

The relationship between early post-stroke cognition and longer term activities and participation: a systematic review.

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The relationship between early post-stroke cognition and longer term activities and participation: a systematic review.

This systematic review examined whether early cognitive impairment after stroke is predictive of outcome within the 'activity' and 'participation' domains of the International Classification of Functioning, Disability and Health (ICF) at 6-12 months post-injury. Studies were included if cognitive functioning was assessed within 6 weeks of injury and outcome was measured at least 6 months post-injury. PsycINFO, MEDLINE, CINAHL and EMBASE databases were searched and 14 studies were identified. Studies were categorised according to whether 'domain-general' or 'domain-specific' cognitive assessment was undertaken and whether outcomes measured the ICF activities or participation domains, as determined by three independent raters using previously established linking rules. Quality of studies was assessed using a modified version of Downs and Black's Quality Index. Overall, early cognitive impairment predicted activities and participation 6-12 months post-stroke. This relationship was more consistent when domain-specific cognitive assessment was used. For the domain of activities, visuospatial perception/construction, visual memory, visual neglect and executive functioning predicted levels of activities 6-12 months post-stroke. Early domain-specific cognitive assessment may be clinically informative of longer term activities. For the domain of participation, further well-controlled studies are needed to determine the relationship with early post-stroke cognitive impairments.

Keywords: stroke; cognitive assessment; outcome; activities; participation.

Introduction

Stroke is the second most frequent cause of death worldwide and the most common cause of adult disability in developed countries (Patel, Woodward, Feigin, Heggenhougen, & Quah, 2010). In addition to physical, psychological and financial consequences for patients and families, stroke has a significant impact on the health and social care system (Barker-Collo & Feigin, 2006) and is estimated to cost the United Kingdom nine-billion pounds a year, with treatment costs accounting for approximately five percent of the National Health Service's total costs (Saka, McGuire, & Wolfe, 2009).

Stroke can result in acute impairments in cognitive domains such as memory, attention, perception, executive functioning and social communication (Lezak, Howieson, Bigler, & Tranel, 2012). In the long-term, stroke patients may experience chronic cognitive impairment, either in a 'domain-specific' form (Nys, Van Zandvoort, de Kort, Jansen, Van der Worp, et al., 2005) or linked to a progressive more 'domain-general' dementia (Huang et al., 2015). In addition, stroke survivors are more likely to experience depression (Nys et al., 2006), have reduced levels of activities and participation (Hartman-Maeir, Soroker, Ring, Avni, & Katz, 2007) and report a lower quality of life (Hackett, Duncan, Anderson, Broad, & Bonita, 2000). It is therefore important for professionals, the individual with the injury and those who have a relationship with that person, to have an understanding about the patient's likely outcome (Barker-Collo & Feigin, 2006).

National clinical guidelines recommend that assessment of patients' cognitive abilities should be conducted within the first 6 weeks of stroke, as they may impact on functioning in daily life (National Institute for Health and Care Excellence, 2010; Royal

College of Physicians, 2016). One purpose of early cognitive assessment is to predict the patient's long-term outcome, based on test performance (Bennett, 2001). For example, the patient's cognitive test scores have been used to predict whether he/she might have difficulties with self-care or independent living or is likely to return to previous employment (Sbordone & Long, 1996). Such outcomes have important implications for the person, family and health and social care professionals.

Traditionally, brief cognitive screening tools, such as the Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975) and the Montreal Cognitive Assessment (MoCA; Nasreddine et al., 2005) are used. Such tools allow quick bedside administration but most are designed to only provide a domain-general cognitive assessment, classifying patients as either cognitively 'impaired' or 'unimpaired'. Although such an approach provides a simple indication of the presence of cognitive impairment, this has drawbacks. For example, many domain-general assessment measures, such as the MMSE (Nys, van Zandvoort, de Kort, Jansen, Kappelle, et al., 2005) and MoCA (Chan et al., 2014; Demeyere et al., 2016), have been found to lack sensitivity to the specific cognitive impairment following stroke. A recent systematic review found that the relationship between early post-stroke cognitive impairment, as measured by the MMSE, and chronic outcome was inconsistent (Van Heugten, Walton, & Hentschel, 2015).

Therefore, the importance of domain-specific cognitive assessment after stroke has been emphasised (Demeyere et al., 2016; Royal College of Physicians, 2016). Some authors have argued that impairments in specific cognitive domains may be more disabling in the long term than other domains (Bennett, 2001; Nys, Van Zandvoort, de Kort, Jansen, Van der Worp, et al., 2005), or might affect outcomes differently (Middleton et al., 2014; Nys et al., 2006). However, domain-specific assessment is often

impractical to conduct early after stroke (Van Heugten et al., 2015). This is because it usually entails conducting a neuropsychological assessment, which can be time consuming and difficult to conduct at the bedside (though see Demeyere et al 2015; 2016).

Following stroke, chronic outcome is typically measured after a period of at least 6 months (Schiemanck, Kwakkel, Post, & Prevo, 2006). This is considered the minimal period required to estimate long-term outcome. Though stroke survivors will continue to change and recover over a long term period (over many years), it has been suggested that the steepest recovery slope is thought to have occurred within this time (Jørgense et al., 2000), and it is recommended that patients' health and care needs are reviewed at 6 and 12 months (Royal College of Physicians, 2012). Most studies are therefore limited to longer term outcomes being defined in this way. Outcome can be measured in a variety of different ways, including overall disability (e.g. modified Rankin Scale; Bonita & Beaglehole, 1988), presence of cognitive impairment, mood and level of caregiver assistance (Van Heugten et al., 2015). However, this broad definition may also contribute to inconsistent findings. For example, it may be that acute cognitive impairment predicts some outcomes but not others and, unless outcomes are more sensitively and specifically defined, important relationships may be overlooked.

The International Classification of Functioning and Disability (ICF; World Health Organisation, 2001) provides a framework for clearly defining outcomes. This model distinguishes between impairments involving a significant deviation or loss in 'body function and body structure'; and problems executing tasks and participating in life situations, referred to as 'activities and participation'. For example, a brain tumour may result in impairments (e.g. visual deficits and paresis), may limit activities (e.g.

mobility and self-care) and may restrict participation (e.g. returning to employment or family roles), all of which may interact with environmental factors (Khan & Amatya, 2013). Although activities and participation are typically grouped together, they are distinguishable and represent different outcomes (World Health Organisation; WHO, 2001). For example, the action of washing oneself may be considered an activity whereas attending a social event may be considered participation. Activities and participation are typically the target for rehabilitation, as they are vital to promoting individuals' quality of life and reducing stroke's economic impact (Andrenelli et al., 2015). There is growing interest in the relationship between activities and participation and cognitive functioning (Middleton et al., 2014; Overdorp, Kessels, Claassen, & Oosterman, 2016).

National clinical guidelines often recommend that early cognitive assessment should be conducted to plan treatments and inform care pathways (e.g. National Institute for Health and Care Excellence, 2010; Royal College of Physicians, 2012). However, whether early cognitive assessment can be used to predict chronic outcome is less clear with recent reviews of evidence yielding mixed conclusions (Van Heugten et al., 2015), given the broad scope of outcome measures typically used. The current review aimed to investigate whether acute cognitive impairment predicts outcome 6-12 months post-stroke, by specifically discussing both domain-general and domain-specific cognitive assessments, as well as individual cognitive domains, and with a clear focus on specific outcomes relating to activities and participation.

In brief, this review will seek to answer two specific questions, about which there is growing interest in the literature: 1) whether domain-general or domain-specific cognitive assessments have a more consistent relationship with outcomes 6-12 months post-stroke, and 2) which cognitive domains are associated with these outcomes.

Method

The current review was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA; Liberati et al., 2009). To reduce risk of error and to promote reliability of data collection, data were extracted using a modified version of Cochrane Public Health's (2016) data extraction and assessment template.

Quality appraisal

Quality was assessed using a version of Downs and Black's (1998) Quality Index that has been modified for use with non-intervention studies (Ferro & Speechley, 2009) and used by previous systematic reviews on ABI (e.g. Grace, Kinsella, Muldoon & Fortune, 2015), although not in stroke specifically. Fifteen items are each scored dichotomously, as 1 (yes), or 0 (no/ unable to determine), and a higher total score represents greater methodological quality. The scale comprises four subscales; reporting (0–7), external validity (0–3), internal validity (0–4) and statistical power (0–1). In the current review, this tool was used to structure and guide the appraisal of articles.

The quality appraisal item, 'confounds', was used to structure the findings. Studies were considered in terms of whether they controlled for motor functioning, age and education. This is because motor impairments have been shown to negatively impact performance on cognitive tests (Lezak et al., 2012) and older age and lower education, but typically not gender, have been associated with worse performance on the Abbreviated Mental Test (AMT; Sahadevan, Lim, Tan, & Chan, 2000), MMSE (Mungas, Marshall, Weldon, Haan, & Reed, 1996), MoCA (Malek-Ahmadi et al., 2015) and a variety of neuropsychological tests (Lezak et al., 2014). Furthermore, several studies reviewed reported that having a younger age and higher education was

associated with higher levels of activities and/or participation (Jehkonen et al., 2000; Nys et al., 2005; 2006; Leśniak et al., 2008; Sveen et al., 1996).

Search Strategy

PsycINFO, MEDLINE, CINAHL and EMBASE were each systematically searched in April 2017. The search terms were grouped into four main areas: population-related, time-related, assessment-related and outcome-related, and were systematically combined. Further studies were identified by searching the reference lists of identified articles and review papers.

Selection criteria

Papers were included if they met the following inclusion criteria: quantitative research with human participants over the age of 18 with a stroke, written in English and published in a peer reviewed journal between 1970 and 2017, articles that conducted cognitive assessment within 6 weeks of injury, a follow-up assessment was conducted using a standardised outcome measure after at least 6 months post-injury, outcome measures related to activities or participation, the relationship between early cognitive assessment and outcome measures was investigated and they were not review papers, meta-analyses, unpublished dissertations or book chapters. The search was limited to articles published since 1970, as it was thought that older articles may not be reflective of current assessment tools, outcome measures and services. Although there is no consensus within the literature about how ‘early’ cognitive assessment should be defined, it was necessary for the current review to apply specific inclusion criteria. Based on clinical guidelines for stroke that recommend that initial cognitive assessment should be undertaken within 6 weeks, cognitive assessment was defined as early if it was conducted within this time period (National Institute for Health and Care Excellence, 2010; Royal College of Physicians, 2016).

Coding of Outcome Measures

To ensure that the current review only included studies that measured activities and participation, and to allow comparisons to be drawn between activities and participation, outcome measures were linked to the ICF framework. This was done using the 'linking rules', set out by Cieza et al. (2005), designed specifically for the ICF. Coding was performed by three blind-raters, the first author and two assistant psychologists. Following Cieza et al.'s (2005) advice, outcome measure items were broken down and analysed separately if they contained more than one meaningful concept. Scores were averaged over the raters and outcome measures were categorised as measuring activities or participation depending on what the majority of meaningful concepts were coded as measuring. To promote consistency and adherence to Cieza et al.'s (2005) linking rules, the raters each spent a minimum of two hours familiarising themselves with the ICF framework, the ICF codes and Cieza et al.'s (2005) linking rules and all three raters worked from an excel spreadsheet with outcome measure items broken down into meaningful concepts in advance. The assistant psychologists were also given an example outcome measure that had been coded by the first author, which was a measure not included in the review. All three researchers spent a minimum of thirty minutes coding each measure. The ICF states that activities and participation can be distinguished (WHO, 2013) by designating some domains 'activities' and others 'participation'. For the purposes of the current review, domains 1-5 ('learning and applying knowledge', 'general tasks and demands', 'communication' and 'mobility' and 'self-care') were categorised as 'activities' and 6-9 ('domestic life', 'interpersonal interactions and relationships', 'major life areas' and 'community, social and civic life') were categorised as participation. This is because the items within the former domains, such as 'putting on clothes', more closely fit the ICF's (2001) definition of activities:

“the execution of a task or action” (p. 12), whereas the items within the latter domains, such as ‘maintaining a job’, more closely fit the ICF’s (2001) definition of participation: “involvement in a life situation” (p. 12). This method of categorising domains is also consistent with how activities of daily living (ADLs) and instrumental ADLs (IADL) are usually differentiated. ADLs involve basic tasks of self-care, such as bathing, eating, dressing, toileting and transferring, whereas IADLs involve more complex tasks, such as shopping, preparing meals, housekeeping, maintaining hobbies, laundering, using transportation and managing finances (LaPlante, 2010). Interrater agreement, at the domain level, was calculated using intraclass correlations, which were all significant ($p < .001$) and indicated excellent levels of reliability for most outcome measures (see Table 1 for a full overview).

<Insert Table 1>

Results

The electronic literature search identified 1,628 results, following the removal of duplicates. The article abstracts were screened and 1,153 were excluded. Seventy-five full text articles were evaluated and fifty-nine were removed, which did not meet the inclusion criteria. In total 14 articles, reporting on 13 studies, were included (see Figure 1 for a flowchart detailing the selection process). The included studies are summarised in Table 2.

<Insert Figure 1>

Overview of studies

Studies were conducted in Australia, Singapore, Hong Kong, South Korea, Sweden, Norway, the Netherlands, Poland, Finland, Canada and the United States of America. Six studies assessed domain-general cognitive functioning (see Table 2); of these, three measured activities (Påhlman, Gutiérrez-Pérez, Sävborg, Knopp, & Tarkowski, 2011; J. Park, Lee, Lee,

& Jung, 2016; Saxena, Ng, Koh, Yong, & Fong, 2007), one measured participation (Thommessen, Bautz-Holter, & Laake, 1999) and two measured both activities and participation (Wong et al., 2014; Zinn et al., 2004). Ten studies assessed domain-specific cognitive functioning; and of these six measured activities (Leśniak, Bak, Czepiel, Seniów, & Członkowska, 2008; Nys et al., 2006; Pålman et al., 2011; J. Park et al., 2016; Rose, Bakal, Fung, Farn, & Weaver, 1994; Van Zandvoort, Kessels, Nys, de Haan, & Kappelle, 2005), one measured participation (Jehkonen et al., 2000) and three measured both activities and participation (Cumming, Brodtmann, Darby, & Bernhardt, 2014; Nys, van Zandvoort, de Kort, van der Worp, et al., 2005; Sveen, Wyller, Ljunggren, & Bautz-Holter, 1996). Two studies measured both domain-general and domain-specific cognitive functioning, both of which measured activities (Pålman et al., 2011; Park et al., 2016). Two of the studies were based on the same cohort of patients (Nys et al., 2005; 2006).

< Insert Table 2 >

Quality assessment and critique of studies

An overview of the assessment of bias for each study based on Downs and Black's (1998) Quality Index modified for use with non-intervention studies (Ferro & Speechley, 2009) is presented in Table 3 (note maximum score =15).

< *Insert Table 3* >

Reporting

All studies clearly stated their aims or hypotheses and methods of outcome measurement. Many did not include demographic information or information specific to the subsample used for their analyses, such as information about age, level of education or both (see Table 2). Five studies provided insufficient information about variability in the data, four provided insufficient information about their results and six did not report exact p values (see Table 3).

External Validity

Thommessen et al. (1999) and van Zandvoort et al. (2005) only included participants living in the community at follow-up, limiting the generalisability of the findings. No study described their source population, so it was not possible to determine whether all participants who were invited or agreed to participate, and were representative of the populations from which they were drawn. It is likely, however, that they were unrepresentative to some extent, as most studies applied strict inclusion criteria. For example, most studies excluded older participants,

specifically those over the age of 59 (Thommessen et al., 1999), 65 (Stenberg et al., 2015), 75 (Leśniak et al., 2008; Jehkonen et al., 2000; Wong et al., 2014), 80 (van Zandvoort et al., 2005), 85 (Nys et al., 2005; 2006) and 90 (Zinn et al., 2004).

Most participants had mild-moderate stroke. Thus, findings from the included studies are unlikely to be representative of patients with the least and most severe injuries. In the studies where information about the relevant subsamples' injuries was given, lesions were evenly distributed across the right and left hemispheres. Wong et al. (2014) and van Zandvoort et al. (2005) only included participant with haemorrhagic and ischemic strokes, respectively, but in the remaining studies the average percentage of participants with ischemic stroke was 87% (Range: 73-95%).

All but four studies (Saxena et al., 2007; Sveen et al., 1996; Thommessen et al., 1999; Ziin et al., 2004) excluded patients with co-morbidities, such as previous stroke, other neurological problems or psychiatric conditions, limiting the generalisability of the findings. Park et al. (2016) excluded patients with visual neglect. Half of the studies excluded patients with aphasia (Cumming et al., 2014; Pålman et al., 2011; Park et al., 2016; Nys et al., 2005; 2006; Saxena et al., 2007; Wong et al., 2014) and four excluded patients who did not speak the native language (Cumming et al., 2014; Pålman et al., 2011; van Zandvoort et al., 2005; Wong et al., 2014).

Internal Validity

Only three domain-general (Saxena et al., 2007; Wong et al., 2014; Zinn et al., 2004) and four domain-specific (Leśniak et al., 2008; Park et al., 2016; Nys et al., 2005; 2006) studies controlled for motor functioning, age and education, and were therefore considered to be 'well-controlled'.

All but one study (van Zandvoort et al., 2005) clearly explained and justified their planned statistical analyses. Except for Pählman et al.'s (2011) study, statistical tests were used appropriately. Although they selected appropriate statistical tests, Pählman et al. (2011) carried out large numbers (> 100) of comparisons. Patients without impairments on the MMSE, and tests of logical deductive ability, motor flexibility, apraxia and aphasia, and with impairments in sensory neglect, improved in BBS scores between discharge and one-year follow-up ($ps = 0.029 - p = 0.049$). However, they did not correct for multiple comparisons and these results may not have survived correction. In addition, the heterogeneous group and small sample means that many non-significant results may have been due to insufficient statistical power. Six studies used the 'stepwise' method of multiple regression (Jehkonen et al., 2000; Leśniak et al., 2008; Nys et al., 2005; 2006; Park et al., 2016; Saxena et al., 2007). This method is atheoretical and important variables can be discarded simply because of other variables already in the model, meaning that results obtained should be interpreted cautiously (Field, 2014).

All studies used valid and reliable outcome measures. However, van Zandvoort et al. (2005) observed ceiling effects on the Barthel Index (Mahoney & Barthel, 1965) and modified Rankin Scale. Jehkonen et al. (2000) and Sveen et al. (1996) removed the Frenchay Activities Index's 'gardening' item (Holbrook & Skilbeck, 1983), which was appropriate, as many participants did not have gardens.

There were several limitations associated with domain-general studies. For example, the AMT (Lees et al., 2013), MMSE (Nys, van Zandvoort, de Kort, Jansen, Kappelle, et al., 2005) and MoCA (Demeyere et al., 2016) have been shown to lack sensitivity to cognitive impairment following stroke. In addition, most measures were not designed for stroke and therefore may be confounded by highly prevalent problems in motor weakness, language and visuospatial abilities, not present in the original target population (e.g. dementia).

Statistical Power

No study reported on statistical power. Based on the number of predictors and the sample size (Cohen, 1992), it is likely that several studies were underpowered to find medium effects (e.g. Nys et al., 2005; van Zandvoort et al., 2005). In Pålman et al.'s (2011) study, the number of participants in different groups varied, so it is likely that power varied according to the comparisons undertaken.

The relationship between outcome and domain-general vs. domain-specific cognitive assessment

The first specific question was whether domain-general or domain-specific cognitive assessments have a more consistent relationship with chronic outcomes. Some domain-general studies, but not all, reported an association between cognitive performance and outcome. Only three (out of six) controlled for the confounding effects of motor functioning, age and education, but the relationship with outcome was inconsistent (Saxena et al., 2007; Wong et al., 2014; Zinn et al., 2004). Acute cognitive functioning predicted outcome in every domain-specific study, apart from van Zandvoort et al. (2005), which was rated the lowest quality (as ranked by Downs and Black's (1998) modified Quality Index (Ferro & Speechley, 2009)) and suffered from limitations relating to ceiling effects and low statistical power. Overall, outcome 6-12 months post-stroke had a more consistent relationship with domain-specific compared to domain-general cognitive assessment. Thus, although there were mixed results, one factor accounting for this appeared to be the type of cognitive assessment undertaken.

The relationship between outcome and individual cognitive domains

The second question that this review sought to answer was which cognitive domains are associated with outcomes 6-12 months post-stroke. Findings are discussed in terms of whether studies met our criteria for controlled or uncontrolled, depending on whether as motor functioning, age and education were not controlled for. It should be noted that, although some controlled studies measured activities none measured participation. Tasks assessing the following cognitive domains were found to be predictive of functioning at the level of activities and/or participation:

Apraxia: In one study, performance on a task of ideational apraxia predicted activities and participation but this study did not meet our definition of well-controlled (Sveen et al., 1996). In this study, ideomotor apraxia predicted participants' ability to use the telephone, to handle finances, and to administer medication but not scores on validated outcome measures (Sveen et al., 1996).

Tactile extinction: Performance on a task of tactile extinction was found to predict activities in one uncontrolled study (Rose et al., 1994).

Visuospatial perception/construction: In uncontrolled studies, performance on tasks of visuospatial perception/construction predicted activities (Sveen et al., 1996) and participation (Nys et al., 2005; Sveen et al., 1996) and predicted functioning at the level of activities in well-controlled studies (Nys et al., 2006; Park et al., 2016).

Visual memory: Functioning at the level of activities was predicted by performance on tasks of visual memory in three studies, all of which met our criteria for being well-controlled (Nys et al., 2005; 2006; Park et al., 2016).

Visual neglect: Impairments in unilateral visual neglect predicted activities in two studies that controlled for motor functioning, age and education (Nys et al., 2005; 2006). In an uncontrolled study visual neglect also predicted participation (Jehkonen et al., 2000).

Attention/Executive functioning: Impairments in attention/executive functioning predicted activity limitations (Leśniak et al., 2008; Nys et al., 2006) and predicted participation in one study classified as uncontrolled (Cumming et al., 2014).

Discussion

This review investigated whether acute cognitive impairment predicts chronic outcome at the level of activities and participation. Most included studies reported a relationship between acute cognitive impairment and chronic activities and participation. However, findings were mixed and one factor accounting for this appeared to be the type of cognitive assessment undertaken, as outcome 6-12 months post-stroke had a more consistent relationship with domain-specific compared to domain-general cognitive assessment. In well-controlled domain-specific studies, activities were predicted by performance on tasks of visuospatial perception/construction, visual neglect, visual memory and executive functioning.

The quality of studies varied but the studies from which the main conclusions were drawn, those rated as well-controlled, were rated as scoring $\geq 10/15$ on the quality appraisal checklist. There appeared to be no difference in overall rating of quality between well-controlled domain-general and domain-specific studies. Provisional evidence from several uncontrolled studies suggests that participation may be related to

apraxia, visuospatial perception/construction, visual neglect and attention/executive-functioning. However, as discussed, no well-controlled study investigated whether domain-specific cognitive functioning could predict participation, limiting the conclusions that can be drawn from this review about this relationship.

The results of this current review suggest acute cognitive impairment can predict levels of activities 6-12 months post-stroke. This has important clinical implications, as understanding cognitive difficulties as early as possible may be informative for professionals, clients and families, helping them to make necessary adjustments and plan interventions, particularly to overcome difficulties in the domains of visuospatial perception/construction, visual neglect, visual memory and executive functioning. In terms of clinical practice, although neuropsychological assessment can be time-consuming, several studies demonstrated that this was feasible (e.g. Nys et al., 2005; 2006; van Zandvoort et al., 2005), shorter tools have become available (particularly stroke-specific screening with the Oxford Cognitive Screen – Demeyere et al., 2015; 2016) and the current evidence provides greater support for domain-specific over domain-general cognitive assessment.

In contrast to previous findings that aphasia may predict activity limitations following stroke (Gialanella, 2011), the domains that predicted outcome were predominantly non-verbal. One could argue that this is because aphasic participants were excluded from five (Cumming et al., 2014; Pålman et al., 2011; Park et al., 2016; Nys et al., 2005; 2006) of the eleven domain-specific studies. However, in studies that did not exclude aphasic participants and measured performance on language tests, language impairments did not predict outcome (e.g. Sveen et al., 1996). Although Pålman et al. (2011) did report a relationship between aphasia and outcome, multiple comparisons were not corrected for, meaning that their finding may not have survived correction. Given that aphasia commonly follows stroke (Flowers, Silver, Fang, Rochon, &

Martino, 2013), future studies should use methods that are more inclusive for people with aphasia, such as the Oxford Cognitive Screen (Demeyere, Riddoch, Slavkova, Bickerton, & Humphreys, 2015).

It is not immediately obvious why these cognitive domains appeared so important to functioning. Cumming et al. (2014) suggested that visuospatial skills may represent a fundamental low-level process, upon which other cognitive functions depend. A similar argument may be made to explain why attention/executive functioning predicted activities. This is a fundamental high-level process responsible for coordinating other cognitive functions (Lezak et al., 2012). For example, Lezak et al. (2012) argue that executive impairments may have such a dramatic impact on functioning, as they can compromise the ability to strategically plan and perform cognitive tasks and monitor and evaluate performance. Dysfunction in attention/executive functioning has been found to be associated with poorer performance on tasks of visuospatial construction (Shin, Park, Park, Seol, & Kwon, 2006), visual and verbal memory (Duff, Schoenberg, Scott, & Adams, 2005) and visual neglect (Woods & Mark, 2007) and to mediate the association between functioning in daily life and performance in the domains of visuospatial/construction, attention, memory and language (O'Bryant et al., 2011). Thus, impairments in low-level visuospatial or high-level attention/executive processes may impact upon functioning both directly and indirectly, through disruption of other cognitive processes.

Methodological issues and implications for future research

Drawing conclusions from the available evidence is challenging, as only **half** of the studies reviewed controlled for important confounds. Further well-controlled research is needed to investigate whether domain-general cognitive assessment predicts chronic activities and participation in

other samples. This review also highlighted statistical problems in several studies. It is therefore important for future research to use and report statistical methods appropriately.

Further research is needed to establish why domain-general assessments had a less consistent relationship with outcome than domain-specific assessments did. One possibility is that impairments in key domains are not fully captured by existing domain-general assessment tools. For example, the AMT does not measure attention/executive functioning and, although the MMSE and MoCA include items that may recruit attention/executive functioning, previous studies have found that these instruments lack sensitivity to executive impairments (Chan et al., 2014; Nys, van Zandvoort, de Kort, Jansen, Kappelle, et al., 2005). In a recent review of the older adult literature, Overdorp et al. (2016) stated that an important question for future research will be whether scores on domain-general assessments and scores on tests of functioning in specific domains, such as attention/executive functioning, predict unique variance on outcome measures.

By coding outcome measures using the procedure set out by Cieza et al. (2005) it was possible to link outcome measured to the ICF framework. Outcome measures that were coded as measuring activities typically included concepts that linked to ICF codes such as: ‘washing oneself’ (e.g. BI; Mahoney & Barthel, 1965), ‘transferring oneself’ (e.g. BBS; Berg et al., 1992) and ‘eating’ (e.g. FIM; Uniform Data System for Medical Rehabilitation, 1993), whereas those coded as measuring participation linked to ICF codes such as: ‘economic self-sufficiency’ (e.g. Lawton IADL; Lawton & Brody, 1969), ‘informal social relationships’ (e.g. AQoL; Hawthorne, et al., 1999) and ‘acquiring, keeping and

terminating a job' (e.g. FAI; Holbrook & Skilbeck, 1983). Based on this, one might expect there to be a difference between the cognitive domains predictive of activities vs participation, for example, with participation being particularly affected by early difficulties in attention/executive-functioning. However, as no well-controlled domain-specific studies measured participation, such comparisons cannot be made until further research is undertaken. Although it was possible to identify outcome measures where the majority of meaningful concepts related to activities or participation, most measures included a mix of activities and participation (see Table 1). This is a limitation of most of the studies reviewed. Further work should investigate the link between acute cognitive impairment and outcome 6-12 months post-stroke using outcome measures that include a higher percentage of items relating to activities, such as the Barthel Index, or participation, such as the participation subscale of the Stroke Impact Scale (Duncan, Bode, Lai, & Perera, 2003), respectively.

Limitations of the review

Across studies, there was variability in which domains were assessed and the tests used to measure those domains. For example, executive dysfunction was associated with poorer outcome in four studies (Hanks et al., 2008; Leśniak et al., 2008; Pålman et al., 2011; Nys 2006) but this domain was not measured in three studies (Cumming et al., 2014; Jehkonen et al., 2000; Rose et al., 1994). Several authors had a theoretical rationale for focussing on specific domains (e.g. Cumming et al., 2014), however the variation across studies in the domains that were assessed makes interpretation difficult. Moreover, most studies attempted to distinguish between cognitive functions by designating some tests as measuring specific domains but this may have led to oversimplification. For example, some authors reported that poor outcomes were associated with impairments in visuospatial construction, when it is likely that their visuospatial construction tasks drew on both visuospatial and executive

processes (e.g. Park et al., 2016). It could also be argued that some cognitive domains were not found to predict outcome because they were not measured, or not measured sensitively enough. However, as shown in Table 2, across the domain-specific studies it appears that the major cognitive domains were assessed.

It is also important to acknowledge that the studies included in this review measured outcome 6-12 month post-stroke, which may not be reflective of outcome observed several years later. Although some authors have argued that functional recovery is complete after a period of 6 months (see Jørgense et al., 2000), there is evidence to suggest that functioning declines between 6 months and 5 years in some patients (Meyers et al., 2015) and contrastingly, other studies have reported ongoing improvements far past the 1 year mark (e.g. Holland et al., 2016) ~~others.~~

As discussed, the studies reviewed came from some Asian, European and Northern American cultures, meaning that the results may not directly apply to other countries, for example, due to differences in health care provision. Studies included patients with a narrow range of injury severity and several excluded older patients, non-native speakers or those with co-morbidities, limiting generalisability.

Conclusion

This review found evidence that acute cognitive impairment predicts activities 6-12 months post-stroke, even when controlling for confounding factors. This relationship was more consistent when domain-specific cognitive assessment was undertaken. This may be because key cognitive domains are not captured by several domain-general assessment tools. In well-controlled studies, visuospatial perception/construction, visual

memory, unilateral visual neglect and executive functioning predicted activities. However, no well-controlled study investigated whether domain-specific cognitive functioning could predict participation, limiting the conclusions that can be drawn about this relationship.

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Table 1. Average Rating of the Percentage of Concepts within Outcome Measures that link to ICF Domains.

Domain & Measure	Body Functions	Structures	Activities	Participation	Environmental	Personal	Uncategorised	ICC	95% CI
A: BI	0%	0%	96.97%	3.03%	0%	0%	0%	.97	.91 - .99
A: MRS	9.09%	0%	87.88%	3.03%	0%	0%	0%	.74	.25 - .93
A: BBS	0%	0%	81.82%	18.18%	0%	0%	0%	.92	.77 - .97
A: FIM	26.32%	0%	70.18%	3.51%	0%	0%	0%	.97	.94 - .99
A: SS QoL	37.41%	0%	40.14%	21.09%	0%	0%	2.04%	.92	.87 - .95
A: SF-36	28.21%	0%	32.82%	27.18%	0%	0%	11.29%	.99	.99 – 1.00
P: FAI*	0%	0%	33.33%	66.67%	0%	0%	0%	.69	.25 - .89
P: Lawton IADL	0%	0%	42.11%	57.89%	0%	0%	0%	.84	.65 - .93
P: AQoL	23.19%	0%	30.43%	36.23%	13.04%	0%	7.25%	.95	.90 - .98

Note: *Sveen et al. (1996) and Jehkonen et al. (2000) removed gardening items but most meaningful concepts still measured participation. A = activities, AQoL = Assessment of Quality of Life (Hawthorne, Richardson, & Osborne, 1999), BBS = Berg Balance Scale (Berg, Wood-Dauphinee, Williams, & Maki, 1992), BI = Barthel Index (Mahoney & Barthel, 1965), CI = confidence interval, FAI = Frenchay Activity Index (Holbrook & Skilbeck, 1983), FIM = Functional Independence Measure (Uniform Data System for Medical Rehabilitation, 1993), ICC = interclass correlations, Lawton IADL (Lawton & Brody, 1969), mRS = Modified Rankin Scale (Bonita & Beaglehole, 1988), P = participation,

SF-36 = 36-Item Short Form Health Survey (Ware & Sherbourne, 1992), SS QoL = Stroke Specific Quality of Life (Williams, Weinberger, Harris, Clark, & Biller, 1999).

Table 2: Study Characteristics and Key Results

Citation; Location	Participant Characteristics	Time of Cognitive Assessment	Cognitive Assessment	Outcome Measure	Method of Data Analysis	Key Findings
Zinn et al. (2004); USA.	Stroke. $N = 119$.	Days between stroke and enrolment: $M = 4.5$ ($SD = 2.5$). MMSE conducted before this.	MMSE.	6 months post-stroke Activities: FIM Participation: Lawton IADL.	Between- groups analyses using t-tests and multiple regression analyses.	Participants impaired on the MMSE scored lower on the FIM than those unimpaired. However, MMSE was not a significant predictor of FIM in the regression analysis. Participants impaired on the MMSE scored lower on the Lawton IADL. MMSE was a significant predictor of Lawton IADL.
Thommessen et al. (1999); Norway.	Stroke. $N = 104$. Ischemic: 100%.	Days post-stroke: $M = 10$.	MMSE.	12 months post-stroke Participation: FAI.	Analysis of variance and linear regression.	S FAI scores were higher for participants with higher MMSE scores. MMSE scores approached significance as a predictor of FAI scores ($p = .06$).

Citation; Location	Participant Characteristics	Time of Cognitive Assessment	Cognitive Assessment	Outcome Measure	Method of Data Analysis	Key Findings
Wong et al. (2014); Hong Kong.	Stroke. $N = 108$. Participants with MoCA scores <18 : $N = 24$, Age: $M = 60$ ($SD = 11$), 29% male. Severity: 79% mild (WFNS grade I or II). Participants with MoCA scores ≥ 18 : $N = 84$. Age: $M = 50$ ($SD = 10$), 32% male. Severity: 92% mild (WFNS Severity grade I or II).	2-4 weeks post-stroke.	MoCA.	1 year post-stroke Activities: mRS score of >2 . Participation: Chinese Lawton IADL scores of <15 .	Hierarchical logistic regression. RoC curves.	MoCA scores predicted mRS and Chinese Lawton IADL scores. MoCA scores distinguished between people with low and high scores on the mRS and Lawton but had low diagnostic accuracy.
Saxena et al. (2007); Singapore.	Stroke. $N = 141$. Age: $M = 71.5$ ($SD = 10.5$), 55% male, 85% ≤ 6 years of education. 88.6% Chinese, 7.8% Malays and 2.5% Indians. Severity: 84% 'mild-moderate' and 15.6% 'severe' (defined as NIHSS ≤ 12 and >12 , respectively). Ischemic: 86%. LH lesions: 48.9%, cortical lesions: 29.1%, subcortical lesions: 62.4%.	Days post-stroke: $M = 14.2$ ($SD 7.5$).	AMT.	6 months. Activities: BI.	Stepwise logistic regression.	Chronic BI scores were predicted by acute AMT scores.
Sveen et al. (1996); Norway	Stroke. $N = 74$. Age: $M = 75.3$ years (range 55-92), 53% males.	Days from admission: $M = 10$ ($SD = 1$). Stroke onset not more than 14 days prior to admission.	ASB.	12 months post-stroke Activities: BI. Participation: FAI.	Logistic multiple regression	BI and FAI predicted by ideational apraxia and visuospatial construction.

Citation; Location	Participant Characteristics	Time of Cognitive Assessment	Cognitive Assessment	Outcome Measure	Method of Data Analysis	Key Findings
Rose et al. (1994); Canada.	Stroke. $N = 26$. Age: $M = 73.64$; 46% male. LH lesions: 19%, RH lesions: 54%, BL lesions: 19%, brain stem infarcts: 8%.	1 month post-stroke.	RPM, WMS-R Visual Paired Associates, Line Bisection, Face-Hand Test.	6 months post- stroke Activities: FIM.	Hierarchical multiple regression. Step one: Performance on cognitive tasks Step two: Tactile extinction	Acute extinction on the left-hand side of the body was the only significant predictor of chronic FIM scores.
Leśniak et al. (2008); Poland.	Stroke. $N = 80$. Age: $M = 64.2$ ($SD = 9.9$); 60% male; years of education: $M = 11.3$ ($SD = 4.3$). Ischemic: 95%, LH lesions: 58.8%, RH lesions: 32.5%, BL lesions: 8.8%.	Days post- stroke: 7 – 14.	WAIS Similarities, TMT, phonemic fluency, go no-go test, as well as other ‘brief bedside neurological assessments’ described by Hodges (1994) and Strub and Black (2000), covering the domains of praxis, attention, orientation, perception, visuospatial function, memory and language.	1 year Activities: BI.	Stepwise multiple regression.	Chronic BI scores were predicted by executive dysfunction.
J. Park et al. (2016); South Korea.	Stroke. $N = 40$. Age: $M = 68.05$ ($SD = 10.17$), 50% male. Severity: Mild – moderate (NIHSS score: $M = 6.25$, $SD = 4.24$). Ischemic: 73%.	Days post- stroke: $M = 19.06$ ($SD = 5.17$). .	Korean BNT, Construction praxis test, Construction recall test, Korean semantic fluency, Korean MMSE.	6 months Activities: Korean mRS.	Stepwise logistic analysis. Five separate analyses using each cognitive task as a predictor variable.	Construction praxis and recall and MMSE predicted Korean mRS scores.

Citation; Location	Participant Characteristics	Time of Cognitive Assessment	Cognitive Assessment	Outcome Measure	Method of Data Analysis	Key Findings
Påhlman et al. (2011); Sweden.	Stroke. $N = 53$ but varied depending on comparison made.	Days post- stroke: 0 – 38.	MMSE, RPM, visual interpretation of pictures and objects, well-known faces and colours, WMS-R Logical Memory, Cronholm-Molander, draw mirror image of a cup, cube copying, cube counting, VOSP Silhouettes, stimulation of hands & visual fields, line bisection, TMT A, Stroop, I-Flex, praxis, neuropsychologist's judgement of speech fluency, auditory comprehension, anomia, paraphasia and reading and writing.	12 months Activities: BBS.	Mann– Whitney tests, Wilcoxon signed ranks tests and logistic regression.	MMSE scores did not predict improvement of balance. Participants with, compared to those without, acute impairments in executive functioning and deductive reasoning had poorer balance chronically. Participants whose balance improved were unimpaired on the MMSE, had sensory neglect and intact deductive reasoning, motor flexibility, apraxia and aphasia.

Citation; Location	Participant Characteristics	Time of Cognitive Assessment	Cognitive Assessment	Outcome Measure	Method of Data Analysis	Key Findings
Van Zandvoort et al. (2005); The Netherlands.	Stroke. $N = 27$. Did not differ to larger sample ($N = 57$) with respect to age ($M = 56$, $SD = 16$) or gender (54% males). Severity: Mild - moderate (only included those with mRS 2-4).	Days post-stroke: $M = 11.2$ ($SD = 6.7$).	WAIS Vocabulary, 12-item RPM, BNS, Dutch semantic & phonemic fluency, WAIS Digit Span, Corsi Block-Tapping Task, RAVLT, Doors Test, ROCF, JLO, Test of Facial Perception, TMT A & B.	Months post-stroke: $M = 20.9$ ($SD = 6.0$). Activities: BI, mRS and SF-36.	Linear regression.	Ceiling effects were observed on the BI and mRS. Performance on cognitive tests did not predict scores on the SF-36.
Cumming et al. (2014); Australia.	Age: $M = 75.5$ ($SD = 11.9$); 76% male. Severity: 79% mild, 21% moderate, 0% severe (Defined as NIHSS scores of 1-7, 8-15 and 16+, respectively). Only 26 and 24 completed simple and choice reaction time tasks, respectively.	Days post-stroke: $M = 5.4$ ($SD = 2.9$).	Simple and choice reaction time tasks from the CogState battery.	12 months post-stroke. Activities: mRS Participation: AQoL.	Correlation between mRS and simple and choice reaction times Two separate linear regression analyses using simple and choice reaction times as predictor variables and AQoL scores are the outcome variable.	MRS scores correlated with choice and simple reaction times. AQoL scores were predicted by faster choice, but not simple, reaction times.

Citation; Location	Participant Characteristics	Time of Cognitive Assessment	Cognitive Assessment	Outcome Measure	Method of Data Analysis	Key Findings
Nys, van Zandvoort, de Kort, van der Worp, et al. (2005); The Netherlands .	Stroke. $N = 111$. Age: $M = 60.1$ ($SD = 14.2$), 54.1% male, years of education: $Med = 9$. Severity: Mild (average NIHSS = 5). Ischemic: 90.1%, LH lesions: 43.8%, cortical lesions: 84.8%.	Days post- stroke: $M =$ 8.3 ($SD =$ 4.5).	RPM short form, WAIS-III Similarities, WAIS-III Block Design, RAVLT, WAIS-III Digit Span, Corsi Blocks, WMS Logical Memory, LLT, WMS Visual Reproduction, Token Test, BNT short form, Chapman Reading task, BIT Star Cancellation, Line Bisection, Brixton Spatial Anticipation Test, TEA Visual Elevator, phonemic and semantic fluency, Stroop, BADS Zoo test, JLO short form, Test of Facial Perception, ROCF.	Months from assessment: $M = 7.4$ (SD $= 1.3$). Activities: BI. Participatio n: FAI.	Step-wise multiple regression analyses.	Scores of <19 on the BI were predicted by impairments in visual memory or unilateral neglect. Scores of < 15 on the FAI were predicted by impairments in visuospatial perception/ construction.
Nys et al. (2006); The Netherlands .	Stroke. Subsample of cohort used by Nys et al., (2005). $N = 91$. Age: $M = 61.6$ ($SD =$ 13.2), 51.6% male, 41.8% 'high education'. Severity: 24.2% "mild" (defined as NIHSS ≤ 7). Ischemic: 92.3%, LH lesions: 42.5%, cortical lesions: 86.2%.	Days post- stroke: $M =$ 7.8 ($SD =$ 4.2).	See Nys et al. (2005).	Months from assessment: $M = 7.5$ (SD $= 1.3$). Activities SS-QOL.	Step-wise univariate and multivariate linear regression analyses.	SS-QOL scores were predicted by impairments in executive functioning, visuospatial perception/construc tion, visual memory and unilateral neglect.

Citation; Location	Participant Characteristics	Time of Cognitive Assessment	Cognitive Assessment	Outcome Measure
Jehkonen et al. (2000); Finland.	Stroke. Sample followed-up at 6 months: $N = 52$, Age: $M = 63.23$ ($SD = 10.23$), 63% male. Sample followed-up at 12 months: $N = 50$, Age: $M = 63.54$ ($SD = 10.38$), 64% male.	Days post-stroke: $M = 6.1$ ($SD = 1.97$).	BIT, WAIS-R Block Design, WMS Visual Reproduction, WMS Logical Memory.	6 and 12 months post-stroke. Participation: FAI.

Note: If information about the relevant subsamples' gender, education, severity, lesion location and laterality it is not presented it was missing. Abbreviations: AMT = Abbreviated Mental Test (Jitapunkul, Pillay, & Ebrahim, 1991), ASB = Assessment of Stroke and other Brain Damage (Sveen, Bautz-Holter, Wyller, & Ljunggren, 1994), BADS = Behavioural Assessment of the Dysexecutive Syndrome (B. A. Wilson, Alderman, Burgess, Emslie, & Evans, 1996), BIT = Behavioural Inattention Test (B. A. Wilson, Cockburn, & Halligan, 1987), BL = Bilateral, BNS = Boston Naming Test (Kaplan, Goodglass, & Weintraub, 1983), Brixton Spatial Anticipation Test (Burgess & Shallice, 1997), Cogstate (Darby, Maruff, Collie, & McStephen, 2003), construction praxis test (Lee et al., 2004), construction recall test (Lee et al., 2004), CNS = Canadian Neurological Scale, Corsi Block-Tapping Task (Kessels, van Zandvoort, Postma, Kappelle, & de Haan, 2000), Cronholm-Molander (Cronholm & Ottosson, 1963), cube copying (Wallin et al., 1996), cube counting (Christensen, 1984), Doors Test (Baddeley, Emslie, & Nimmo-Smith, 1994), Dutch semantic and phonemic fluency (Deelman, Koning-Haanst, & Liebrand, 1981), Face-Hand Test (Gordon et al., 1984), I-Flex = Investigation of Flexibility (Royall, Mahurin, & Gray, 1992), JLO = Judgement of Line Orientation Test (Benton, deS Hamsher, Varney, & Spreen, 1983), Korean BNT (Kim & Na, 1997), Korean Mini-Mental State Examination (J. H. Park & Kwon, 1991), Korean semantic fluency (Lee et al., 2004), Line Bisection Test (Schenkenberg, Bradford, & Ajax, 1980), LH = Left hemisphere, LLT = Location Learning Test (Bucks, Willison, & Byrne, 2000), M = Mean, Med = Medium, MMSE = Mini-Mental State Examination (Folstein et al., 1975), MoCA = Montreal Cognitive Assessment (Nasreddine et al., 2005), neuropsychologist's judgement of speech fluency (Fuller, 1999), NIHSS = NIH Stroke Scale (Brott et al., 1989), praxis (Fuller, 1999), RH = Right hemisphere, RPM = Raven Advanced Progressive Matrices (Raven, Raven, & Court, 1993), recognition of well-known faces and colours (R. S. Wilson, Kaszniak, Bacon, Fox, & Kelly, 1982), ROCF = Rey Osterrieth Complex Figure (Rey, 1941), RAVLT = Rey Auditory Verbal Learning Test (Schmidt, 1996), SD = Standard Deviation, SF-36 = 36-Item Short Form Health Survey (Ware & Sherbourne, 1992), Stroop (Stroop, 1935; Troyer, Leach, & Strauss, 2006), stimulation of hands (Heilman & Adams, 2003), stimulation of visual fields (Adams et al., 1999), TEA = Test of Everyday Attention (Robertson, Ward, Ridgeway, & Nimmo-Smith, 1994), Test of Facial Perception (Benton et al., 1983), token test (DeRenzi & Vignolo, 1962), Visual Discrimination Test (Benton,

Sivan, Hamsher, Varney, & Spreen, 1994), Visual interpretation of pictures and objects (Wallin et al., 1996), VOSP = Visual and Object Space Perception Battery (Warrington & James, 1991), WAIS = Wechsler Adult Intelligence Scale (Wechsler, 1955), WAIS-III = Wechsler Adult Intelligence Scale – Third edition (Wechsler, 1997), WFNS = World Federation of Neurosurgical Societies (Drake, 1988), WMS = Wechsler Memory Scale (Wechsler, 1945), WMS–R = Wechsler Memory Scale – Revised (Wechsler, 1987)

Table 3: Quality Appraisal of Included Studies

Citation	Reporting							External Validity		Internal Validity		
	Hypothesis	Outcome	Sample	Findings	Variance	P Values	Response Rate	Those Asked	Those Agreed	Location	Data-dredging	Statistical Tests
Saxena et al. (2007)	Y	Y	Y	Y	Y	N	Y	N	N	Y	Y	Y
Thommessen et al. (1999)	Y	Y	N	Y	Y	Y	N	N	N	N	Y	Y
Wong et al. (2014)	Y	Y	N	Y	Y	Y	Y	N	N	Y	Y	Y
Zinn et al. (2004)	Y	Y	N	Y	Y	Y	Y	N	N	Y	Y	Y
Park et al. (2016)	Y	Y	N	Y	Y	Y	N	N	N	Y	Y	Y
Påhlman et al. (2011)	Y	Y	N	Y	Y	Y	Y	N	N	Y	Y	N
Cumming et al. (2014)	Y	Y	N	N	N	Y	Y	N	N	Y	Y	Y
Jehkonen et al. (2000)	Y	Y	N	Y	Y	Y	Y	N	N	Y	Y	Y
Leśniak et al. (2008)	Y	Y	Y	Y	Y	N	Y	N	N	Y	Y	Y
Nys et al. (2005)	Y	Y	Y	Y	Y	Y	Y	N	N	Y	Y	Y
Nys et al. (2006)	Y	Y	Y	Y	N	N	Y	N	N	Y	Y	Y
Rose et al. (1994)	Y	Y	N	N	N	N	N	N	N	Y	Y	Y
Sveen et al. (1996)	Y	Y	N	Y	N	Y	Y	N	N	Y	Y	Y
van Zandvoort et al. (2005)	Y	Y	N	N	Y	N	N	N	N	N	N	Y