 (59)	34 (71)
Education, years mean (SD)	15 (3.4)	15 (4.1)	14 (2.7)
ETHNICITY			
Caucasian	36 (44)	19 (56)	17 (35)
African American	45 (55)	14 (41)	31 (65)
Other	1 (1)	1 (3)	0 (0)
LANGUAGE COMPETENCY INDEX			
Expression		74.8 (21.8)	
Comprehension		75.5 (21.0)	
Total		75.1 (20.3)	

PWA, People with aphasia; PWOA, People without aphasia; PWA were longer post-onset than PWOA ($p = 0.013$); Ethnicity differed marginally across groups ($p = 0.07$).

screened were excluded as participants and no data on these individuals were collected.

Once enrolled in the study, PWA received the short form of the Boston Diagnostic Aphasia Examination-III (45) to characterize their language impairment with the Language Competency Index (LCI). These scores are included in **Table 1**. LCI Expression scores ranged from 22.5 to 100; LCI Comprehension scores ranged from 20 to 100; LCI Total scores ranged from 28.75 to 100. Three PWA obtained LCI scores of 100, indicating no language impairment. None of these 3 individuals rated themselves as not experiencing a communication deficit on the Stroke Impact Scale.

People Without Aphasia (PWOA)

Participants with stroke, but no aphasia as determined by the NIHSS aphasia item (a score of 0) at the acute hospital stay were included. All PWA and PWOA were participants in a larger investigation.

Table 1 describes characteristics of the participants. For the purposes of this study, the absolute value of $p < 0.05$ was considered statistically significant. There were no statistically significant differences between groups on age or education. Gender did not differ by group, X^2 (2) $= 1.3$, $p = 0.26$. There was a marginally statistically significant different distribution of race/ethnicity by group, X^2 (2) $= 5.3$, $p = 0.07$, with more African American participants in the PWOA group than in the PWA group.

MEASURES

Self-report measures depend on the respondent's ability to process language both receptively and expressively. Aphasia can be a significant barrier for participating in subjective aspects of stroke outcome research (46–48). This study employed general principles for supportive techniques that can be utilized with any assessment without compromising the assessment's psychometric properties for PWA (44). These principles have been derived from prior studies on communication support: written support can increase auditory comprehension (49–51); reading comprehension can be enhanced by changing font style, size, and letter and line spacing (52, 53). Three types of supported communication techniques were used in this study: test administration modifications, response format modifications, and a systematic hierarchy of examiner supports [see Tucker et al. (44) for details]. Only two potential participants were not able to be included after using these supports; their data were excluded from this study.

Each participant was assessed with the objective assessment, the *National Institutes of Health Stroke Scale,* to characterize stroke impairment and the *Stroke Impact Scale* to assess self-perception of abilities across eight domains.

The *National Institutes of Health Stroke Scale* [NIHSS; (54)] was administered by certified assessors to ascertain cognitive, sensory, and motor impairments resulting from a stroke. The 13-item test is based on a score ranging from zero to 42; lower scores indicate lower levels of neurological impairment. Reliability is good to excellent and validity is high (55).

Self-Perception of Abilities and Stroke Impact

The Stroke Impact Scale, version 2.0 [SIS: (56)] assesses self-perceived impairments, disabilities, and participation following a stroke. The maximum score is 100. The eight domains of the SIS include: Strength, Hand Function, ADL/IADL, Mobility, Communication, Emotion, Memory and Thinking, and Participation/Role Function (56). The three domains included in this investigation were as follows: (a) as a measure of self-perception of physical functioning we averaged the scores from the Strength (four questions), Hand Function (5 questions), and Mobility (ten questions) domains; (b) as a measure of self-perception of communication we used the score from the Communication domain (seven questions), and (c) as a measure of self-perception of cognition, we used the score from the Memory and Thinking domain (8 questions). These scales have high reliability, with alphas ranging from 0.83 to 0.90. Inter-class correlation coefficients ranged from 0.70 to 0.92. Validity was established by correlating SIS domain scores with other measures of that function (57). The items on the SIS that were used for these measures are in **Appendix II**.

Participation

The *Activity Card Sort* (ACS), 2nd Edition, Recovering version, was used as the dependent measure to assess participation in instrumental, social, and high- and low-physical-demand leisure activities (35). Participants group and sort each pictured item into categories that indicate whether they continue to do each activity, have given it up, do the activity less, or have started the activity since their stroke. Percent retained is the number of current activities, which is the number of activities they continue to do (1 point each) + do less (0.5 points each) + started (1 point each), divided by the number of previous activities, which is the

TABLE 2 | Scores on the physical exertion, communication, and cognitive skill dimensions for two different activities: bicycling and talking on the telephone.

Rated dimensions	Activity: bicycling	Activity: talking on the telephone
Physical exertion	2.9	0.3
Communication	0.4	2.7
Cognitive skill	1.2	1.5

number of activities they continue to do (1 point each) + the number of activities they have given up (1 point each). This ratio is then multiplied by 100 to obtain the percent retained score. The ACS has high internal consistency ($\alpha \geq 0.83$ for the 4 domains) (58). Test-retest reliability is high, with intra-class correlations ranging from 0.71 (58) to 0.98 (59). ACS scores have content, construct, and predictive validity (35). The internal consistency and construct validity of the new scales is unknown.

In the unpublished study mentioned earlier, 43 healthy adult raters, primarily occupational therapy students, and other volunteers who worked in the medical school environment, judged the extent to which nine dimensions of activity were needed for a person to be able to participate in each of the 89 activities of the ACS. The nine dimensions that each activity was rated on were: physical exertion, a partner to do the activity with, mobility, expressive communication, language comprehension, cognitive skills, fine motor skills, financial resources, and need for transportation. Each activity received a rating from 0 to 3 (none = 0, some = 1, a fair amount = 2, a lot = 3) on each of the nine dimensions. Average ratings for each item for each dimension were then calculated across the raters. Scores were then regrouped into three categories based on average ratings: The activity required a little amount (0–0.99); a fair amount (1–1.99); or a lot (>2.0) of the activity demand for the nine dimensions. Individual ACS activities may receive ratings of *"A lot"* across few, several, or most of the nine dimensions, resulting in a complex mix of requirements for each activity. To illustrate further, **Table 2** shows the scores for two activities, *bicycling* and *talking on the telephone* on the dimensions that we considered in this study (communication, cognition, and physical functioning).

This study used items (activities) from the ACS in a novel manner to derive three participation scores for communicatively-, cognitively-, and physically-demanding activities, areas that many people experience difficulties with after stroke. While the 89 activities within the ACS are categorized into the four separate domains mentioned earlier, participation in each activity requires differing demands that may influence an individual's ability to participate in any given activity. For the purposes of the current study, the ACS activities were regrouped into categories involving demands in three particular dimensions: communicative, cognitive, or physical exertion requirements. Scores were found to be high (≥2.0) on one or more of these three dimensions on 59 of the ACS activities, comprising 2/3 of the ACS items. Results of this regrouping produced: (a) *High-Communitive items-* 35 activities requiring a lot of communicative skill; for this we used scores from the communication comprehension dimension, which happened to also include all items that were high on expressive communication. About half of these (17 items) were high on only the communication dimension (not cognition or physical), and half were high on communication plus at least one other dimension; (b) *High-Cognitive items-* 27 activities required a lot of cognitive skill and 5 of these were high on only the cognitive dimension. Many high-cognitive activities were also high on the communication dimension (18 of 27); (c) *High-Physical items-* 23 activities required a lot of physical exertion and the majority (15 items) of these were high on only this dimension. The specific ACS activities belonging to each category are found in **Appendix I**. Ratings for each item for each of the three dimensions and the percent retained for each item for the entire sample are shown in the appendix as well.

DATA ANALYSIS

Separate linear regression models were used to examine three dependent variables measuring participation using the ACS: the percent retained activities for (a) communicatively-demanding activities, (b) cognitively-demanding activities, and (c) physically-demanding activities. The predictor variables used in the regression analyses were the three self-perception scores derived from the SIS questions relevant to communicative function, cognitive function, and physical function. In addition, months post onset (MPO) and the total NIHSS score were included as covariates. The hypothesis was that the predictors should account for variability in percentage retained on the ACS only for those items with high scores in the dimensions that matched the outcome domain. For example, perceived level of communication impairment (quite relevant because we explicitly included people with aphasia in our sample) should predict the extent to which people retain activities that are highly demanding of communication skills. Likewise, perceived cognitive abilities should only uniquely predict the extent to which individuals retain cognitively demanding activities and perceived physical function should uniquely predict the retention of physically demanding activities. Before testing the linear regression models, we compared PWA and PWOA on the dependent variables.

RESULTS

Scores obtained on each of the measures for all participants and separated into PWA and PWOA are displayed in **Table 3**.

Differences Between Participants on the Dependent and Predictor Measures

Appendix I shows the percent-retained data post-stroke for each of the 59 activities that were considered in this investigation. Retention rates for the various ACS activities ranged from a low of 24% on item 65 "Playing tennis or racquet sports" and 26% on item 20 "Work (paid)," to a high of 98% on item 52, "Watching television."

There were no statistically significant differences between groups (PWA, PWOA) on any of the three percent-retained

TABLE 3 | Means (M) and standard deviations (SD) for PWA and PWOA for self-perceptions, months post-onset, stroke severity, and participation percent retained.

Measure	All ($N = 82$)	PWA ($N = 34$)	PWOA ($N = 48$)
	M (SD)	M (SD)	M (SD)
SELF-PERCEPTIONS AND OTHER PREDICTORS			
SIS Physical Function	63.0 (25.5)	66.3 (27.6)	60.8 (24.1)
SIS Cognition	75.2 (21.9)	71.0 (21.4)	78.1 (22.0)
SIS Communication*	80.6 (21.0)	70.2 (22.1)	87.7 (17.2)
NIHSS Total Score	2.5 (2.2)	2.5 (2.4)	2.5 (2.1)
MPO*	23.6 (32.2)	34.5 (48.5)	16.4 (7.8)
ACS ACTIVITIES PERCENT RETAINED			
High Communicative Skill	74.9 (17.3)	75.2 (18.3)	74.7 (16.8)
High Cognitive Skill	64.5 (21.6)	67.2 (21.6)	62.6 (21.6)
High Physical Skill	47.2 (28.7)	50.4 (28.6)	44.9 (28.8)

**Significant differences between groups: PWA, People with aphasia; PWOA, People without aphasia; SIS, Stroke Impact Scale, version 2.0; NIHSS, National Institutes of Health Stroke Scale; MPO, months post-onset; ACS, Activity Card Sort, version 2.*

TABLE 4 | Regression models examining self-perceptions and participation in high-communicative activities with parameter estimates and standard errors in parentheses.

	Communication tasks % retained	
	Without covariates	With covariates
Intercept	41.504***	42.468**
	(6.216)	(14.991)
Age		−0.196
		(0.149)
Education		1.173
		(0.627)
Gender		−1.249
		(3.676)
NIH stroke scale		−0.693
		(0.940)
SIS physical	0.191*	0.153
	(0.074)	(0.084)
SIS memory	0.123	0.063
	(0.099)	(0.107)
SIS communication	0.148	0.194
	(0.101)	(0.108)
Observations	81	78
R^2	0.298	0.314
Adjusted R^2	0.271	0.245
Residual Std. Error	15.339 (df = 77)	15.270 (df = 70)
F statistic	10.916*** (df = 3; 77)	4.570*** (df = 7; 70)

**p < 0.05; **p < 0.01; ***p < 0.001.*

participation scores (see **Table 3**), all $p_s > 0.15$: (1) *High-Communication items*, or (2) *High-Cognitive items*, or (3) *High-Physical items*. In terms of percent retained activities, most people post-stroke continued to participate in communicatively- and cognitively-demanding activities at moderately high rates, regardless of whether they had aphasia or not. Percent retained participation in physically demanding activities was somewhat less than 50% for both groups. Because there were no differences between the groups on the participation measures, regression analyses were conducted on the combined sample.

For measures that were included as predictors of participation on the ACS (see **Table 3**), only SIS Communication scores, $t_{(79)} = 4.0$, $p = 0.001$ and months post onset, $t_{(78)} = 2.55$, $p = 0.013$, differed by group with PWA reporting significantly lower self-perceptions of communication ability and being longer post-stroke onset. NIHSS scores did not differ between groups.

Differences in Percent Retained Between ACS Scales

Because there were no group differences in ACS percent retained, we conducted analyses of the differences between ACS scales collapsing across group. Percent retained for ACS High Communicative Skill was greater than percent retained for ACS High Cognitive Skill, $t_{(31)} = 9.19, p < 0.0001$. Percent retained for High Cognitive Skill was greater than percent retained for High Physical Skill, $t_{(81)} = 9.03, p < 0.0001$. Percent retained for High Communicative Skill was greater than for High Physical Skill, $t_{(81)} = 12.12, p < 0.0001$.

Relation of Self-Perception of Impairment in Three Domains to Participation

We examined whether self-perceptions of communicative, cognitive, and physical impairment predicted participation in these domains using linear regression models. For each outcome, we tested models with and without the inclusion of covariates (age, gender, education, and the NIH Stroke Scale Total score).

For participation in high-communicative activities, self-perception of *physical function* was significantly and positively related to participation, $ps < 0.05$, adjusted $R^2 = 0.27$. Once covariates were included, however, the effect was no longer significant, indicating that no single variable predicted participation in high-communicative activities, adjusted $R^2 = 0.25$. Results of the models are presented in **Table 4**.

For participation in *High-Cognitive activities*, self-perceptions of both *physical* and *cognitive function* were significantly and positively related to participation, $p < 0.05$, adjusted $R^2 = 0.34$. Once covariates were included, only perception of *physical function* significantly predicted participation in *High-Cognitive activities*, $p < 0.05$, adjusted $R^2 = 0.33$. Results of the models are presented in **Table 5**.

For participation in *High-Physical activities*, self-perceptions of both *physical* and *cognitive function* were significantly and positively related to participation, $p_s < 0.05$, adjusted $R^2 = 0.22$. Once covariates were included, *age* and self-perception of *physical function* were the only significant predictors of participation in physically-demanding activities, $p < 0.01$, adjusted $R^2 = 0.28$. Results of the models are presented in **Table 6**.

TABLE 5 | Regression models examining self-perceptions and participation in high-cognitive activities with parameter estimates and standard errors in parentheses.

	Cognitive skill % retained	
	Without covariates	**With covariates**
Intercept	24.652**	32.349
	(7.425)	(17.541)
Age		−0.224
		(0.174)
Education		1.382
		(0.734)
Gender		1.390
		(4.302)
NIH stroke scale		−1.897
		(1.100)
SIS physical	0.348***	0.259*
	(0.089)	(0.098)
SIS cognition	0.307*	0.234
	(0.119)	(0.125)
SIS communication	−0.066	−0.050
	(0.121)	(0.127)
Observations	81	78
R^2	0.365	0.394
Adjusted R^2	0.340	0.334
Residual Std. Error	18.322 (df = 77)	17.867 (df = 70)
F statistic	14.739*** (df = 3; 77)	6.514*** (df = 7; 70)

*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

TABLE 6 | Regression models examining self-perceptions and participation in high-physical activities with parameter estimates and standard errors in parentheses.

	Physical exertion skill % retained	
	Without covariates	**With covariates**
Intercept	14.179	43.867
	(10.400)	(24.141)
Age		−0.690**
		(0.239)
Education		1.123
		(1.010)
Gender		1.964
		(5.921)
NIH stroke scale		−1.399
		(1.514)
SIS physical	0.420**	0.377**
	(0.124)	(0.136)
SIS cognition	0.391*	0.329
	(0.166)	(0.172)
SIS communication	−0.280	−0.210
	(0.170)	(0.174)
Observations	81	78
R^2	0.247	0.347
Adjusted R^2	0.218	0.282
Residual Std. Error	25.663 (df = 77)	24.590 (df = 70)
F statistic	8.439*** (df = 3; 77)	5.311*** (df = 7; 70)

*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

DISCUSSION

Participants in this sample could be considered as having relatively mild strokes, based on their chronic NIHSS scores that ranged from 0 to 10 with a mean of 2.5. It is interesting and somewhat surprising, therefore, to note that their activity participation retention rates indicate they are giving up between 30 and 50% of their activities in the three groupings of activities examined in this study, that is, activities requiring high levels of communicative skill, cognitive skill, and/or physical exertion. However, contrary to our expectations, there were no statistically significant differences between groups based on presence/absence of aphasia (PWA, PWOA) on any of the three percent-retained participation dimensions. People with and without aphasia showed similar participation retention for physically demanding activities of between 45% and 49%; and both groups retained participation in communicatively- and cognitively-demanding activities at higher rates of about 60–70%. Having aphasia, at least in this sample of post-stroke individuals, does not constitute a greater barrier to participation in several different types of activities than having a stroke alone, using the participation measures we derived for this study. Of course, individuals with more severe post-stroke deficits, both in the motor or language domains, may experience greater restrictions in participation. Although participation rates are reduced in this "milder" stroke sample, the fact that 60–70% of high-communicative or high-cognitive activities are retained may also reflect the value that people post-stroke place on these particular activities. For example, 15 of the 35 high-communicative activities are within the ACS domain of "social activities," and as such, these activities are likely important to quality of life post-stroke.

The regression analyses that examined whether self-perception of impairments in the three domains predicted participation post-stroke also revealed some interesting and unexpected findings. Self-perception of physical functioning and chronological age emerged as predictors of participation in physically demanding activities as expected. The fact that age was a predictor is not unexpected given known changes in physical functioning related to age even in healthy aging, let alone post-stroke. But self-perception of physical functioning also uniquely predicted participation in cognitively demanding activities, which was not expected. A weaker relationship was also seen between self-perception of physical function and participation in communicatively-demanding activities in the original regression without covarying for age, education, gender, and NIHSS score.

Why should self-perception of physical functioning emerge as the prominent predictor for activity retention of high-cognitive or high-communicative activities? Some of the effect may be explained by the fact that some activities are high on two or more of the dimensions. For example, of the 23 high-cognitive activities, 8 are also high-physical; of the 35 high-communicative, 4 are also high physical. When people are rating themselves on the Stroke Impact Scale are they perceiving their physical impairments as more important than impairments in other areas? Are they poor judges of their non-physical selves? Or do they just know something is wrong and cannot attribute it to a specific cause?

Considering the lack of relationship obtained between self-perception of communication and cognitive skills and retention of communicatively- or cognitively-demanding activities, we can ask the same question: Why do self-perceptions of communicative or cognitive challenges appear *not* to predict retention of communicatively- or cognitively-demanding activities? There are several possibilities. One is that self-perception ratings, particularly in these non-physical domains, may not be reliable, in the sense that they may not coincide with actual performance measures. Tucker et al. (44) found a systematicity in self-report for various measures of self-perception ratings within domains like social and physical functioning, such that people were consistent in how they perceived themselves across measures, even if the self- perception scores did not coincide with reality on more objective measures.

Furthermore, individuals post-stroke have varied personal reactions to changes in functioning. For example, some individuals with mild aphasia may perceive their impairment as severe, whereas other individuals with moderate to severe aphasia do not perceive their communication impairment as debilitating. Some people with right hemisphere damage may frankly not perceive any communication or cognitive impairment when compared to outside observers and on objective measurements their communication and cognition fall in the disordered range. When using patient-reported measures such as those in this study, there may be an impression of unreliability to outside observers; nevertheless this may reflect the patient's true perception of their reality.

Another possibility is that people are resourceful post-stroke and have developed numerous compensations for their communication and cognitive challenges such that despite aphasia and other cognitive impairments they find ways to express themselves and participate in valued life activities, though not to the degree they did before, thus reporting that their impairments are few. In contrast, they may perceive (rightly or wrongly) that there are fewer ways to easily compensate for physical impairments, thereby diminishing the relationship between perceptions of physical function and reported participation in physically-demanding activities. In fact, some activities requiring high physical exertion may simply not be able to be easily adapted and thus result in lower retention rates.

Future study should also consider how best to interpret patient-centered or self-perception measures. Could a valid measure of self-awareness inform how self-perception scores are interpreted by assisting in sorting out people with poor self-awareness from those with good self-awareness? Self-perception ratings serve an important purpose in insuring that targets of interventions are important to individuals and allow us to measure outcomes of importance to people post-stroke. But they may not be as useful for people who are poor judges of their own abilities. In a subsequent investigation we aim to conduct a similar study but use objective measures, rather than self-perception measures of functioning in these three domains (communication, cognition, and physical function). Comparisons of self-perception scores to objective measures may highlight different groups of individuals in which these scores are congruent or not. It is also possible that objective measures would show a more direct relationship to retention of participation in the three domains covered in this study than the self-perception measures.

Beyond the limitations discussed above with respect to self-perception measures, other limitations of this study include the fact that the sample was somewhat limited in range of stroke severity and that we had more individuals who were women than men. It is also possible that the group of people with aphasia had milder aphasia, resulting in lack of group differences between those with and without aphasia. Although we accommodated the communication deficit in the group of people with aphasia using the strategies outlined in Tucker et al. (44) it is also possible that in some cases these accommodations were not sufficient to render fully reliable results on the self-perception measures used in this study. Another limitation in exploring factors related to participation is that we only looked at three dimensions (communication, cognition, and physical exertion). Some of the other dimensions that ACS items may be rated high on (for example needing a partner to do the activity with, financial resources, or need for transportation) could have been more important to activity retention rates than the factors that were considered [see Foley et al. (3)]. Future research will need to more fully address the variety of personal as well as environmental factors that ultimately affect participation in life activities post-stroke.

Moreover, this study is limited in that a modest proportion of variance was accounted for by the examined regression models. For the six models tested (three participation outcomes × with/without covariates) the R^2 values ranged from 0.22 to 0.34. Clearly, there is a large proportion of the total variance in participation unaccounted for in this investigation. Future work will be needed to test other possible predictors of participation and more complex relationships among the predictors themselves to account for variance in participation.

Further, because this study used the ACS as its primary outcome measure there are limits to the interpretation of the results of this study. The ACS focuses on the retention of pre-stroke activities. Although there were no differences in the retention of pre-stroke activities, we do not know the perceived quality of participation based on the ACS. It is quite possible that PWA are more dissatisfied or feel some restrictions in their capabilities to engage in activities after stroke. Even though they continue to participate, PWA may feel that their language impairment reduces their satisfaction with participation or may alter their engagement or enjoyment of those activities. Futher work, perhaps including a qualitative study, is warranted to understand the nature of activity participation after stroke and potential predictors of participation satisfaction.

Rehabilitation professionals may want to consider the results of this study in their clinical practice. First, even those with mild stroke will experience significant restrictions in their pre-stroke activities, even after rehabilitation—on the order of 30–50%. In addition, self-perception of physical function is the only self-perception rating that relates to participation retention in cognitively-demanding activities and physically-demanding activities. No self-perception rating that we examined related to participation in communicatively-demanding activities. Importantly, a significant proportion of the variance in participation scores was unaccounted for by self-perception and stroke severity ratings. Therefore, there is still much to learn about facilitators and inhibitors of post-stroke activity participation.

DATA AVAILABILITY STATEMENT

The datasets generated for this study are available on request to the corresponding author.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Washington University Human Research Protection Office and Partners HealthCare Institutional Review Board. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

LC and MN contributed to the conception, design of the work, interpretation of the findings, and drafted the manuscript. KB and JM acquired the data. AF designed the statistical approach and conducted the analyses. KB, JM, and CB revised it critically for important intellectual content. All authors contributed to manuscript revision, read, and approved the submitted version.

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SUPPLEMENTARY MATERIAL

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