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Frequency of domain-specific cognitive impairment in sub-acute and chronic stroke

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Abstract.
BACKGROUND: Functional contributions of cognitive impairment may vary by domain and severity.
OBJECTIVE: (1) To characterize frequency of cognitive impairment by domain after stroke by severity (mild: $-1.5 \leq$ z-score < -2; severe: $Z \leq -2$) and time (sub-acute: $<$ 90d; chronic: 90d–2yrs); and (2) To assess the association of cognitive impairment with function in chronic stroke.
METHODS: Cognitive function was characterized among 215 people with sub-acute or chronic stroke (66.8 years, 43.3% female). Z-scores by cognitive domain were determined from normative data. Function was defined as the number of IADLs minimally independent.
RESULTS: 76.3% of sub-acute and 67.3% of chronic stroke participants had cognitive impairment in ≥ 1 domain (p-for-difference = 0.09). Severe impairment was most common in psychomotor speed (sub-acute: 53.5%; chronic: 33.7%). Impairment in executive function was common (sub-acute: 39.5%; chronic: 30.7%) but was usually mild. Severe impairment in psychomotor speed, visuospatial function, and language and any impairment in executive function and memory was associated with IADL impairment ($p < 0.03$).
CONCLUSIONS: Mild cognitive impairment is common after stroke but is not associated with functional disability. Impairment in psychomotor speed, executive function, and visuospatial function is common and associated with functional impairment so should be a focus of screening and rehabilitation post-stroke.

1. Introduction

Cognitive impairment is an increasingly recognized sequela of stroke that contributes to functional disability (Claesson, Linden, Skoog, & Blomstrand, 2005; Hlman, Guti, Vborg, Knopp, & Tarkowski, 2011). Estimates of the prevalence of cognitive impairment post-stroke range from 12% to 60% and vary according to setting (hospital versus community), time since stroke, and inclusion of pre-stroke dementia (Appelros, 2005; Ebrahim, Nouri, & Barer, 1985; Liman et al., 2011; Oksala et al., 2009; Patel, Coshall,

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Rudd, & Wolfe, 2002, Pendlebury & Rothwell, 2009; Tetemichi et al., 1994). The prevalence of cognitive impairment after stroke has also fluctuated over the past several decades (Bejot et al., 2011).

Few studies have characterized the frequency of post-stroke cognitive impairment by domain (Dickey et al., 2010; Lesniak, Back, Czepiel, & Seniow, 2008; Nys et al., 2005, 2007; Pohjavarra et al., 2002; Rasquin et al., 2004; Stewart, Sunderland, & Sluman, 1996), with several of these studies only considering a single cognitive domain (Dickey et al., 2010; Phjasvaara et al., 2002; Stewart et al., 1996). This is despite the fact that the impact of cognitive impairment on functional abilities varies is dependent on the domain affected. For example, visuomotor slowing strongly predicts functional disability, while memory appears to have relatively little effect (Narasimhalu et al., 2011). Of the studies comparing cognitive impairment across domains, three excluded older participants ($\geq$75 or 85 years), which is the age group most prone to strokes (Lesniak et al., 2008; Nys et al., 2005; 2007; Shiue, 2011). In addition, these studies all used a mild criterion to define cognitive impairment (z-score of approximately 1.5) that is consistent with a diagnosis of mild cognitive impairment (MCI) (Morris, 2012), not dementia. The frequency of severe cognitive impairment (using a more stringent criteria of z-score < -2) that is more likely to impact function is poorly characterized. Thus, the objective of this cross-sectional analysis was to characterize and compare the frequency of cognitive impairment by domain and severity in a sample of people in the sub-acute versus chronic phase of stroke recovery, and to determine how these patterns were associated with daily function (instrumental activities of daily living, IADLs) in chronic stroke recovery.

2. Methods

This is a cross-sectional analysis of the Rehabilitation Affiliates Study, a multi-center prospective cohort study of people post-stroke instigated by the Heart and Stroke Foundation Centre for Stroke Recovery. The objective of the Rehabilitation Affiliates study is to characterize physical and cognitive recovery among people after stroke. The study uses convenience sampling to identify adults who suffered a recent stroke from four Canadian centres, two acute care facilities (Baycrest, Toronto, Canada; Sunnybrook Health Sciences Centre, Toronto, Canada) and two rehabilitation facilities (Grand River Hospital–Freeport Site, Kitchener, Canada; Providence Healthcare, Toronto, Canada). The sample was intended to be inclusive—all patients from the centres with a primary diagnosis of ischemic or hemorrhagic stroke occurring within the past 2 years and who are eligible for, participating in, or have graduated from stroke rehabilitation were eligible for enrolment. Participants or their substitute decision maker provided informed consent. The study was approved by the ethics board at all participating sites.

Between September 2008 and March 2011, there were 281 people enrolled to the Rehabilitation Affiliates study. Our sample includes participants who had cognitive test results either $\leq$ 90 days post-stroke (sub-acute recovery, $n = 114$) or 90 days–2 years post-stroke (chronic recovery, $n = 101$) in each of six cognitive domains (executive function, memory, attention, psychomotor speed, visuospatial, and language) ($n = 220$). Those with a history of symptoms consistent with pre-stroke cognitive impairment (retrospectively reported pre-stroke Functional Independence Measure (FIM) cognitive score of < 30, approximately equivalent to a MMSE of 24) (Heruti et al., 2002), were excluded ($n = 5$), leaving a sample size of 215.

2.1. Neuropsychological assessment

The neuropsychological test battery included the Montreal Cognitive Assessment (MoCA) (Nasreddine et al., 2005), digit span (Wechsler, 1997), the Trail Making Test (Reitan & Wolfson, 1985), semantic fluency (Spreen & Strauss, 1998), a modified Snodgrass picture naming and recall test (Snodgrass & Vanderwart, 1980), and line bisection. In the line bisection test, participants were required to mark the centre of three 20 cm lines; the distance from the mark to the lines true midpoint was averaged between trials. The 5-word recall (recall, cued recall, and recognition) and clock drawing test were part of the MoCA (Nasreddine et al., 2005).

Cognitive tests were grouped according to primary cognitive domain (Table 1). The score for each test was normalized according to either published norms (Trail Making Test, Digit Span, and semantic fluency) or internal norms (95 adults aged 28 to 87 years, which matches the age range of our cohort) to produce a z-score. To reduce the effect of outliers, scores outside $\pm$ 3 were set to 3 or -3, as appropriate. The average z-score for tests within each cognitive domain was determined. Mild impairment was defined as an average cognitive domain z-score between -1.5 and -2. Severe cognitive impairment was defined by an aver-

Table 1
Neuropsychological assessments by domain. Impairment was defined by an average cognitive domain z-score ≤ -1.5

Cognitive domain	Neuropsychological Test
Executive Function	Digit span backwards
	Trails B
Memory	Modified Snodgrass recall
	5-word list free recall
	5-word list cued recall
	5-word list recognition
Simple attention	Digit span forwards
Psychomotor speed	Trails A
Visuospatial	Line-bisection
	Clock drawing
Language	Semantic fluency (animals)
	Modified Snodgrass naming

age cognitive domain z-score ≤ -2.0. Total cognitive impairment was the total of the two (z-score of ≤ -1.5, consistent with definitions in previous literature) (Nys et al., 2005; 2007; Pohjasvaara et al., 2002).

2.2. Other measures

Stroke characteristics including type (ischemic, hemorrhagic), side of impairment (left, right, or both), and region (frontal, posterior) were determined from medical records. Severity of stroke deficits was evaluated using the National Institutes of Health Stroke Scale (NIHSS) (Brott et al., 1989). Current and pre-stroke functional ability was reported using the Functional Independence Measure (FIM) (Keith, Granger, Hamilton, & Sherwin, 1987). Participants self-reported age, sex, gender, race, smoking history, vascular comorbidities (hypertension, diabetes, hyperlipidemia, cardiac disease), and history of previous strokes or transient ischemic attacks (TIAs). Depressive symptoms were evaluated using the 20-item Center for Epidemiological Studies Depression scale (CES-D) (Radloff, 1977). Those who scored ≥ 16 were considered to have depressive symptoms. Instrumental activities of daily living (IADLs) were evaluated among chronic stroke participants using Lawton and Brody's 8-point scale (Lawton & Brody, 1969). For these analyses, participants received a score of one if the IADL was impaired and zero if they were minimally independent for each task for a maximum score of eight.

2.3. Analysis

Characteristics of our study sample by recovery period were described by mean (standard deviation, SD) or percent (n) and compared between recovery periods independent t-tests, Wilcoxon's sum-rank test, or chi-square as appropriate.

Frequency of mild impairment, severe impairment, and total impairment by cognitive domain was calculated and compared between recovery periods using chi-square (χ^2). The number of domains impaired (mild, severe, and total) was calculated and compared between recovery periods using Wilcoxon's sum rank test.

The association between cognitive status and IADL performance was evaluated using unadjusted and adjusted linear regression (age, sex, and education, and days post-stroke were included as potential confounders). All analyses were performed with SPSS version 21.

3. Results

Study participants had average age of 66.6 years (standard deviation, SD 13.0 years) and an average of 13.1 (SD3.6) years of education; 43.3% were female and 18.6% had sustained a previous stroke or TIA. The majority of strokes were ischemic (65.3% versus 22.4% hemorrhagic; 12.2% not recorded). Strokes were approximately evenly distributed between hemispheres (43.5% left, 49.7% right, 6.8% bilateral). The chronic sample had less severe symptoms (NIHSS), better functional abilities (FIM), and better MoCA scores ($p < 0.03$ for all) (Table 2).

Cognitive impairment was common after stroke; 76.3% and 67.3% of sub-acute and chronic stroke participants, respectively, had at least mild impairment in one or more cognitive domains (p-for-difference = 0.09). Severe impairment was most common in psychomotor speed, but the frequency was lower in the chronic than the sub-acute sample (33.7% of sub-acute vs. 53.5% of chronic sample, p-for-difference = 0.003). Severe impairment was relatively rare in other domains (<15% of participants in both samples). The frequency of mild impairment in executive function was significantly lower among the chronic sample than the acute sample (15.8% of chronic versus 28.1% of sub-acute sample, $p = 0.02$). In contrast, the frequency of mild impairment in psychomotor speed was higher among the chronic than the acute sample (11.9% of chronic vs. 4.4% of sub-acute sample, $p = 0.05$). (For full description of the frequency of impairment by cognitive domain, severity, and recovery period, see Table 3.)

Table 2
Participant characteristics (mean, SD or %, *n*) by time (sub-acute: ≤ 90 days; chronic: > 90 days post-stroke)

Characteristics	Sub-acute (*n* = 114)	Chronic (*n* = 101)	*p*-value for difference
Patient Characteristics			
Age, years	68.2 (12.6)	65.1 (13.1)	0.08
Female	49.1 (56)	36.6 (37)	0.07
Education, years	12.6 (3.8)	13.6 (3.4)	0.05
Depressive Symptoms, CES-D ≥ 16*	37.5% (36)	35.4% (29)	0.88
MoCA	20.1 (5.4)	22.8 (4.8)	<0.001
Previous Stroke/TIA	21.9% (25)	14.9% (15)	0.22
Days Post-stroke	47.1 (21.6)	353.6 (144.7)	<0.001
NIH Stroke Scale	5.5 (5.1)	3.9 (4.4)	0.03
FIM	99.6 (20.3)	111.3 (17.0)	0.03
Stroke Characteristics			
Type			0.89
Ischemic	66.6 (76)	63.4 (64)	
Hemorrhagic	19.3 (22)	23.8 (24)	
Hemisphere			0.76
Left	42.1 (48)	41.6 (42)	
Right	44.7 (51)	49.5 (50)	
Both	13.1 (15)	7.9 (8)	
Region			0.73
Frontal	21.4% (22)	24.1% (21)	
Other	78.6% (81)	75.9% (66)	

*CES-D = Centre for Epidemiologic Studies Depression Scale.

Table 3
Frequency of cognitive impairment (%, *n*), by domain, severity, and time (sub-acute: ≤ 90 days; chronic: > 90 days post-stroke)

Cognitive domain	Mean Z-score	Mild impairment (−1.5 ≤ Z ≤ −2)	Severe impairment (Z ≤ −2.0)	Total (mild & severe) impairment (Z ≤ −1.5)
Sub-acute (*n* = 101)				
Executive Function	−1.1 (0.9)	28.1% (32)	11.4% (13)	39.5% (45)
Memory	−0.2 (1.0)	8.8% (10)	4.4% (5)	13.2% (15)
Simple Attention	−0.1 (1.0)	14.9% (17)	0.9% (1)	15.8% (18)
Psychomotor Speed	−1.8 (1.4)	4.4% (5)	53.5% (61)	57.9% (66)
Visuospatial	−0.9 (0.9)	8.8% (10)	14.0% (16)	22.8% (26)
Language	−0.4 (1.3)	4.4% (5)	11.4% (13)	15.8% (18)
Any Domain	–	48.2% (61)	59.6% (69)	76.3% (87)
Chronic (*n* = 101)				
Executive Function	−0.9 (0.9)	15.8% (16)*	14.9% (15)	30.7% (31)
Memory	−0.2 (0.9)	7.9% (8)	3.0% (3)	10.9% (11)
Simple Attention	−0.2 (1.0)	8.9% (9)	2.0% (2)	10.9% (11)
Psychomotor Speed	−1.3 (1.4)*	11.9% (12)*	33.7% (34)*	45.5% (46)*
Visuospatial	−0.7 (0.8)*	6.9% (7)	10.9% (11)	17.8% (18)
Language	0.1 (1.6)*	6.9% (7)	5.9% (6)	12.9% (13)
Any Domain	–	43.6% (51)	43.6% (45)*	67.3% (68)

*$p < 0.05$ for difference between sub-acute and chronic samples.

The number of cognitive domains with mild impairment was similar among sub-acute and chronic samples (median, interquartile range: sub-acute 0, 0–1 and chronic 0, 0–1, *p*-for-difference = 0.38). The number of domains with severe or any impairment, however, was higher among the sub-acute than the chronic sample (severe: sub-acute 1, 0–2 and chronic 0, 0–1, p-for-difference = 0.02; any: sub-acute 1, 1–2 and chronic 1, 0–2, p-for difference = 0.04). The distribution of cognitive impairment by number of domains affected is presented in Fig. 1.

In unadjusted and adjusted analyses, people who had severe impairment in psychomotor speed, visuospatial function, and language had more IADLs impaired than those without ($p < 0.02$). In addition, those with any impairment in or total impairment in executive function, memory, psychomotor speed, and visuospatial skills also had increased number of IADLs impaired

($p < 0.04$). Mild impairment alone was not associated with IADL performance in any domain (Table 4).

4. Discussion

In this study, we quantified the frequency of mild and severe cognitive impairment across several cognitive domains in a sample of people in the sub-acute or chronic phase of stroke recovery. Over two-thirds of our sub-acute and chronic stroke samples had at least mild impairment in ≥ 1 cognitive domain. Severe impairment in psychomotor speed was most frequent and was also associated with greater IADLs impairment. Executive function, visuospatial function, and language impairment also contributed to IADL deficits. Our results indicate that the frequency and functional impact of cognitive impairment is dependent on the specific domain affected and severity of impairment. The relative frequency and consequences by domain may be important for determine targets for cognitive rehabilitation programs.

Frequency estimates for cognitive impairment after stroke are highly variable (Liman et al., 2011; Pendlebury & Rothwell, 2009). In our cohort of Canadian stroke survivors recruited from acute care or rehabilitation facilities, over two-thirds had at least mild impairment in one domain, which is high compared to prior studies (Appelros, 2005; Ebrahim et al., 1985; Liman et al., 2011; Oksala et al. 2009; Patel et al., 2002; Pendlebury & Rothwell, 2009; Tatemichi et al., 1994). There are several possible explanations. First, we defined cognitive impairment as impairment in any cognitive domain and may have included people who did not meet diagnostic criteria for MCI or dementia. Studies looking at single domain impairment yielded similar results to ours (55–80% with impairment) (Lesniak et al., 2008; Nys et al., 2005). Second, although we excluded people who reported symptoms consistent with pre-stroke cognitive impairment, this strategy is vulnerable to recall bias and may have allowed for the inclusion of already impaired individuals.

Reports of the most commonly affected domains also vary widely. Rasquin and colleagues (2004) reported that psychomotor speed was most frequently affected, similar to our results. Nys and colleagues (2005, 2007) reported that executive function and visuospatial function were most common impaired but did not include a measure of psychomotor speed. Lezniak and colleagues (2008) reported that attention was the most frequently affected domain. However, their attention measures included significant executive control demands. Use of different cognitive measures may explain the variability across studies. Our results indicate that psychomotor speed along with executive function and visuospatial function were commonly impaired, in partial agreement with three of the four previous studies (Nys et al., 2005, 2007; Rasquin et al., 2004). Our study also agrees with another previous report that approximately 40% of people with sub-acute stroke have impaired executive function (Pohjasvaara et al., 2002).

We did not identify a previous study that examined the frequency of severe impairment by cognitive domain after stroke. Extant studies instead used a cut-off of $Z < -1.5$, which defines our mild impairment group and is consistent with cut-offs for mild cognitive impairment (Morris, 2012). Our results indicate that severe impairment was much more common in psychomotor speed than in other domains, with over 50% of the sub-acute sample severely affected compared to less than 15% for other domains. This figure dropped to just over 30% among chronic stroke participants and the average z-score for psychomotor speed increased, suggesting that impairment in psychomotor speed may improve over time.

Along similar lines, we found that the frequency of any cognitive impairment (mild + severe) in any domain was almost 10% lower among the chronic stroke sample than among the sub-acute stroke sample, though not statistically significant. Any drop in frequency appeared to be primarily attributable primarily to lower frequency of impairment in psychomotor speed ($p = 0.05$). This is similar to previous studies that found that the rates of cognitive impairment declined from acute to chronic stroke (Del Ser et al., 2005; Hochstenbach, den Otter, & Mulder, 2003; Lesniak et al, 2008; Liman et al., 2011; Patel, Coshall, Rudd, & Wolfe 2003; Rasquin et al., 2004). Additional longitudinal studies are needed to confirm these trends.

Impairment in psychomotor speed, visuospatial function, language, executive function, and memory was associated with IADL deficits. A previous report that visuomotor speed most strongly predicted functional disability (Narasimhalu et al., 2011). In partial alignment with this study, any impairment (mild to severe) in psychomotor speed, memory, and visuospatial function were strongly associated with greater impairment in IADLs. Due to high frequency of severe impairment in psychomotor speed, this deficit likely has the greatest population impact on functional abilities after stroke. Only severe impairment and not mild impairment in language was associated with impaired

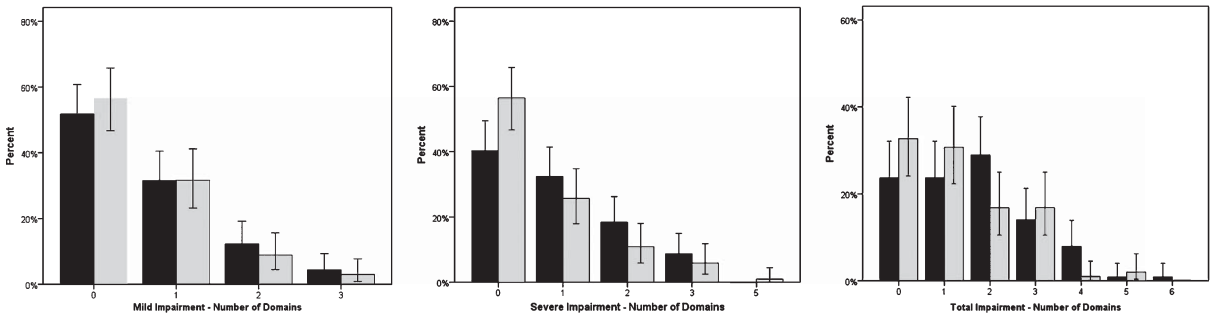

Fig. 1. Number of domains with (a) mild impairment ($-2 <$ z-score ≤ -1.5), (b) severe impairment (z-score ≤ -2), and (c) any (mild or severe) impairment (z-score ≤ -1.5) in sub-acute ($\leq$90days, black) and chronic (90 days – 2 years, grey) stroke.

Table 4
Association between cognitive impairment by domain and number of IADLs impaired

Cognitive domain	Mild impairment	Severe impairment	Total impairment
Unadjusted			
Executive Function	0.87 (−0.40, 2.15)	1.09 (−0.31, 2.50)	1.03 (0.03, 2.03)
Memory	1.20 (−0.43, 2.833)	1.58 (−0.88, 4.05)	1.32 (−0.08, 2.72)
Simple Attention	0.50 (−1.01, 2.01)	0.28 (−2.76, 3.33)	0.47 (−0.89, 1.83)
Psychomotor Speed	0.12 (−1.09, 1.32)	2.00 (1.07, 2.94)	1.37 (0.51, 2.23)
Visuospatial	−0.01 (−1.73, 1.70)	2.21 (0.79, 3.63)	1.32 (0.15, 2.49)
Language	0.12 (−1.46, 1.69)	1.86 (−0.29, 4.00)	0.70 (−0.61, 2.01)
Adjusted			
Executive Function	1.04 (−0.20, 2.28)	1.09 (−1.82, 4.94)	1.14 (0.12, 2.15)
Memory	1.50 (−0.12, 3.11)	1.19 (−1.25, 3.63)	1.44 (0.04, 2.84)
Simple Attention	0.33 (−1.11, 1.77)	−0.93 (−5.08, 3.22)	0.21 (−1.16, 1.58)
Psychomotor Speed	0.38 (−0.84, 1.60)	2.15 (1.25, 3.04)	1.65 (0.82, 2.47)
Visuospatial	0.09 (−1.53, 1.70)	2.31 (0.89, 3.73)	1.34 (0.20, 2.48)
Language	0.21 (−1.29, 1.71)	2.65 (0.34, 4.95)	0.90 (−0.39, 2.19)

*Adjusted analyses included age, sex, education and days post-stroke as potential confounding variables.

IADLs, possibly explaining why a previous study did not find a strong association between function and language impairment defined by scoring below the sample mean (Narasimhalu et al., 2011). Total impairment in executive function was also associated with IADL deficits, though neither mild nor severe reached statistical significance individually. Due to the relatively high prevalence of impairment in executive function, impairment in this domain is also likely to have significant population impact on function even though the relative risk of IADL impairment associated with executive function impairment was lower than for memory or visuospatial skills.

Given that psychomotor speed, visuospatial function, and executive function are relatively common and are associated with poor functional abilities, cognitive rehabilitation focusing on these domains after stroke is vital. Unfortunately, little work has focused on cognitive rehabilitation after stroke relative to physical rehabilitation. Some programs show promise in improving visuospatial neglect after stroke (Bowen & Lincoln, 2007; Ianes et al., 2011; Lim, Kang, & Paik, 2010; Miniussi et al., 2008). However, executive function and psychomotor speed have rarely been targeted. Previous studies regarding rehabilitation for executive function included both acquired and traumatic brain injury participants with few reports specifically in stroke (Levine, turner, & Stuss 2008; Turner & Levine, 2004). One executive function intervention, Goal Management Training (Cicerone et al., 2005), was recommended as a practice standard for rehabilitating executive function impairment based on evidence from acute brain injury and aging populations. Work is underway to investigate its efficacy in cerebrovascular disease and stroke.

Our study has strengths. We studied a large, recent, well-characterized, and inclusive cohort of stroke survivors who were recruited from both acute care academic hospitals and community-based rehabilitation centres. Our study also has limitations. Our screening

for pre-stroke cognitive impairment was based on self-report of symptoms and may not have been sensitive enough to detect all cases, which is likely the reason that few pre-stroke cases of cognitive impairment were detected and excluded. Sensorimotor impairments may have influenced our frequency estimates for cognitive impairment, particularly on timed tests or tests that required motor speed or accuracy, which always a concern when both cognitive and motor impairments are common. In addition, since our sample required cognitive scores across all domains, it is likely that people with more severe cognitive impairment, particularly severe language deficits, may have been excluded from our study sample. However, our frequency estimates for language impairment is within the range of previous studies (Berthier, 2005; Lesniak et al., 2008). Furthermore, FIM scores of our sample were similar to discharge FIM score reported from the Ontario Stroke Registry (Hall et al., 2011).

5. Conclusions

In our study, cognitive impairment in psychomotor speed, executive function, and visuospatial function was both common after stroke and was associated with poorer IADL performance. These domains may be important targets to cognitive rehabilitation and should be assessed carefully following stroke. Future studies should track the frequency of cognitive impairment by domain longitudinally from acute to sub-acute and chronic phases of stroke recovery to confirm changes in frequency of cognitive impairment between sub-acute and chronic stroke and determine association with functional recovery.

Declaration of interest

The authors have no conflicts of interest or additional disclosures relevant to this manuscript.

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