5. Rehabilitation of Cognitive Impairment Post Stroke

Robert Teasell MD, Norhayati Hussein MD, Marcus Saikaley BSc, Jerome Iruthayarajah MSc, Mitchell Longval BSc

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5.1 The Nature of Cognitive Impairment Post Stroke

Post stroke cognitive impairment (CI) is common but remains underdiagnosed and carries a poor prognosis (Godefroy et al. 2011). Some form of cognitive impairment is observed in 40-70% of stroke patients (Godefroy et al. 2011). At three months, 1, 2 and 3 years post stroke, the prevalence rates of cognitive impairment were 39%, 35%, 30% and 32% respectively (Pater et al. 2003).

Cognitive impairments are generally divided into various domains which include:

- Attention
- Memory
- Executive function
- Perception and praxis
- Language

Attention	•Focus attention, sustained attention, selective attention, divided attention
Memory	•Visual memory, auditory memory, working memory, eispodic memory, semantic memory, working memory, procedural memory
Executive Function	•Initiation, processing speed, problem solving, planning
Perception, praxis	•Visuo-spatial, visuo-perceptual, Unilateral neglect, inattention, apraxia, agnosia, prosopagnosia
Language	•Aphasia: Broca's, Wernicke's,transcortical motor/sensory or mixed, conductive, global

Cognition includes multiple domains (Sachdev et al. 2014; Cummings et al. 2013):

- Attention, which can be broadly defined as focusing, shifting, dividing, or sustaining attention on a particular stimulus or task.
- Executive function which is involved in planning, abstract thinking, organization of thoughts, inhibition and conflict monitoring.
- Visuospatial ability which describes one's aptitude to visual search or scan for information, to draw or recreate visual images, and mentally manipulate objects two- and three-dimensional objects.
- Learning and memory describes one's ability to recall and recognition of visual and verbal information, be it episodic or semantic.

- Language which is the ability to express and be receptive of oneself through language through writing and reading comprehension.
- Social cognition which is the recognition of one's own and other's emotional state, and an understanding of the theory of mind.

Importantly these domains are not independent of each other.

5.2 Vascular Cognitive Impairment

5.2.1 Definition of Vascular Cognitive Impairment (VCI)

VCI encompasses a wide range of cognitive deficits, from relatively Mild Cognitive Impairment of Vascular Origin (VaMCI) to Vascular Dementia (VaD), the most severe form of VCI. **VCI** is a syndrome with cognitive impairment affecting **at least one cognitive domain** (e.g., attention, memory, executive function, perception or language) with **evidence of clinical stroke or subclinical vascular brain injury.**

Vascular cognitive impairment (VCI) refers to a heterogenous group of conditions (including: mild neurocognitive disorder, dementia, vascular dementia and mixed dementia) in which vascular lesions cause or contribute to impaired cognitive function (Barbay et al. 2017). Currently, there are three terms used to describe VCI.

- VCI-no dementia (VCI-ND) describes individuals *"whose symptoms are not associated with substantial functional impairment, including a high proportion with subcortical ischemia with cognitive impairment of presumed vascular cause"* (Moorhouse & Rockwood, 2008).
- Vascular dementia is defined as a loss of cognitive function resulting from ischemic, hypoperfusive, or hemorrhagic brain lesions due to cerebrovascular disease or cardiovascular pathology (Roman, 2003) and includes disorders that are in the original vascular dementia construct, such as post-stroke dementia and multi-infarct dementia (Moorhouse & Rockwood, 2008).
- Mixed dementia describes the "presentation of individuals with clinical, and commonly neuro pathological, features of Alzheimer's disease and vascular dementia" (Moorhouse & Rockwood, 2008).

Clinical presentation of VCI commonly includes decreased executive functioning, mental slowing, and impairment of goal formulation, initiation, planning, organizing, sequencing, executing, abstracting and attention (Lesniak et al. 2008; Roman 2003; Srikanth et al. 2003; Desmond et al. 1999; Looi & Sachdev 1999; Hochstenbach et al. 1998). Memory, however, may be relatively preserved (Roman 2003; Desmond et al. 1999; Looi & Sachdev 1999). In a study of elderly residents, Rao et al. (1999) found that individuals with VCI displayed significantly poorer performance than controls on abstract thinking, attention, calculation, language, memory, orientation, perception, praxis, and Mini Mental State Examination (MMSE) scores.

As suggested by Rockwood et al. (2000), the concept of VCI-ND is useful in identifying patients with stroke at risk for developing vascular dementia. Ballard et al. (2003; 2002) reported that a third of elderly stroke survivors who were free of dementia at 3 months post-stroke met the criteria for VCI-ND. Compared to

elderly controls, the stroke survivors with VCI-ND had greater impairments of attention and executive function but had preservation of memory compared to those with dementia.

5.2.2 Characteristics of Cognitive Deficits in VCI

The pattern of cognitive deficits in VCI may include variable degree of deficits in any of the cognitive domains, including focal stroke syndromes. Cumming et al. (2013) notes that, *"It is now thought that stroke tends to have greater deleterious impact on attention and executive function than on memory".*
In a community-based comparison of stroke patients with population controls, stroke patients were **more frequently impaired than controls in spatial ability, executive function, attention and language but were not more impaired in orientation or memory** (Srikanth et al. 2003, Cumming et al. 2013). Cumming et al. (2013) noted that, *"Cognitive slowing is a common complaint after stroke, and a majority of patients exhibit marked slowness of information processing (Hochstenbach et al. 1998; Rasquin et al. 2005). Processing speed is clinically relevant, as it makes an independent contribution to functional outcome after stroke (Barker-Collo et al. 2010) and is independently predictive of dependency in stroke survivors (Narasimhalu et al. 2011)".* Cumming et al. (2013) also noted that, *"It is possible that attention and executive deficits appear to predominate after stroke these domains are more often tested using time-sensitive tasks (e.g., Trail-Making and verbal fluency) than the domains of memory or language".*

Conclusions
Vascular cognitive impairment (VCI) is the current term that reflects the range of cognitive deficits due to the impact of cerebrovascular disease, including stroke.
VCI without dementia reflects deficits in one or more domains not severe enough to cause functional decline, reflecting a single strategic lesion or multiple infarcts that impact functional activities.
Impairments of attention, executive function, and processing speed appear to be a consistent pattern of deficits in all subtypes.
Since 30% of all stroke survivors progress to a dementia syndrome, more research is needed to identify biomarkers for those at risk.

5.2.3 Vascular Pathology in VCI

Cognitive impairment seen in VCI result from a range of vascular pathology, including multiple cortical infarcts, multiple subcortical infarcts, "silent" infarcts, small-vessel disease with white matter lesions (leukoaraiosis) and lacunae, and brain hemorrhage. Cumming et al. (2013) notes that, *"There is a broad distinction between focal damage, which can lead to selective cognitive impairments, and diffuse neuronal dysfunction, which produces a more uniform profile of mental slowing, memory problems and executive deficits (de Haan et al. 2006) … Diffuse dysfunction typically results from underlying sub-clinical cerebrovascular disease, such as white matter disease, or an accumulation of small infarcts as in small-vessel disease (Pantoni 2010). Over the four years following a stroke, higher load of white matter hyperintensities (WMHs) is strongly associated with dementia and cognitive decline (Dufouil et al. 2009). Stroke patients with white matter lesions and silent infarcts were worse on cognitive tasks at baseline and two-year follow-up than those without this damage (Rasquin et al. 2005)".*

Conclusion
The severity of white matter change is associated with poorer cognitive performance and increasing limitations in activities of daily living post stroke.

5.2.4 Impact of Vascular Cognitive Impairment

It has been suggested that cognitive abilities such as abstract thinking, judgment, short-term verbal memory, comprehension and orientation are important in predicting the stroke survivor's functional status at discharge (Jongbloed, 1986; Mysiw et al., 1989; Tatemichi et al., 1994). Reduced cognition has been associated with a decreased ability to perform activities of daily living (ADL), with poorer physical functioning at discharge and with a greater likelihood of mortality within 1 year of discharge (Arfken et al. 1999; Prencipe et al. 1997; Desmond et al. 2000; Lin et al. 2003; Claesson et al. 2005; Leys et al. 2005; Hinkle 2006; Cederfeldt et al. 2010; Lichtenberg et al. 1994; Tatemichi et al. 1994; Ruchinskas & Curyto 2003). Narasimhalu et al. (2011) found post-stroke cognitive impairment to be predictive of dependency and Zinn et al. (2004) reported fewer discharges home among patients with cognitive impairment than among cognitively intact patients (85.9% vs. 93.4%, p=0.07). A recent 15-year longitudinal study found that, on average, the relative risk of disability following stroke was twice as high for those with cognitive impairment than in those without: 3-month RR=2.4, 95%CI 1.93-3.08; 1-year RR=1.9, 95%CI 1.38-2.6; 5-year RR=1.8, 95%CI 1.27-2.55 (Douiri et al., 2013).

Although the presence of cognitive impairment may be associated with decreased ADL function, it has been demonstrated that it is not a significant predictor of ADL function at 6 months post-stroke (Zinn et al., 2004). Rather, instrumental function may be more severely impacted by the presence of cognitive ability. At 6 months post-stroke, the presence of cognitive impairment was associated with and predictive of decreased instrumental ADL (IADL) function (Zinn et al., 2004). Similarly, Mok et al. (2004) determined that higher levels of cognitive impairment post-stroke were associated with greater deficits in IADL function and greater levels of pre-stroke cognitive decline. Identified predictors of IADL performance were stroke severity, executive dysfunction, age and pre-stroke cognitive decline (Mok et al., 2004). Patients with cognitive impairments may require more therapy over a longer period of time (Zinn et al., 2004). In addition, participation in rehabilitation may be adversely affected by the presence of attention and executive dysfunction (Robertson et al., 1997; Skidmore et al., 2010). However, this is associated with greater expenditure of healthcare resources (Claesson et al. 2005).

VCI affects functional abilities. It is often associated with depression which can also affect functional abilities. VCI is often associated with depression. VCI can result in higher mortality rate, 2-6 times higher among those with post-stroke dementia, after adjusting for stroke severity, stroke recurrence, co-morbid cardiac disease and demographic factors (Leys et al. 2005).

Conclusion
Cognitive impairment is associated with decreased ADL and IADL function, and patients may require longer-term, ongoing rehabilitation.

5.2.5 Prevalence of Dementia Post-Stroke

As many as two-thirds of stroke patients go on to experience cognitive impairment or decline following stroke. Risk of developing dementia may be 10x greater among individuals with stroke than those without stroke. The presence of white matter changes (leukoaraiosis) is related to development of dementia. The LADIS study (2011) reported that severe white matter changes pose a 3-fold risk of developing dementia independent of age and sex. Independent predictors of post-stroke dementia were older age, lower education, history of stroke, diabetes, atrial fibrillation, stroke severity and existing cognitive impairment. (Pendlebury & Rothwell 2009) Additionally, the above risk factors as well as cerebral amyloid angiopathy,

low physical activity, HTN, both hyper- and hypoglycemia, smoking, and carotid and intracranial atherosclerosis have been correlated with an increased risk of VCI (Farooq & Gorelick 2013, Pendlebury & Rothwell 2009). The above risk factors as well as cerebral amyloid angiopathy, low physical activity, HTN, both hyper- and hypoglycemia, smoking, and carotid and intracranial atherosclerosis have been correlated with increased risk of VCI (Farooq & Gorelick 2013). 10% have existing dementia at the time of stroke, 10% develop dementia after first-ever stroke, and approximately one-third of patients experience dementia following recurrent stroke (Pendlebury & Rothwell 2009).

Conclusions
Following stroke, as many as two-thirds of patients experience cognitive impairment or decline.
The presence of cognitive impairment is associated with a substantial increase in risk for dementia.
Risk for developing dementia may be up to 10 times greater among individuals with stroke than for those without.
At the time of stroke, 10% of patients may have existing dementia. Another 10% may develop dementia shortly after a first-ever stroke. More than 33% of patients may experience dementia after a recurrent stroke.

5.3 Vascular Cognitive Impairment Recovery

5.3.1 Natural Course of Vascular Cognitive Impairment

While cognitive decline may continue post stroke, approximately 16-20% of patients with cognitive impairment improve. While most improvements occur in the first 3 months, recovery may continue for at a minimum the first year post-stroke. There appears to be domain -specific trend in the prevalence and the temporal evolution of the stroke -related cognitive impairment (Hurford et al. 2013). Attention and speed was the most impaired domain at < 1 month after stroke, but had the greatest trend for decreasing impairment, from 72.4% acutely to 37.9% after 3 months ($p<0.01$). Perceptual skill impairment showed a high prevalence of impairment in the acute stage (29.5% impaired, 95% CI: 21.8 to 38.1) but a strikingly lower prevalence of impairment at 1 month (9.5%, 95%CI: 2.7 to 22.6) and 3 months (8.1%, 95% CI: 1.7 to 21.9; $p=0.002$). Cumming et al. notes that, *"At one year poststroke, a majority of patients still had attention deficits, while deficits in language and memory were more likely to have resolved (2013)".* Mortality rates among stroke patients with dementia are 2-6x greater than those without.

Conclusions
While cognitive decline may progress post stroke, approximately 16-20% of patients with cognitive impairment improve.
While most improvements occur in the first three months, recovery may continue for the first year post stroke.
The presence of post-stroke cognitive impairment has been associated with a 3-fold increase in risk for mortality.
Mortality rates among patients with stroke and dementia are 2 to 6 times greater than among those without dementia.

5.3.2 Diagnosis of Vascular Cognitive Impairment

The clinical diagnosis of VCI are based on clinical assessment of the cognitive domains of attention, executive function, memory, visuospatial function and language.

Classification of VaMCI and VaDementia

	Mild Vascular Cognitive Impairment (VaMCI)	**Vascular Dementia (VaD)**
The classification of VaMCI and VaD must be based on cognitive testing. A minimum of 4domains should be assessed: executive /attention, memory, visuospatial function, language	Decline in cognitive function from prior baseline and impairment performance in **at least 1 cognitive domain.**	Decline in cognitive function from prior baseline and impairment performance in **at least 2 cognitive domains.**
Function	Instrumental ADLs may be **normal or mildly impaired**; independent of motor and sensory deficits.	ADLs sufficiently **severely impaired**; independent of motor and sensory deficits.
Other related categories	Probable VaMCI * Possible VaMCI* Unstable VaMCI*	Probable VaD* Possible VaD*

*Detailed diagnostic criteria: Refer to Gorelick et al. (2011)

5.3.3 Vascular Dementia

Vascular dementia is the second most common cause of dementia after Alzheimer's disease. It is often confused with Alzheimer's Dementia, and the two may even co-exist. The distinguishing features of vascular dementia versus Alzheimer's disease are as below.

Vascular Dementia vs. Alzheimer's Dementia

Characteristic	**Vascular Dementia**	**Alzheimer's Disease**
Onset	Sudden or gradual	Gradual
Progression	Slow, stepwise fluctuation	Constant insidious decline
Neurological findings	Evidence of focal deficits	Subtle or absent
Memory	Mildly affected	Early and severe deficit
Executive function	Early and severe	Late
Dementia Type	Subcortical	Cortical
Neuroimaging	Infarcts or white matter lesions (leukoraiosis)	Normal; hippocampal atrophy
Gait	Often disturbed early	Usually normal

Cardiovascular history	TIAs, strokes (including covert/silent stroke), vascular risk factors	Less common

Cognitive Syndrome of Post-Stroke Vascular Dementia (Kalaria and Ballard 2001)

- Occurs in up to 30% of patients with stroke
- Progresses slowly
- Predominantly executive function
- Subcortical and frontal lobe functions are affected
- Memory and language deficits are less obvious
- Late stage memory deficits and dementia

Memory Function Post Stroke

Studies have shown that patients with vascular dementia had superior long-term memory but suffered from more frontal executive impairment when compared to Alzheimer's patients (Looi and Sachdev 1999). However, memory is not necessarily spared after a stroke or in patients with a diagnosis of vascular cognitive impairment. Cumming et al. (2013) notes that, *"The presence of sub-cortical infarcts in older people has been associated with lower episodic, semantic, and working memory performance (Schneider et al. 2007). Memory deficits, though, appear to be less prevalent than deficits in other cognitive domains, and when they do occur, they are likely to have a different genesis to those seen in Alzheimer patients, Recognition memory, which tests retention of information without effortful search and retrieval, may be less affected than non-cued recall after stroke (Hochstenbach et al. 1998; Sachdev et al. 2004), suggesting that the underlying cause may be less amnestic and more executive".*

Conclusions

At present, there is no gold standard for the diagnosis and assessment of VCI.
Harmonized standards for brief and more extensive testing protocols have been developed for clinical and research use.

5.4 Screening and Assessment of Cognitive Impairment Post Stroke

Many of the existing cognitive screening tools were developed for dementia and are weighted towards memory and orientation (e.g., the Mini-Mental State Examination) (Folstein et al. 1975). The Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MOCA) are two of the most commonly employed screening instruments fro detecting CI post stroke.

Category	Rationale	Individual Assessment Tools
Attention	These outcome measures assessed an individual's ability to attend as well as identify target stimuli and remain focused on a particular goal.	• Attentive Matrices Test • Charron Test • Colour Trails Test • Continuous Performance Task (CPT • EEG Signal Detection • Ruff 2 & 7 Selective Attention Test • Schulte's Tests

		• Symbol Digit Substitution Test (Symbol Digit Modalities Test) • Talking-While-Walking Test • Test of Everyday Attention (TEA) • Trail-making Test A • Useful Field of View
Executive function	These outcome measures assessed an individual's ability to plan, follow rules and self-monitor.	• Controlled Oral Word Association Test (COWAT) • Categorical Word Fluency (Verbal Fluency Test) • Corsi Block Tapping (Block Span) Test (Backwards) • Digit Span Test (Backward) • Flanker Task • Frontal Assessment Battery (FAB) • Go/No-Go Task • Stroop Interference Test • Tower of London Test • Trail-making Test B • Verbal Fluency Test • Wisconsin Card Sorting Task
Learning and Memory	These outcomes measures assessed an individual's ability to explicitly and implicitly learn and recall information.	• 10-word recall test (RBANS) • California Verbal Learning Test (CVLT) • Claeson-Dahl Test • Corsi Block Tapping (Block Span) Test (Forward) • Delayed Recognition Span Test (DRST) • Digit Span Test (Forward) • Fuld Object-Memory Evaluation (FOME) • Memory Interference Tasks • Oxford Recurring Faces Test • Paced auditory serial addition test (PASAT) • Paired Associates Test • Rey Auditory Verbal Learning Test • Rivermead Behavioural Memory Test • Serial Reaction Time Task • Stroke Impact Scale (Memory Subsection) • Stylus Maze Task • Wechsler Memory Scale (WMS) • Word List Recall/Delayed Recall Test • Word List Memory Test • Word List Recognition Test
Global Cognition	These outcome measures assessed an individual's overall cognitive processing capability factoring in multiple domains.	• Abbreviated Mental Test • Clock Drawing Test • Addenbrooke's Cognitive Examination (ACE) • Alzheimer's Disease Assessment Scale, Cogntitive (ADAS-COG) • Category Test (from the Halstead-Reitan Neuropsychological Test Battery) • Cognitive Capacity Screening Examination (CCSE) • Cognitive Failures Questionnaire (CFQ)

		• Functional Independence Measure Cognitive Subscale (FIM-Cog) • Global Deterioration Scale • Loewenstein Occupational Therapy Cognitive Assessment-Geriatric (LOTCA-G) • Mini Mental Status Examination (MMSE) • Montreal Cognitive Assessment (MoCA) • Raven's Progressive Matrices • Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) • Wechsler Adult Intelligence Scale (WAIS)
Visuospatial perception and orientation	These outcome measures assessed an individual's ability to correctly process and mentally manipulate visuospatial information.	• Benton's Temporal Orientation • Benton Visual Retention Test • Money Road Map Test • Motor-Free Visual Perception Test (MVPT) • Rey-Osterrieth Complex Figure Test • Toulouse-Pieron Test
Amusia	These outcome measures assessed an individual's ability to perceive pitch and recognize music.	• Montreal Battery of Amusia
Activities of Daily Living	These outcome measures assessed an individual's proficiency at performing everyday activities.	• Alzheimer's Disease Cooperative Study, ADLs (ADCS-ADL) • Alzheimer's Disease Functional Assessment and Change Scale (ADFACS) • Barthel Index (BI) • Disability Assessment for Dementia (DAD) • Functional Independence Measure (FIM) • Lawton Instrumental Activities of Daily Life Scale • Stroke Impact Scale (ADL Subsection)

5.4.1 Attention

Attention, which can be broadly defined as focusing, shifting, dividing, or sustaining attention on a stimulus or task.

Trail-making Test A

The Trail Making Test A is a neuropsychological instrument often used in patients with suspected cognitive impairment to measure the cognitive domains of processing speed, sequencing, mental flexibility, and visual-motor skills. The most widely used version comprises of 2 parts: A and B. In part A, the patient uses a pencil to connect a series of 25 encircled numbers in numerical order. In part B, the patient connects 25 encircled numbers and letters in numerical and alphabetical order, alternating between the numbers and letters. The primary variable of interest is the total time to completion for parts A and B, which is used to obtain a ratio of total time to complete part B/A for all trials. A lower value (closer to 1.0) is indicative of

better performance. Part A of the measure is thought to be a test of visual search and motor speed skills, whereas part B is considered also to be a test of higher-level cognitive skills such as mental flexibility. The measure has excellent construct validity and interrater reliability; however, it may be susceptible to practice effects at shorter intervals (Bowie & Harvey 2006; Piper et al. 2015).

5.4.2 Executive Function

These outcome measures assessed an individual's ability to plan, follow rules and self-monitor. Executive function is involved in planning, abstract thinking, organization of thoughts, inhibition and conflict monitoring.

Trail-making Test B

Trail-making Test B is a neuropsychological instrument often used in patients with suspected cognitive impairment to measure the cognitive domains of processing speed, sequencing, mental flexibility, and visual-motor skills. The most widely used version comprises of 2 parts: A and B. In part B, the patient connects 25 encircled numbers and letters in numerical and alphabetical order, alternating between the numbers and letters. The primary variable of interest is the total time to completion for parts A and B, which is used to obtain a ratio of total time to complete part B/A for all trials. A lower value (closer to 1.0) is indicative of better performance. Part A of the measure is thought to be a test of visual search and motor speed skills, whereas part B is considered also to be a test of higher-level cognitive skills such as mental flexibility. The measure has excellent construct validity and interrater reliability; however , it may be susceptible to practice effects at shorter intervals (Bowie & Harvey 2006; Piper et al. 2015).

5.4.3 Learning and Memory

These outcomes measures assessed an individual's ability to explicitly and implicitly learn and recall information.

Rivermead Behavioural Memory Test

The Rivermead Behavioural Memory Test is a test used to evaluate memory abilities when performing everyday tasks. The test consists of 11 subtests that assess verbal and visual recognition and recall, learning and recall of instructions, and recall of a spatial root. Subtests include remembering a name, belonging, appointment, pictures, story (immediate and delayed), faces, route (immediate and delayed), message, orientation, and date. All subtests use simple, everyday items. The test has been validated in a stroke population (Man et al. 2009).

Stroke Impact Scale (Memory Subsection)

The Memory Subsection of the Stroke Impact Scale is a patient-reported measure of multi-dimensional stroke outcomes. The measure consists of 59 functional tasks (e.g. dynamometer, reach and grab, walking, reading out loud, rating emotional regulation, word recall, number of tasks completed, and shoe tying). These tasks are then divided into 8 distinct subscales which include: strength, hand function, mobility, communication, emotion, memory, participation and activities of daily living (ADL). Each task is measured on a 5-point scale (1=an inability to complete the task, 5=not difficult at all). The measure has been shown to have good reliability and validity (Mulder et al. 2016; Richardson et al. 2016).

Wechsler Memory Scale (WMS)

The WMS is a measure designed to provide a rapid, simple and practical memory examination. The original scale was developed in 1945 by Wechsler, however there have been many revisions since, including WMS-R, WMS-III, and WMS-IV. The current edition, WMS-IV, consists of 7 subtests: spatial addition, symbol span, design memory, general cognitive screener, logical memory (I & II), verbal paired associates (I & II), and visual reproduction (I & II). A subject's performance is reflected in 5 "Index" scores: auditory memory, visual memory, visual working memory, immediate memory, and delayed memory. The logical memory subtest of the WMS is the most frequently used subtest and has an immediate (I) and delayed (II) condition. The test consists of two stories/paragraphs that are orally presented to the subject at a conversational pace. The subject is then asked to recall as much of the stories as possible, immediately (LM I), and again after 25-35 minutes (LM II). All relevant utterances and thematic units are then scored. The WMS has demonstrated high internal consistency and reliability overall, and within the logical memory subtest, with each newer version showing stronger psychometric properties (Morris et al. 2014; Gerhart 2005).

5.4.4 Visual Perception and Orientation

These outcome measures assessed an individual's ability to correctly process and mentally manipulate visuospatial information.

Motor-Free Visual Perception Test (MVPT)
The MVPT is a measure of visual- perceptual ability independent of motor ability. Spatial relationships, visual discrimination, figure-ground, visual closure and visual memory are assessed. A total raw score is obtained based on the number of correct responses and standard score, percentile rank and age-equivalent score are generated. In the current version (MVPT-4), the test contains 45 items. The MVPT exhibits acceptable construct, content and criterion validity as well as good test-retest reliability and internal consistency (Brown & Peres, 2018).

Rey-Osterrieth Complex Figure Test
The Rey-Osterrieth Complex Figure Test is a measure of visuo-spatial abilities and visual memory. The test requires the subject to copy a complex geometrical figure and, after an interval, reproduce the figure from memory without forewarning. The most used method of scoring the test is the Osterrieth method, a scoring system that provides a 36-point summary score based to the presence and accuracy of 18 units of the figure. The test has been shown to have excellent interrater reliability and good discriminant validity in differentiating healthy controls from patients with Parkinson's disease, OCD, ADHD, schizophrenia, alcohol abuse, and traumatic brain injury (Salvadori et al. 2018).

5.4.5 Global Cognition

These outcome measures assessed an individual's overall cognitive processing capability factoring in multiple domains.

Clock Drawing Test
The Clock Drawing Test s a very brief screening tool used to detect cognitive impairment. It can also detect neglect and executive dysfunction. Participants are asked to draw a clock along with numbers and hands denoting a specified time. There are multiple different rating systems, with most classifying the number

and type of errors made. The test is valid and reliable as a screening tool, with a high sensitivity and specificity (Duro et al, 2018; Sheehan, 2012).

The Clock-Drawing Test

Questions	Answer
What does it measure?	The CDT provides a quick assessment of visuospatial and praxis abilities and may detect deficits in both attention and executive dysfunction (Adunsky et al. 2002; Suhr et al. 1998; McDowell & Newell 1996).
What is the scale?	The CDT involves having the patient draw a clock, place the numbers on the clock in their proper positioning and then place the arms of the clock at a requested time. The task itself is viewed as being highly complex, involving a number of neuropsychological abilities (Suhr et al. 1998).
What are the key scores?	Numerous scoring systems for the CDT have been suggested, ranging from simple to complex as well as from quantitative to qualitative. In general, however, they all evaluate errors and/or distortions in the form of omissions of numbers and errors in their placement such as perseverations, transpositions, and spacing (McDowell & Newell 1996).
What are its strengths?	The CDT is brief, inexpensive and easy to administer. The CDT may help to create a more complete picture of cognitive function when it is used with other assessment tools (Ruchinskas & Curyto 2003; McDowell & Newell 1996; Suhr & Grace, 1999). Despite different scoring systems, The CDT has demonstrated acceptable levels of reliability and has been shown to correlate highly with other cognitive screening measures. (Scanlan et al. 2002; Ruchinskas and Curyto 2003; McDowell and Newell 1996).
What are its limitations?	Like most other neuropsychological screening measures, the CDT is negatively influenced by increasing age, reduced education and the presence of depression (Ruchinskas & Curyto 2003; Lorentz et al. 2002). The CDT may also be affected by visual neglect, hemiparesis and motor dis-coordination (Ruchinskas & Curyto 2003). The most effective use of the CDT may be as a supplement to other cognitive assessments rather than as the sole, independent screening device for cognitive impairment (McDowell & Newell 1996). For example, it is an effective supplement to the MMSE and the CAMCOG.

Functional Independence Measure Cognitive Subscale (FIM-Cog)

The FIM-Cog is an 18-item outcome measure composed of both cognitive (5-items) and motor (13-items) subscales. Each item assesses the level of assistance required to complete an activity of daily living on a 7-point scale. The summation of all the item scores ranges from 18 to 126, with higher scores being indicative of greater functional independence. This measure has been shown to have excellent reliability and concurrent validity in its full form (Granger et al. 1998, Linacre et al. 1994; Granger et al. 1993).

Mini Mental Status Examination (MMSE)

The MMSE is a brief screening tool and quantitative assessment of cognitive impairment. It is one of the most commonly used instruments for this purpose. The exam consists of 11 questions/tasks in 7 cognitive domains: 1) orientation to time; 2) orientation to place; 3) registration of 3 words; 4) attention and calculation; 5) recall of 3 words; 6) language; and 7) visual construction. The test is scored out of 30

possible points, with a score between18 to24 denoting mild impairment and a score between 0 to17 denoting severe impairment. The test has been found to be valid as a screening tool, and is sensitive for detecting moderate/severe impairment, but not mild impairment. It has good interrater reliability. The MMSE is appropriate for screening for post-stroke cognitive impairment (Bour et al. 2010; Tombaugh & McIntyre, 1992; Dick et al. 1984).

Although the MMSE is the most widely used screening tool for CI, its greatest limitation is **lack of sensitivity in identifying small changes in cognitive impairment**. Individuals who meet criteria for mild cognitive impairment can score in normal range on MMSE. MMSE has been shown to be insensitive to conditions associated with frontal-executive and subcortical dysfunction and to milder forms of cognitive impairment (Pendlebury et al. 2010).

Mini-Mental State Examination

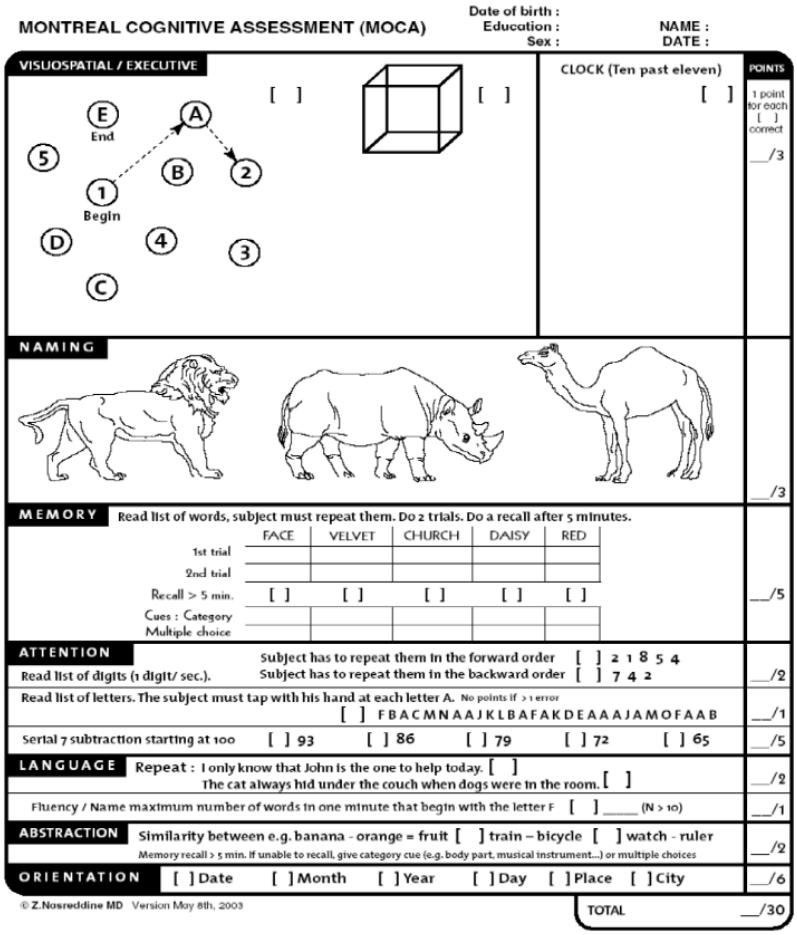
Questions	Answer
What does it measure?	The MMSE is a brief screening tool that provides a quantitative assessment of cognitive impairment (Folstein et al. 1975).
What is the scale?	The MMSE consists of 11 simple questions or tasks, typically grouped into 7 cognitive domains: orientation to time, orientation to place, registration of three words, attention and calculation, recall of three words, language and visual construction.
What are the key scores?	The test yields a total score of 30, with a score of 23 or less generally accepted as the cut-off score indicating the presence of cognitive impairment (Dick et al. 1984). Levels of impairment have also been classified as none (24-30); mild (18-24) and severe (0-17) (Tombaugh and McIntyre 1992).
What are its strengths?	Only requiring 10 minutes to complete, the MMSE is brief, inexpensive and simple to administer; does not require training. Its widespread use and accepted cut-off scores increase its interpretability.
What are its limitations?	Low levels of sensitivity have been reported, particularly among individuals with mild cognitive impairment and patients with right-sided strokes (Tombaugh & McIntyre, 1992; de Koning et al. 1998, Dick et al. 1984). Lacks an evaluation of executive function. The MMSE has been shown to be affected by age, level of education and sociocultural background, which may lead to misclassification (Tombaugh & McIntyre 1992, Bleeker et al. 1988, Lorentz et al. 2002).

Improving the MMSE

Suggested solutions to the MMSE's poor sensitivity rates include the use of age-specific norms (Bleecker et al. 1988) and the addition of a clock-drawing task to the test (Suhr & Grace, 1999). **Clock-drawing tests** themselves have been assessed as acceptable to patients, easily scored and less affected by education, age and other non-dementia variables than other very brief measures of cognitive impairment (Lorentz et al. 2002) and would have little effect on the simplicity and accessibility of the test (see below).

Montreal Cognitive Assessment (MoCA)

The MOCA is one of the most commonly used tools designed to detect mild cognitive impairment. It is a brief, 30-item test that consists of various subtests evaluating: short-term memory, visuospatial abilities, executive function, attention, concentration, working memory, language, and orientation to time and space. A cut-off score ≤26 represents cognitive impairment. The MoCA was found to be valid and exhibits excellent sensitivity in mild cognitive impairment. It was therefore found to be superior to the MMSE in screening for mild cognitive impairment (Pendlebury et al. 2010; Popovic et al. 2007). It exhibited good sensitivity in detecting moderate and severe impairment. Specificity was also high. It is sensitive and appropriate for use in detecting post-stroke cognitive impairment (Dong et al. 2010; Nasreddine et al. 2005).



Montreal Cognitive Assessment

Questions	Answer
What does it measure?	Designed as a screening tool to detect mild cognitive impairment (Nasreddine et al. 2005).
What is the scale?	The MoCA uses tasks such as picture naming, clock drawing and recall to assess the following domains: attention and concentration, executive functions, memory, language, visuoconstructional skills, conceptual thinking, calculations, and orientation.
What are the key scores?	The MoCA yields a total score out of 30 with scores of 26 or lower indicating the presence of cognitive impairment.
What are its strengths?	The MoCA is able to detect mild forms of impairment in patients that score in the normal range on other assessment measures (i.e., the MMSE) (Nasreddine et al. 2005).
What are its limitations?	The MoCA is a relatively new measurement tool; thus, its reliability and validity may not yet be thoroughly tested.

Wechsler Adult Intelligence Scale (WAIS)

The WAIS is a widely used IQ test designed to measure a person's intelligence and cognitive ability. The original WAIS was created in 1955, and there have been many revisions since, including the WAIS-R, WAIS-III, and WAIS-IV. WAIS-R is a revised form of the WAIS and consists of six verbal (information,

comprehension, arithmetic, digit span, similarities, vocabulary) and five performance (picture arrangement, picture completion, block design, object assembly, digit symbol) subtests. The current edition, WAIS-IV, includes four core indices measuring verbal comprehension, perceptual reasoning, working memory, and processing speed. The WAIS scales have long been considered the gold standard measure of intellectual functioning and have demonstrated excellent validity and reliability in healthy individuals (Weschler 2008; Denhart 2018).

5.4.6 Activities of Daily Living

These outcome measures assessed an individual's proficiency at performing everyday activities.

Barthel Index (BI)
The Barthel Index is a measure of one's ability to perform activities of daily living. The scale consists of 10 items: personal hygiene, bathing, feeding, toilet use, stair climbing, dressing, bowel control, bladder control, ambulation or wheelchair mobility and chair/bed transfers. Each item has a five-stage scoring system and a maximum score of 100 points, where higher scores indicate better performance. The scale is suitable for monitoring on the phone, and is shown to have a high inter-rater reliability (Park 2018).

Functional Independence Measure (FIM)
FIM is an 18-item outcome measure composed of both cognitive (5-items) and motor (13-items) subscales. Each item assesses the level of assistance required to complete an activity of daily living on a 7-point scale. The summation of all the item scores ranges from 18 to 126, with higher scores being indicative of greater functional independence. This measure has been shown to have excellent reliability and concurrent validity in its full form (Granger et al. 1998, Linacre et al. 1994; Granger et al. 1993).

Stroke Impact Scale (ADL Subsection)
The ADL Subsection of the Stroke Impact Scale is a patient-reported measure of multi-dimensional stroke outcomes. The measure consists of 59 functional tasks (e.g. dynamometer, reach and grab, walking, reading out loud, rating emotional regulation, word recall, number of tasks completed, and shoe tying). These tasks are then divided into 8 distinct subscales which include: strength, hand function, mobility, communication, emotion, memory, participation and activities of daily living (ADL). Each task is measured on a 5-point scale (1=an inability to complete the task, 5=not difficult at all). The measure has been shown to have good reliability and validity (Mulder et al. 2016; Richardson et al. 2016).

5.4.7 Neuropsychological Testing

The accepted "gold standard" for assessment of cognitive impairment is a battery of neuropsychological tests which covers various domains, with domain-specific deficits being determined using normative data (Cumming et al. 2013).

5.5 Management for Vascular Cognitive Impairment

5.5.1 Non-Pharmacological Management

General Management Strategy (Farooq & Gorelick 2013)

Focus on managing modifiable risk factors for stroke:

- Life style: smoking cessation, moderate alcohol intake, healthy diet, weight control and physical activity.
- Medical: hypertension, hyperglycemia, hyperlipidemia, smoking and atrial fibrillation.

5.5.2 Pharmacotherapy for Vascular Cognitive Impairment

The main aims of pharmacological management in vascular cognitive impairment are:

- Disease modifying -to prevent further decline in cognitive function, reduce white matter changes and stroke recurrence.
- Symptomatic management - to improve current level of cognitive function.

5.5.2.1 Disease-Modifying Pharmacological Management in VCI

Antihypertensives

Many blood pressure reduction trials have been conducted and, while some report the effects of treatment on cognition outcomes. The contribution of hypertension to the risk for dementia post-stroke may be masked, in part, by its large contribution to the risk for stroke. The slow development of cognitive impairment related to the presence of hypertension is greatly augmented by the presence of stroke. Reduction of hypertension could reduce the risk for cognitive decline by preventing further cardio or cerebrovascular disease (Mackowiak-Cordoliani et al. 2005, Williams 2004).

Perindopril and Indapamide (PROGRESS)

Highlighted Study

Collaborative PR, Neal B, MacMahon S. Effects of blood pressure lowering with perindopril and indapamide therapy on dementia and cognitive decline in patients with cerebrovascular disease. Arch Intern Med. 2003;163:1069-75.		
RCT (8) N_{Start}=6105 N_{End}=5888 TPS=Chronic	E: Perindopril (4mg/d) (+ Indapamide 2-2.5mg/d) C: Placebo Duration: 3.9yr	• Mini Mental State Exam (+exp)
PROGRESS was a RCT (N=6105) people with prior stroke or TIA. Participants were assigned to either active treatment (perindopril for all participants and indapamide for those with neither an indication for nor a contraindication to a diuretic) or matching placebo(s). The primary outcomes for these analyses were dementia.During a mean follow-up of 3.9 years, dementia was documented in 193 (6.3%) of the 3051 randomized participants in the actively treated group and 217 (7.1%) of the 3054 randomized participants in the placebo group (relative risk reduction, 12% [95% confidence interval, -8% to 28%]; P =.2). Cognitive decline occurred in 9.1% of the actively treated group and 11.0% of the placebo group (risk reduction, 19% [95% confidence interval, 4% to 32%]; p=0.01). The risks of the composite outcomes of dementia with recurrent stroke and of cognitivedecline with recurrent stroke were reduced by 34% (95% CI: 3% to 55%, p =.03) and 45% (95% CI: 21% to 61%) p<0.001), respectively, with no clear effect on either dementia or		

cognitive decline in the absence of recurrent stroke (using DSM-IV criteria) and cognitive decline (a decline of 3 or more points in the Mini-Mental State Examination score).

Highlighted Study

Diener HC, Sacco RL, Yusuf S, Cotton D, Ôunpuu S, Lawton WA, Palesch Y, Martin RH, Albers GW, Bath P, Bornstein N. Effects of aspirin plus extended-release dipyridamole versus clopidogrel and telmisartan on disability and cognitive function after recurrent stroke in patients with ischaemic stroke in the Prevention Regimen for Effectively Avoiding Second Strokes (PRoFESS) trial: a double-blind, active and placebo-controlled study. The Lancet Neurology. 2008 Oct 1;7(10):875-84.		
RCT (10) N_{Start}=20332 N_{End}=18712 TPS=Subacute	E1: Telmisartan (80mg/d) + Aspirin (25mg 2/d) + Extended-release Dipyridamole (200mg 2/d) E2: Telmisartan (80mg/d) + Clopidogrel (75mg/d) E3: Placebo + Aspirin (25mg 2/d) + Extended-release Dipyridamole (200mg 2/d) E4: Placebo + Clopidogrel (75mg/d) Duration: 2.5yr	• Mini Mental State Exam (-) • Barthel Index (-)

Of the summarized studies (Table 12.4.2.1.1), four (PROGRESS, MOSES, PRoFESS, and Ihle-Hansen et al. (2014) were secondary prevention trials focusing on individuals with previous history of stroke or transient ischemic attack (TIA). Only the PROGRESS study reported a significant association between treatment of hypertension and reduced risk for cognitive decline or dementia. Both the MOSES and PRoFESS trials compared the relative effectiveness of antihypertensive regimens. Neither reported significant between group differences on MMSE scores. Ihle-Hansen et al. (2014) not only optimised medical treatments such as antihypertensives, antiplatelet agents, statins, vitamin B complex supplements, and anti-diabetic medications, but also offered nutritional advice. Although the intervention did succeed in improving cognitive performance, these improvements did not differ significantly compared to a control group. The authors speculate that a follow-up time of one year may be insufficient as dementia develops over several years and therefore longitudinal study designs may allow for greater observations.

Levels of Evidence for Antihypertensives

Intervention	Attention	Learning and Memory	Global Cognition	ADLs
Antihypertensives	**1b** **1 RCT**	**1b** **1 RCT**	**1a** **3 RCTs**	**1b** **1 RCT**

<u>Conclusions</u>
The effect of treatment for hypertension on risk for cognitive decline and dementia is uncertain. In individuals with previous stroke or TIA, treatment has been associated with reduced risk.
There is no evidence that one particular antihypertensive agent is superior to another for the prevention of cognitive decline.

5.5.2.2 **Symptomatic Pharmacological Management in VCI**

Cholinesterase Inhibitors

Cholinergic agents – donepezil, rivastigmine and galantamine – have been used in the treatment of vascular dementia. While there has been evidence from large RCTs supporting the effectiveness of these compounds in the treatment of Alzheimer's dementia, the evidence supporting their use in the treatment of vascular dementia is less clear (Craig & Birks 2005). A meta-analysis by Kavirajan and Schneider (2007) found that cholinesterase inhibitors may produce small benefits in cognition of uncertain clinical significance in patients with mild to moderate vascular dementia, but evidence was insufficient to support their widespread use.

Donepezil in Vascular Dementia

Donepezil is a selective acetylcholinesterase inhibitor which has been well studied in treatment of mild to moderate Alzheimer's dementia. Effectiveness among patients with vascular dementia has been shown in 2 large RCTs (Black et al. 2003; Wilkinson et al. 2003) (see below). There is strong evidence, based on 2 RCTs, donepezil taken for 24 weeks improves cognitive function in patients with probable or possible vascular dementia (Black et al. 2003; Wilkinson et al. 2003).

Highlighted Study

Black S, Roman GC, Geldmacher DS, Salloway S, Hecker J, Burns A, Perdomo C, Kumar D, Pratt R. Efficacy and tolerability of donepezil in vascular dementia: Positive results of a 24-week, multicenter, international, randomized, placebo-controlled clinical trial. Stroke 2003; 34(10):2323-2330.		
RCT (7) N_{Start}=603 N_{End}=478	E1: Donepezil (5mg/d) E2: Donepezil (5mg/d for 28d, 10mg/d thereafter) C: Placebo Duration: 24wks	• Alzheimer's Disease Assessment Scale-Cognitive subscale (+exp) • Clinician's Interview-Based Impression of Change (+exp) Sum of the Boxes of the Clinical Dementia Rating (+exp)
603 patients with probable (70.5%) or possible (29.5%) VaD randomized to 24 weeks of Donepezil 5mg/day or 5mg/day x28days then 10mg/day or placebo. Groups receiving Donepezil showed significant improvement in cognition vs placebo. Withdrawal due to adverse reactions was 11.1% in 5mg/d, 11.1% in placebo and 21.8% in 10mg/day (p=0.005).		

Highlighted Study

Wilkinson D, Doody R, Helme R, Taubman K, Mintzer J, Kertesz A, Pratt RD. Donepezil 308 Study Group. Donepezil in vascular dementia: a randomized, placebo-controlled study. Neurology 2003; 61(4):479-486.		
RCT (7) N_{Start}=616 N_{End}=491	E1: Donepezil (5mg/d) E2: Donepezil (5mg/d for 28d, 10mg/d after) C: Placebo Duration: 24wks	• Alzheimer's Disease Assessment Scale-Cognitive subscale (+exp) Clinician's Interview-Based Impression of Change-Plus (+exp)
616 patients with probable (76%) or possible (24%) VaD randomized to Donepezil 5mg/day or 5mg/day x 28d then 10 mg/day or placebo x 24 weeks. Both Donepezil groups showed significant improvements in cognition outcomes vs. placebo. Withdrawal due to adverse events: placebo - 8.8%, donezepril - 5mg/day 10.1%, 10mg/day - 16.3%.		

Conclusion

Treatment with donepezil may improve cognitive and global function in patients with vascular dementia.

Rivastigmine in Vascular Dementia

Rivastigmine is an acetylcholine-esterase inhibitor and a butyrylcholine-esterase inhibitor. In non-randomized, open-label clinical studies, there have been benefits associated with Rivastigmine among patients with subcortical VaD. There is limited evidence treatment with Rivastigmine is associated with more stable cognitive performance and improved behavioural outcomes among patients with subcortical vascular dementia.

Highlighted Study

Ballard C, Sauter M, Scheltens P, He Y, Barkhof F, Van Straaten EC, Van Der Flier WM, Hsu C, Wu S, Lane R. Efficacy, safety and tolerability of rivastigmine capsules in patients with probable vascular dementia: the VantagE study. Current medical research and opinion. 2008 Sep 1;24(9):2561-74.		
RCT (9) N_{Start}=719 N_{End}=572	E: Rivastigmine (3-12 mg/d) C: Placebo Duration: 24wks	• Vascular Dementia Assessment Scale (+exp) • Alzheimer's Disease Assessment Scale-Cognitive subscale (+exp) • Mini Mental State Exam (+exp) • Alzheimer's Disease Cooperative Study-Activities of Daily Living (-) • Global Deterioration Scale (-) • Neuropsychiatric Inventory (-)
Ballard et al. (2008) found inconsistent results regarding the efficacy of rivastigmine treatment for vascular dementia, with significant improvements on some outcome measures and none on others. As well, the authors argued that any improved cognitive outcomes were derived from effects in older patients with mixed dementia.		

In a Cochrane Review, Birks et al. (2013) found three RCTs examining the use of rivastigmine for patients with VCI and vascular dementia. The authors concluded that there was insufficient evidence to support or refute the use of rivastigmine in the treatment of dementia, given that only one study detected a benefit on cognition. As such, they recommended that further studies be conducted.

Levels of Evidence for Rivastigmine

Intervention	Attention	Executive Function	Learning and Memory	Global Cognition	ADLs
Rivastigmine	**1b 1 RCT**	**1b 1 RCT**	**1b 1 RCT**	**1b 1 RCT**	**1b 1 RCT**

<u>Conclusion</u>
Treatment with rivastigmine may stabilize cognitive performance and improve behaviour in patients with vascular dementia. Further research is required.

Galantamine in Vascular Dementia

Galantamine is an acetylcholinesterase inhibitor that also modulates nicotinic receptors (Erkinjuntti et al. 2002, Erkinjuntti et al. 2004).There is moderate evidence based on a single RCT of excellent quality (see below), galantamine associated with improvements in cognitive and functional ability (Erkinjuntii et al. 2002).

Highlighted Study

Auchus AP, Brashear HR, Salloway S, Korczyn AD, De Deyn PP, Gassmann-Mayer C. Galantamine treatment of vascular dementia: a randomized trial. Neurology. 2007 Jul 31;69(5):448-58.		
RCT (9) N_{Start}=786 N_{End}=634	E: Galantamine (24mg/d) C: Placebo Duration: 26wks	• Alzheimer's Disease Assessment Scale-Cognitive subscale (+exp) • Alzheimer's Disease Cooperative Study-Activities of Daily Living (-) • Clinician's Interview-Based Impression of Change-Plus (-) • Neuropsychiatric Inventory (-) • Executive Interview-25 (+exp)
This RCT reported that taking up to 24 mg of galantamine over the course of 26 weeks was effective in improving cognitive abilities, including executive function, in patients with vascular dementia. However, improvements in activities of daily living with galantamine were not significantly different from those achieved with placebo.		

Highlighted Study

Erkinjuntti T, Kurz A, Gauthier S, Bullock R, Lilienfeld S, Damaraju CV. Efficacy of galantamine in probable vascular dementia and Alzheimer's disease combined with cerebrovascular disease: a randomised trial. Lancet 2002; 359:1283-1290		
RCT (8) N_{Start}=592 N_{End}=457	E: Galantamine (24mg/d) C: Placebo Duration: 6mo	• Alzheimer's Disease Assessment Scale-Cognitive subscale (+exp) • Clinician's Interview-Based Impression of Change-Plus (+exp)
Studied 592 patients with probable vascular dementia or mixed dementia randomized to 24 mg/day galantamine or matching placebo x 6 months. Galantamine associated with improvements in cognitive and functional ability. However, benefits more clearly demonstrated among patients with mixed dementia than vascular dementia.		

Conclusions

Treatment with galantamine may improve cognitive and global function in patients with mixed dementia. However, its impact on patients with post-stroke cognitive impairments is less clear. Further research is required.

Summary Comments on Cholinesterase Inhibitors

Three reversible acetylcholinesterase inhibitors, donepezil, rivastigmine, and galantamine, have been investigated in the treatment of vascular dementia. Donepezil and galantamine can be helpful in VaD or mixed Alzheimer's disease and cerebrovascular disease. Limited evidence for treatment with rivastigmine. Although there is strong evidence that Donepezil is effective in vascular dementia; several meta-analyses have not recommended these drugs for Mild Cognitive Impairment which is what is most common post stroke (Tricco et al., 2013; Russ & Morling, 2012; Birks & Flicker, 2006)

Nimotidine in Vascular Dementia

Nimotidine is a calcium-channel blocker that readily crosses the blood-brain barrier. It has a know vasoactive effect and may improve blood flow to hypoperfused areas. Recent meta-analysis treatment with nimotidine with vascular dementia is associated with non-significant improvements in global function and ADLs when compared to placebo. Well tolerated with few side-effects.

In a Cochrane Review, Birks and Lopez-Arrieta (2002) found fifteen RCTs examining the use of nimodipine in patients with Alzheimer's, vascular, or mixed dementia. The authors reported short-term improvements in global function and activities of daily living associated with nimodipine treatment. They recommended extending studies in order to better assess long-term outcomes.

Highlighted Study

Sze KH, Sim TC, Wong E, Cheng S, Woo J. Effect of nimodipine on memory after cerebral infarction. Acta neurologica scandinavica. 1998 Jun;97(6):386-92.		
RCT (6) N_{Start}=100 N_{End}=92 TPS=Acute	E: Nimodipine (90mg/d) C: No treatment Duration: 12wk	• Fuld Object-Memory Evaluation (+exp) • Mini Mental State Exam (+exp) • Barthel Index (-)

Levels of Evidence for Nimodipine

Intervention	Learning and Memory	Global Cognition	ADLs
Nimodipine	**1b** **1 RCT**	**1b** **1 RCT**	**1b** **1 RCT**

Conclusions

Nimodipine may be beneficial for improving learning and memory, and global cognition.
Nimodipine may not be beneficial for improving activities of daily living.

Memantidine in Vascular Dementia

Memantine is an antagonist of the N-methyl-D-aspartate (NMDA) receptor. Its use has been evaluated among patients with Alzheimer's Dementia and those with vascular dementia.

Highlighted Study

Orgogozo JM, Rigaud AS, Stöffler A, Möbius HJ, Forette F. Efficacy and safety of memantine in patients with mild to moderate vascular dementia: a randomized, placebo-controlled trial (MMM 300). Stroke. 2002 Jul 1;33(7):1834-9.		
RCT (8) N_{Start}=321 N_{End}=288	E: Memantine (20mg/d) C: Placebo Duration: 28wks	• Alzheimer's Disease Assessment Scale-Cognitive subscale (+exp) • Mini Mental State Exam (+exp) • Gottfries-Brâne-Steen Scale (+exp) • Nurses' Observation Scale for Geriatric Patients (+exp) • Clinician's Interview-Based Impression of Change-Plus (-)

Highlighted Study

Wilcock G, Möbius HJ, Stöffler AM. A double-blind, placebo-controlled multicentre study of memantine in mild to moderate vascular dementia (MMM500). International clinical psychopharmacology. 2002 Nov 1;17(6):297-305.		
RCT (8) N_{Start}=579 N_{End}=548	E: Memantine (20mg/d) C: Placebo Duration: 28wks	• Alzheimer's Disease Assessment Scale-Cognitive subscale (+exp) • Clinician's Interview-Based Impression of Change-Plus (-)

Both Orgogozo et al. (2002) and Wilcock et al. (2002) found significant stabilization and improvement on the Alzheimer's Disease Assessment Scale-Cognitive Subscale, but not on the Clinician's Interview-Based Impression of Change-Plus, after 28 weeks of memantine treatment for vascular dementia relative to placebo. In addition, Wilcock et al. (2002) noted that treatment effects may be larger among patients with greater cognitive impairment (Mini Mental State Exam<15) or with small vessel disease.

In a Cochrane Review, McShane et al. (2006) found twelve RCTs examining the use of memantine in patients with Alzheimer's, vascular, or mixed dementia. The authors reported a small benefit of memantine in moderate to severe Alzheimer's dementia, which was not clinically detectable in patients with mild to moderate vascular dementia. As such, they recommended that further studies be conducted regarding vascular dementia.

Conclusion

Treatment with memantine may be associated with stabilization or improvement of cognitive function in patients with vascular dementia.

Pentoxyfylline in Vascular Dementia

Pentoxifylline is a methylzanthine compound that has been associated with a significant increase in cerebral blood flow (Hartmann 1983).

Highlighted Study

Oizumi K, Baumann P, Siira P, Vanharanta H, Myllylä VV, Chiu MJ, Chen RC, Tseng CY, Rossi A, Iidaka T, Nakajima T. European pentoxifylline multi-infarct dementia study. European Neurology. 1996;36(5):315-21.		
RCT (7) N_{Start}=289 N_{End}=269	E: Pentoxifylline (400 mg 3/d) C: Placebo Duration: 9mo	• Sandoz Clinical Assessment Geriatric Scale (+exp) • Sandoz Clinical Assessment Geriatric Scale-Cognitive subscale (+exp) • Gottfries-Brâne-Steen Scale (+exp) • Gottfries-Brâne-Steen Scale (ITT sample) (-)
In a multi-centre trial conducted by the EPMID Study Group (1996), patients treated with pentoxifylline demonstrated significantly greater improvement in overall cognitive function compared to patients treated with a placebo. Adverse events were reported by both groups, but side effects such as nausea and vomiting were experienced mostly by the pentoxifylline group. The study group noted that some centres enrolled only 1 patient, while the largest cohort was 32 patients. Despite this heterogeneity, significant results were consistent within the treatment group.		

Conclusion

Treatment with pentoxifylline may improve cognitive function in patients with multi-infarct dementia.

Antidepressants

Tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs) and serotonin norepinephrine reuptake inhibitors (SNRIs) are used in the treatment of depression following stroke. Depression is one of many possible symptoms displayed post-stroke but is often in conjunction with cognitive impairment. The frequency and severity of cognitive impairment has been positively correlated with the presence of depression immediately after injury (Downhill & Robinson, 1994). In addition, depressive symptoms can persist longer into recovery if the individual also has cognitive impairment, and cognitive impairment will last longer if the individual is depressed (Robinson et al. 1986). Given the association between the presence of depression and cognitive dysfunction, studies have investigated the effect of antidepressants on cognition post-stroke.

Highlighted Study

Jorge RE, Acion L, Moser D, Adams HP, Robinson RG. Escitalopram and enhancement of cognitive recovery following stroke. Archives of general psychiatry. 2010 Feb 1;67(2):187-96.		
RCT (7) N_{Start}=129 N_{End}=110 TPS=Subacute	E: Escitalopram (10mg/d) C: Placebo Duration: 12mo	• Repeatable Battery for the Assessment of Neuropsychological Status Total Score (+exp) RBANS Subcategories: • Delayed Memory (+exp) • Immediate Memory (+exp) • Attention (-) • Visuospatial/Constructional (-) • Trail-Making Tests A (-) • Trail-Making Test B (-) • Controlled Oral Word Association Test Raw Scores (-) • Stroop Test (-) • Wechsler Adult Intelligence Scale-III Similarities Scores (-)
Jorge et al. (2010) evaluated the effect of escitalopram on cognitive function in a group of patients with stroke but no depression. The authors identified a significant improvement in global cognitive function and memory (immediate and delayed recall) associated with treatment. This effect was independent of the impact of treatment on depression, time since the index event, and type or mechanism of stroke.		

Levels of Evidence for Antidepressants

Intervention	Attention	Executive Function	Learning and Memory	Global Cognition	Visual-Spatial
Antidepressants	**1b 1 RCT**	**1b 1 RCT**	**1b 1 RCT**	**1b 1 RCT**	**1b 1 RCT**

<u>Conclusions</u>

Antidepressants may be beneficial for improving learning and memory but may not be beneficial for improving other cognitive outcomes.

Methylphenidate (Ritalin)

Methylphenidate (0.25 -.30 mg/kg bid) is recommended in adults to enhance attention and speed of cognitive processing in the adult population. Consider in treating patients with difficulty in attention and focus.

5.6 Depression and Cognitive Disorders

5.6.1 Impact of Depression on Cognitive Disorders

Depression is an important issue which must be considered when managing cognitive disorders. Depression may affect the results of the cognitive tests (Ruchinskas & Curyto 2003). Depression in patients with amnestic mild cognitive impairment is associated with risk of developing Alzheimer's type dementia and cognitive deterioration may proceed at a more rapid pace (Modrego & Ferrández 2004). A significant and independent association between presence of depression and cognitive impairment has been demonstrated in stroke survivors one year following the stroke event (Kalaria & Ballard 2001, Talelli et al. 2004). Brodaty et al. (2007) have demonstrated a greater frequency of dementia among stroke patients with depression (27.8%) when compared to patients without depression (17.3%) at three months post-stroke (though this difference was not significance). By 15 months post-stroke 54.2% of patients with depression were diagnosed with dementia vs. 7.1% of non-depressed with significant difference.

Conclusion
It is unclear whether depression is associated with cognitive impairment post stroke.

5.6.2 Pseudo Dementia

Depression-related cognitive impairment can sometimes mimic the signs of dementia and is referred to as pseudodementia. Pseudodementia tends to be more sudden onset, more rapid progression, with a previous history of depression. It is characterized by more variable, effort-related cognitive deficits with little nocturnal exacerbation.

Dementia vs. Pseudodementia

Feature	Dementia	Pseudodementia
Onset	Often insidious	Usually acute or subacute
Progression	Usually slow, early changes often missed	Usually rapid
Symptom duration at presentation	Long	Short
Psychiatric history or recent life crisis	Uncommon	Common
Extensive self-report of mental impairment	Uncommon	Common
Mental status or psychometric testing	Progressive decline	Variable, effort-related

Memory impairment	Common, most severe for recent events	Common, often selective amnesia, inconsistent deficits over time
Affective changes	Apathy, shallow emotions	Depression common
Nocturnal exacerbation of symptoms	Common	Uncommon

5.7 Cognitive Rehabilitation for Attention, Memory, Executive Function Post Stroke

Interventions for cognitive rehabilitation are broadly classified as:

1. Direct remediation/cognitive skill training to re-establish previously learned patterns of behaviour.
2. Compensatory strategy training, either establishing new patterns of cognitive activity through internal compensatory cognitive mechanisms or establishing new patterns of activity through external compensatory mechanisms such as external aids, environmental structuring and support.

Cognitive rehabilitation interventions aim to:

1. Reinforce, strengthen or **re-establish previously learned patterns of behavior.**
2. Establish new patterns of cognitive activity through **internal compensatory cognitive mechanisms** for impaired neurological systems.
3. Establish new patterns of activity through **external compensatory mechanism** such as external aids, or environmental structuring and support.
4. **Enable persons to adapt** to their cognitive disability.

5.7.1 Evidence on Cognitive Rehabilitation

Evidence for cognitive rehabilitation post stroke is less than for motor rehab as there are fewer RCTs (about one fifth) and effectiveness for interventions less clear (Cumming et al. 2013). Many studies of cognitive rehabilitation were performed in a heterogeneous population consisting of stroke and traumatic brain injury. Overall, cognitive rehabilitation interventions were associated with small but significant treatment effects. There is good evidence that cognitive rehabilitation is effective in treating more focal deficits such as visual spatial rehabilitation or rehab interventions for aphasia (Cicerone et al. 2011; Brady et al. 2012). Review by Cicerone et al. (2011) reported that existing evidence supports visual spatial rehabilitation, interventions for aphasia and apraxia. Effective treatments for memory and executive function, often associated with more diffuse lesions, are lacking (Ballard et al. 2003).

Overall, the four Cochrane reviews examining interventions for cognitive impairment post stroke that have been conducted to date are largely inconclusive. Few randomized controlled trials have been conducted, and many are lacking methodological quality. The general consensus of these four reviews is that, although various interventions for cognitive impairment following stroke appear to have some promise, more studies need to be conducted in order to support their use.

5.7.2 Remediation of Attention

Attention is a cognitive function that will ultimately affect all aspects of cognition and processing. No matter the nature of a task, attention is required to pick out salient information, and ignore non-relevant stimuli. For this reason, training attention specifically can improve a variety of mental processes and training effects can ideally permeate to almost all levels of cognitive functioning. Training of attention can take on two very broad classifications. One way is repetition of task-specific activities that require an attention network (network training). Another is through activities like meditation and mindfulness training that seek to change the brain's overall state (state training) (Posner, Rothbart & Tang, 2015). Most interventions relied on drills and practice used within stimulus-response paradigm. Gains made during speeded tasks are less durable than gains made via non-speeded tasks. Greater benefit observed from attention training on complex tasks requiring selective or divided attention when compared to attention training on basic tasks of reaction time or vigilance.

Highlighted Study

Mazer BL, Sofer S, Korner-Bitensky N, Gelinas I, Hanley J, Wood-Dauphinee S. Effectiveness of a visual attention retraining program on the driving performance of clients with stroke. Arch Phys Med Rehabil 2003; 84(4):541-550.		
RCT (7) N_{Start}=97 N_{End}=84 TPS=Subacute	E: Useful Field of View (UFOV) training C: Traditional computerized training Duration: 30-60min/session, 2-4 sessions/wk until 20 sessions	• Useful Field of View (-) • Functional Independence Measure (-) • Test of Everyday Attention (-) • Motor-Free Visual Perception Test (-) • Money Road Map Test of Direction Sense (-) • Trail-Making Test A (-) • Trail-Making Test B (-) • Charron Test (-) • On-road Evaluation (-)
84 hemispheric stroke patients (<6months) who wanted to return to driving randomized to training of visual processing speed, divided attention and selective attention vs traditional computerized visuoperceptual retraining for 20 sessions each. No significant differences except 2X improvement in rate of success on on-road driving test.		

Highlighted Study

Barker-Collo SL, Feigin VL, Lawe CM, Parag V, Senior H, Rodgers A. Reducing attention deficits after stroke using attention process training; A randomized controlled trial. Stroke 2009; 40:3293-3298.		
RCT (8) N_{Start}=78 N_{End}=66 TPS=Acute	E: Attention Process Training C: Usual care Duration: 1hr/d, 5d/wk for 4 wk	• Integrated Visual and Auditory Continuous Performance Test (+exp) • Trail-Making Test A (-) • Trail-Making Test B (-) • Paced Auditory Serial Addition Test (-)
78 acute stroke patients with attention deficits identified by neuropsychological assessment. Participants were randomly allocated to standard care plus 30 hours of Attention Process Training (APT) or standard care alone. APT training consisted of 1 hour sessions provided for a total of 4 weeks. The primary outcome was Integrated Visual Auditory Continuous Performance Test Full-Scale Attention Quotient (IVA-CPT). Patients in the intervention group performed significantly better on the primary outcome, as compared		

to patients in the control group (p < 0.05). No other significant differences were reported between the two groups.

Remediation of Attention Levels of Evidence

Intervention	Attention	Executive Function	Learning and Memory	ADLs
Attentional Training	**1b** **2 RCTs**	**1b** **1 RCT**	**1b** **1 RCT**	**1b** **1 RCT**

Conclusions

Attention training may have a positive effect on specific, targeted outcomes but overall attentional training may not be helpful for improving attentional deficits.

Further research within the stroke population is required using like outcome measures to better evaluate comparisons between studies.

5.7.3 Remediation of Memory Deficits

There are many different types of memory, and therefore many types of memory training. Most of the research available tends to focus on training working memory, but other methods are available for training semantic or episodic memory as well. Because all types of memory play such a crucial role in our ability to live independent lives, it is a major target for rehabilitation in those affected by memory deficits. Although the nature of the tasks may differ, training generally consist of a learning phase of some form where the information is intended to be encoded, and a recall phase. In addition, training certain strategies as opposed to simply task-specific repetition is also another way to ameliorate memory deficits (Zarit, Cole & Guider, 1981).

There has been strong evidence that compensatory strategies are effective in improving memory outcomes post traumatic brain injury; relatively few of the study participants had suffered a stroke. However, a recent large study (Aben et al. 2014) found it worked in stroke. Strategies include imagery-based training and the use of assistive, electronic devices. Intensive computerized training programs improve memory.

Highlighted Study

Aben L, Heijenbrok-Kal MH, Ponds RW, Busschbach JJ, Ribbers GM. Long-lasting effects of a new memory self-efficacy training for stroke patients: a randomized controlled trial. Neurorehabilitation and neural repair. 2014 Mar;28(3):199-206.		
RCT (8) N_{Start}=153 N_{End}=139 TPS=Chronic	E: Memory self-efficacy training program C: Educational program Duration: 9 sessions, 1hr/session, 2 sessions/wk	• Auditory verbal Learning Test (-) • Rivermead Behavioural Memory Test (-)
The authors suggested that combining compensatory techniques with psychoeducation with an emphasis on self-efficacy results in positive improvements in memory.		

Remediation of Memory Levels of Evidence

Intervention	Attention	Executive Function	Learning and Memory	Global Cognition
Memory Training	1b 1 RCT	1b 1 RCT	1b 1 RCT	1b 1 RCT

Conclusions

Compensatory strategies can be used to improve memory outcomes post stroke. Further research within the stroke population is required.

There is limited research investigating group therapy post stroke, and little evidence supporting the use of group-based interventions for the improvement of memory.

5.7.4 Remediation of Executive Functioning and Problem Solving

Executive functioning defined as *"those integrative cognitive processes that determine goal directed and purposeful behaviour and are superordinate in the orderly execution of daily life functions"* (Cicerone et al. 2000). Functions affected include: ability to formulate goals; to initiate behaviour; to anticipate the consequences of actions; to plan and organize behavior according to spatial, temporal, topical, or logical sequences; and to monitor and adapt behavior to fit a particular task or context (Cicerone et al. 2000). Cicerone et al. (2011) studied 17 studies on executive function involving patients with TBI. There were no stroke patients in the studies included in the review (Chung et al. 2013) also concluded that there is insufficient evidence for cognitive rehabilitation in improving executive function post stroke.

Highlighted Review

Chung CSY, Pollock A, Campbell T, Durward BR, Hagen S. Cognitive rehabilitation for executive dysfunction in adults with stroke or other adult non-progressive acquired brain damage. Cochrane Database of Systematic Reviews 2013, Issue 4. Art. No.: CD008391.
DOI: 10.1002/14651858.CD008391.pub2.

Methods

19 studies (907 participants) met the inclusion criteria for this review. 13 studies (770 participants) were included in meta-analyses (417 traumatic brain injury, 304 strokes, 49 other acquired brain injuries) reducing to 660 participants once non-included intervention groups were removed from three and four group studies.

Results

The authors identified insufficient high-quality evidence to reach any generalised conclusions about the effect of cognitive rehabilitation on executive function, or other secondary outcome measures.

Remediation of Executive Functioning and Problem-Solving Levels of Evidence

Interventions	Learning and Memory	Global Cognition	ADLs

Occupational Workplace Interventions		**1b** **1 RCT**	**1b** **1 RCT**
Trial and Error Learning	**2** **1 RCT**		**2** **1 RCT**
Problem Solving Therapy			**1b** **1 RCT**

Conclusions

The standardization of both intervention and outcome measures would help resolve the conflicts seen between individual studies.

Analogical problem-solving skills training may improve problem solving abilities and instrumental activities of daily living, but there is conflicting evidence.

Tailored interventions to improve return to work are not effective in improving cognition.

5.7.5 Physical Activity

Although it is well known that physiotherapy and exercise are effective for rehabilitation, it is still not clear as to what type is most effective (Langhorne, Wagenaar & Patridge, 1996; Cho & Cha, 2016). Besides the more obvious physical benefits associated with exercise, psycho-social benefits also exist, and attempts are made to maximize these residual benefits as well (Saunders, Greig & Mead, 2014). Many studies have shown how aerobic exercise can help improve cognitive function, and importantly protect it through ageing in healthy individuals (Quaney et al. 2009).

A review by Cumming et al. (2011) examined the impact of exercise on cognitive performance in patients with stroke. The authors identified 12 RCTs but only nine had sufficient data to be included in meta-analysis. The large variability between study interventions prevents drawing firm conclusions regarding frequency, intensity, and type of physical activity provided. As well, the measures used to assess cognitive performance were limited and were rarely the primary focus of these articles. Although the authors reported a significant treatment effect favoring the use of exercise, this body of literature is methodologically limited, which highlights the need for further research in this area.

Highlighted Study

Tang A, Eng JJ, Tsang TS, Liu-Ambrose T. High-and low-intensity exercise do not improve cognitive function after stroke: A randomized controlled trial. Journal of rehabilitation medicine. 2016 Nov 5;48(10):841-6.		
RCT (6) N_{Start}=50 N_{End}=47 TPS=Chronic	E: High intensity aerobic exercise C: Balance/Flexibility Control Group Duration: 60min/d, 3d/wk for 6mo	• Verbal Digit Span (-) • Stroop Test (-)

Levels of Evidence for Physical Activity and Cognition

Interventions	Attention	Executive Function	Learning and Memory	Global Cognition	ADLs
Exercise Programs	**1a**	**1a**	**1a**	**1a**	**1b**

	4 RCTs	4 RCTs	4 RCTs	3 RCTs	1 RCT

Conclusions

Exercise may be beneficial for improving learning and memory, and overall cognitive abilities.
Exercise may not be beneficial for improving attention or executive function.
Higher intensity exercises may not be more beneficial than lower intensity exercises for improving cognition.

5.7.6 Multimodal Treatment

Multimodal training refers to combinations of various types of interventions used simultaneously to produce better outcomes than the individual interventions could alone.

Highlighted Study

Bo W, Lei M, Tao S, Jie LT, Qian L, Lin FQ, Ping WX. Effects of combined intervention of physical exercise and cognitive training on cognitive function in stroke survivors with vascular cognitive impairment: a randomized controlled trial. Clinical rehabilitation. 2019 Jan;33(1):54-63.		
RCT (6) Nstart = 225 Nend = 178 TPS =Subacute	E1: Computer-assisted cognitive training + physical exercise (3x/wk) E2: computer-assisted cognitive training (60min 3x/wk) E3: physical exercise (50min 3x/wk) C: Control (45min video documentaries, 3x/wk) Duration: 12 wks	E1 vs C: • Trail Making B (+exp1) • Stroop Test (+exp1) • Forward Digit Span (+exp1) • Mental Rotation Test (+exp1) E1 vs E2: • Trail Making B (-) • Stroop Test (-) • Forward Digit Span (-) • Mental Rotation Test (+exp1) E1 vs E3: • Trail Making B (-) • Stroop Test (-) • Forward Digit Span (+exp1) • Mental Rotation Test (+exp1)

Highlighted Study

Cheng C, Liu X, Fan W, Bai X, Liu Z. Comprehensive rehabilitation training decreases cognitive impairment, anxiety, and depression in poststroke patients: a randomized, controlled study. Journal of Stroke and Cerebrovascular Diseases. 2018 Oct 1;27(10):2613-22.		
RCT (6) N_{Start}=168 N_{End}=136 TPS=Acute	E: Comprehensive rehabilitation therapy (patient and family education, cognitive training, rehabilitation training, regular check-ups) C: Conventional therapy Duration: 4 wks	• Montreal Cognitive Assessment (+exp) • Mini-Mental State Examination (-)

Levels of Evidence for MultiModal Treatment

Intervention	Executive Function	Learning and Memory	Global Cognition	Visual-Spatial	ADLs

Multimodal training (exercise and cognitive training)	**1b 1 RCT**	**1b 1 RCT**	**1a 2 RCTs**	**1b 1 RCT**	**1b 1 RCT**

Conclusion
The literature is mixed regarding multimodal interventions for improving cognitive rehabilitation.

5.7.7 Mental Imagery

The use of mental practice was adopted from the field of sports psychology where the technique has been shown to improve athletic performance, when used as an adjunct to standard training methods (Page et al. 2014). There has also been a large amount of work done showing imagery's ability to improve memory recall, and learning (Bower, 1970). Therefore, this technique could be used to not only enhance memory, but other functions as well.

Liu KP, Chan CC, Lee TM, Hui-Chan CW. Mental imagery for promoting relearning for people after stroke: a randomized controlled trial. Archives of physical medicine and rehabilitation. 2004 Sep 1;85(9):1403-8.		
RCT (6) N_{Start}=49 N_{End}=46 TPS=Acute	E: Mental imagery training C: Functional rehabilitation Duration: 1hr/d, 5d/wk for 3wk	• Score of Trained Tasks at 3wk (+exp) • Score of Untrained Tasks (+exp) • Color Trails Test (+exp)

Level of Evidence for Mental Imagery

Intervention	Attention	Learning and Memory	ADLs
Mental Imagery	**1b 1 RCT**	**2 1 RCT**	**1b 2 RCTs**

Conclusions
Mental imagery may be beneficial for improving attention, and activities of daily living.
Mental imagery may not be beneficial for improving learning and memory.

5.7.8 Cognitive-Motor Interference

Dual-tasking training requires subjects to simultaneously perform complex tasks, such as cognitive and motor tasks, allowing them to improve their coordination of various tasks (Kim et al. 2014). Cognitive-motor tasks are important for various activities of daily living, such as walking while holding a conversation (Liu et al. 2017). Additionally, dual tasks can be two motor tasks to allow for different motor processes to occur simultaneously to further stimulate the damaged brain.

Highlighted Study

Liu KP, Chan CC. Pilot randomized controlled trial of self-regulation in promoting function in acute poststroke patients. Archives of physical medicine and rehabilitation. 2014 Jul 1;95(7):1262-7.		
RCT (7) N_{Start}=46 N_{End}=44 TPS=Acute	E: Self-regulation of motor and cognitive performance C: Functional rehabilitation Duration: five 1hr sessions	• Tasks of Daily Living (+exp) • Functional Independence Measure-Cognition (-) • Color Trails Test (-)

Cognitive-Motor Interference Level of Evidence

Intervention	Attention	Global Cognition	ADLs
Cognitive Motor Interference	**1b** **1 RCT**	**1b** **1 RCT**	**1b** **1 RCT**

Conclusion

The literature is mixed regarding cognitive-motor interference for cognitive rehabilitation.

5.7.9 Music Impacting Cognition

For humans, listening to music activates a wide array of brain regions past the auditory cortex, including frontal, parietal, temporal and subcortical structures (Sarkamo et al. 2008). For this reason, further enriching a stroke survivors' environment with music could help to improve several cognitive functions.

Highlighted Study

Särkämö T, Tervaniemi M, Laitinen S, Forsblom A, Soinila S, Mikkonen M, Autti T, Silvennoinen HM, Erkkilä J, Laine M, Peretz I. Music listening enhances cognitive recovery and mood after middle cerebral artery stroke. Brain. 2008 Mar 1;131(3):866-76.		
RCT (6) N_{Start}=60 N_{End}=54 TPS=Acute	E1: Music listening (≥1hr/d) E2: Language listening C: No listening material Duration: 6 months	• Rivermead Behavioural Memory Test (+exp_1) • Auditory List-Learning Task (-) • Digit Span Test (-) • Memory Interference Task (-) • Verbal Fluency Test (-) • Clock Drawing Test (-) • Benton Visual Retention Test (-) • Montreal Battery of Evaluation of Amusia (-) • Frontal Assessment Battery (FAB): • Stroop Subtest and Mental Subtraction Test of FAB – Summed Correct Responses (+exp_1) • Stroop Subtest and Mental Subtraction Test of FAB – Reaction Times (-) • Vigilance Subtest of FAB – Correct Responses (-) • Simple Reaction Time Subtest of FAB – Reaction Time (-)
Sarkamo et al. (2008) compared three conditions: listening to music, listening to narrated audiobooks, and no treatment. Although no significant effect of group was found between groups, a significant time-by-group interaction was revealed for verbal memory and focused attention. Post-hoc analysis revealed		

that the music group performed significantly better than the audiobook and control groups in verbal memory recovery, and the control group on focused attention recovery. No significant difference was noted between the music listening group and the audiobook group for focused attention, but the difference approached statistical significance in favour of the music listening group. The authors suggested that listening to music, especially with lyrics, activates a wider and broader range of neural networks and therefore increasing neural plasticity. Patients in the music-listening group reported lower levels of depression and confused mood as well, suggesting that music may also help alleviate emotional issues experienced post-stroke.

Level of Evidence for Music Therapy

Intervention	Attention	Executive Function	Learning and Memory	Global Cognition	Visual-Spatial	Amusia
Music Therapy	1b 1 RCT	1b 1 RCT	1b 1 RCT	1b 1 RCT	1b 1 RCT	1b 1 RCT

<u>Conclusion</u>
Music may not be helpful for improving cognitive function. Further research is required.

5.7.10 Computer-Based Cognitive Training

A computer-based approach is generally more accessible and cost-effective than the same session under the direction of a human therapist. For this reason, computer-based rehabilitation can free up more hospital resources and allow patients to begin rehabilitation as quickly as possible. Furthermore, patients can take a more involved role in their own care, and training can theoretically be performed as often, and whenever the patient wants

Highlighted Study

Wentink MM, Berger MA, de Kloet AJ, Meesters J, Band GP, Wolterbeek R, Goossens PH, Vliet Vlieland TP. The effects of an 8-week computer-based brain training programme on cognitive functioning, QoL and self-efficacy after stroke. Neuropsychological rehabilitation. 2016 Sep 2;26(5-6):847-65.		
RCT (10) N_{Start}=115 N_{End}=107 TPS=Chronic	E: Luminosity computer training C: Stroke Info group Duration: 15-20min/d, 5d/wk for 8wk	• Corsi Forward Block Span (Block Tapping) Test (+exp) • Corsi Backward Block Span (Block Tapping) Test (-) • Forward Digit Span Test (-) • Backwards Digit Span Test (-) • Trail-making Test A (-) • Trail-making Test B (-) • Flanker Task Congruent Reaction Time (-) • Flanker Task Incongruent Reaction Time (+exp) • Raven's Progressive Matrices (-) • Cognitive Failures Questionnaire (-)

Computer Based Cognitive Training Levels of Evidence

Intervention	Attention	Executive Function	Learning and Memory	Global Cognition	Visual-Spatial	ADLs
Computer Based Cognitive Training	1a 2 RCTs	1a 4 RCTs	1b 1 RCT	1a 3 RCTs	1b 1 RCT	1a 2 RCTs

Conclusions
The literature is mixed regarding computer-based training for improving attention.
Computer -based training may not be helpful for improving executive function or global cognition.

5.7.11 Virtual Reality in Improving Cognition

Virtual reality (VR) is a technology that allows individuals to experience and interact with virtual environments, often through a game. VR simulates life-like learning and can be used to increase intensity of training while providing three-dimensional feedback of a visual, sensory, and auditory nature (Saposnik et al. 2010). VR tools are classified as either immersive (i.e. three-dimensional environment via head-mounted display) or non-immersive (i.e. two-dimensional environment via conventional computer monitor or projector screen). Customized VR programs have been created and tested in rehabilitation research, although commercial gaming consoles (e.g. Nintendo Wii) have also been used to deliver VR training.

Highlighted Study

Faria AL, Cameirão MS, Couras JF, Aguiar JR, Costa GM, Bermúdez i Badia S. Combined cognitive-motor rehabilitation in virtual reality improves motor outcomes in chronic stroke–a pilot study. Frontiers in psychology. 2018 May 30;9:854.		
RCT (3) N_{Start}=32 N_{End}=24 TPS=Chronic	E: Virtual reality (Reh@Task) + conventional therapy (45min X 3/wk) C: Conventional therapy. Duration: 1 month	• Montreal Cognitive Assessment (-) • Barthel Index (-)

Virtual Reality Levels of Evidence

Intervention	Attention	Executive Function	Learning and Memory	Global Cognition	Visual-Spatial	ADLs
Virtual Reality Training	2 1 RCT	2 1 RCT	2 1 RCT	2 1 RCT	2 1 RCT	2 1 RCT

Conclusion
Virtual reality may not be beneficial for improving cognition.

5.7.12 Repetitive Transcranial Magnetic Stimulation (rTMS)

Repetitive transcranial magnetic stimulation (rTMS) is a form of non-invasive brain stimulation in which magnetic pulses are delivered to the cerebral cortex through the scalp.). The neuromodulatory effects of transcranial magnetic stimulation are attributed largely to neural membrane polarization shifts that can lead to changes in neuron activity, synaptic transmission, and activation of neural networks (Peterchev et al. 2012). Repetitive transcranial magnetic stimulation (rTMS) is the application of repetitive trains of transcranial magnetic stimulation at regular intervals.

After a stroke, interhemispheric competition is altered; with cortical excitability increasing in the unaffected hemisphere and decreasing in the affected hemisphere (Zhang et al. 2017). rTMS can be used to help modulate this interhemispheric competition, with low stimulation frequencies (≤1Hz) decreasing cortical excitability and inhibiting activity of the contralesional hemisphere, while high frequency (>1Hz) stimulation increases excitability and have a facilitatory effect on activity of the ipsilesional hemisphere (Dionisio et al. 2018).

Highlighted Study

Lu H, Zhang T, Wen M, Sun L. Impact of repetitive transcranial magnetic stimulation on post-stroke dysmnesia and the role of BDNF Val66Met SNP. Medical science monitor: international medical journal of experimental and clinical research. 2015;21:761.		
RCT (6) N_{Start}=54 N_{End}=50 TPS=Subacute	E: Low-frequency (1Hz) rTMS C: Sham therapy Duration: 1 session/d, 5d/wk for 4wk	• Montreal Cognitive Assessment (+exp) • Loewenstein Occupational Therapy Cognitive Assessment (+exp) • Rivermead Behavior Memory Test (+exp)
This study demonstrated that specific rTMS interventions can be very effective in improving cognition.		

rTMS Levels of Evidence

Intervention	Attention	Executive Function	Learning and Memory	Global Cognition	Visual-Spatial	ADLs
rTMS	1b 1 RCT	1b 1 RCT	1a 2 RCTs	1b 1 RCT	1b 1 RCT	1b 1 RCT

Conclusions

rRTMS may have a positive effect on cognitive function following stroke although much of the research has not shown a positive effect.

Further research is required to determine if this effect is a result of a specific placement or frequency of the rTMS therapy.

5.7.13 Transcranial Direct Current Stimulation (tDCS)

In transcranial direct current stimulation (tDCS), a weak, non-invasive electrical current is delivered to induce changes in cortical excitability (Fregni et al. 2005). Previous studies have demonstrated that anodal tDCS may be associated with improvements in cognitive function in healthy populations (Antal et al. 2004,

Fregni et al. 2005, Kincses et al. 2004, Nitsche et al. 2003). Working memory and attention are of particular importance in relearning and recovery post stroke. The results of two crossover studies suggest that anodal tDCS to the left dorsolateral prefrontal cortex may result in some improvement to these areas of cognitive function (Jo et al. 2009, Kang et al. 2009). However, due to limits in sample sizes and methodologies, further research is required.

tDCS Levels of Evidence

Intervention	Attention	Learning and Memory
tDCS	2 1 RCT	1b 1 RCT

Conclusion

Anodal tDCS to the left dorsolateral prefrontal cortex may not help to improve working memory and attention. Further research is required.

5.7.14 Acupuncture, Electroacupuncture and TENS

Acupuncture

With respect to stroke rehabilitation, the benefit of acupuncture has been evaluated most frequently for pain relief and recovery from motor deficits, but some research has examined its effectiveness in improving cognitive outcomes.

Highlighted Study

Chen L, Fang J, Ma R, Gu X, Chen L, Li J, Xu S. Additional effects of acupuncture on early comprehensive rehabilitation in patients with mild to moderate acute ischemic stroke: a multicenter randomized controlled trial. BMC complementary and alternative medicine. 2016 Dec;16(1):226.		
RCT (8) N_{Start}=250 N_{End}=241 TPS=Acute	E: Acupuncture therapy C: Standard rehabilitation care Duration: 30min/d, 6d/wk for 3wk	• Montreal Cognitive Assessment (+exp) • Mini Mental State Exam (+exp)

Electroacupuncture

Electroacupuncture is a variant of acupuncture techniques practiced in traditional Chinese medicine, the difference being that a minute electrical current of similar intensity to that of a bioelectric current produced endogenously in the body is applied to the needles used (Wang et al. 2014).

Acupuncture and Electroacupuncture Levels of Evidence

Interventions	Attention	Executive Function	Learning & Memory	Global Cognition	Visual-Spatial	ADLs
Acupuncture				1b 2 RCTs		2 1 RCT

Electroacupuncture	**1b 1 RCT**	**1b 1 RCT**	**1b 1 RCT**	**1b 1 RCT**	**1b 1 RCT**	

Conclusions
Acupuncture may be beneficial for improving global cognition and activities of daily living Electroacupuncture may be beneficial for improving attention, and visuospatial perception and orientation, but not other cognitive outcomes.

5.8 Rehabilitation for Perceptual Disorders Post-Stroke

Titus et al. (1991) defined perceptual performance as "*the ability to organize, process, and interpret incoming visual information, tactile-kinesthetic information, or both, and to act appropriately on the basis of the information received".*

5.8.1 Unilateral Spatial Neglect

Unilateral Spatial Neglect (USN) is defined as a failure to report, respond, or orient to sensory stimuli presented to the side contralateral to the stroke lesion. USN is found in about 23% of stroke patients. USN is more common in patients with Right sided lesions (42%) than Left sided lesions (8%) and is more persistent with Right sided strokes. Recovery of USN is common; most recovery occurs in the first 6 months and later recovery is less common. USN is associated with negative prognosis for functional outcome, poorer mobility, longer LOS in rehab, and slower rates of improvement; tend to be more functionally disabled at discharge (Wee & Hopman 2008).

Unilateral spatial neglect can be classified as **egocentric or allocentric**:

a) Egocentric neglect: Neglect of the body or personal space, tendency to neglect the opposite side of the lesion, in reference to the midline the body.
b) Allocentric neglect: Can be peripersonal or extrapersonal.

- Peripersonal space refers to space within the patient's normal reach.
- Extrapersonal refers to object /environment beyond the patient's normal reach.
- In allocentric neglect, the neglect is to the contralesional side of each object/environment in the peri/extrapersonal space.

More obvious forms of neglect involve colliding with environment on involved side, ignoring food on one side of plate, and attending to only one side of body. More subtle forms are more common, more apparent during high levels of activity such as driving, work, or interacting with others. Milder neglect involves various degrees of ignoring the affected side when faced with stimulation on the unaffected side (extinction).

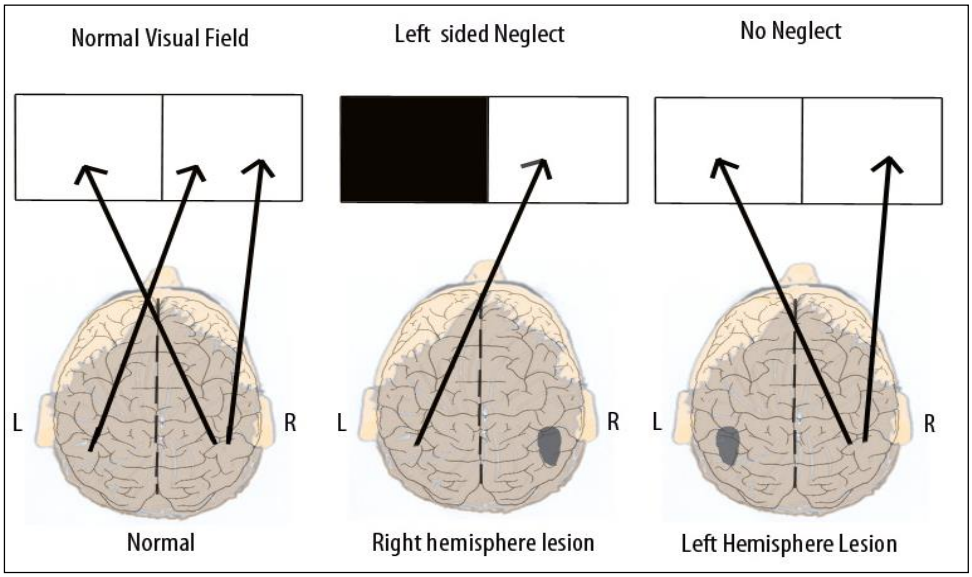
Anasognosia
Anasognosia refers to unawareness of loss of an important bodily function, primarily hemiplegia. It involves primarily large right hemispheric strokes which involve the parietal region.

5.8.2 Why is Left Sided Neglect More Common than Right Sided Neglect?

Unilateral spatial neglect is more common in patients with right-sided lesions than left. In the Copenhagen Stroke Study (Pedersen et al., 1997), 42% of individuals with a right-sided lesion were reported to have unilateral spatial neglect compared to only 8% of patients with a left hemisphere lesion. A study of 1,282 acute stroke patients (Ringman et al., 2004) revealed that 43% of patients with right-sided lesions experienced neglect compared to 20% of patients with left-sided lesions ($p<0.001$). At 3 months following stroke onset, 17% of patients with right-sided lesions continued to suffer from neglect compared to only 5% of patients with left-sided lesions.

There is evidence from positron emission tomographic (PET) scan analyses (Corbetta et al., 1993) and a systematic review of 17 studies (Bowen et al., 1999) that the right hemisphere regulates attention. Neuroanatomical findings have identified that the left hemisphere is responsible for modulating arousal and attention for the right visual field, whereas the right hemisphere controls these processes in both right and left visual fields (Feinberg et al., 1990). This may explain why unilateral spatial neglect is not typical for those with left hemisphere damage (LHD) post-stroke because the intact right hemisphere is capable of compensating for perceptual deficits that result from LHD (Feinberg et al., 1990)

Regulation of Attention by Cerebral Hemispheres



5.8.3 Spontaneous Recovery and Neglect

It has been reported that incidence of unilateral spatial neglect declines one month or more following the stroke event (Katz et al., 1999; Paolucci et al., 2001). In their 1999 review, Ferro and colleagues reported that, in many cases, the most conspicuous manifestations of hemi-spatial neglect resolved spontaneously within the first 4 weeks following a stroke event (Ferro et al., 1999). While further recovery may continue over the period of one year, it is not as significant as the recovery seen in the acute phase post stroke.

The degree of recovery may vary according to type of neglect. Appelros and colleagues demonstrated that patients experiencing neglect of peripersonal space experienced complete recovery less often than those

patients experiencing either neglect of far space or of personal space (Appelros et al., 2004). In the latter cases, complete recovery was seen by 6 months post stroke in 52% and 46% of cases, respectively compared with 13% of patients experiencing neglect of peripersonal space. For all three types of neglect, there were no further significant improvements seen from 6 months to one-year post stroke (Appelros et al., 2004).

5.8.4 The Impact of Neglect Post-Stroke

Unilateral spatial neglect has been reported to have a negative impact on functional recovery, length of rehabilitation stay, and need for assistance after discharge. While the majority of patients diagnosed with visuospatial inattention post-stroke recover by three months, those with severe visuospatial inattention on initial presentation have the worst prognosis (Diamond, 2001). Paolucci et al. (2001) reported unilateral spatial neglect to be a clearly negative prognostic factor. The presence of unilateral spatial neglect was associated with poorer functional outcome, poorer mobility, longer length of stay in rehabilitation and a greater chance of institutionalization upon discharge from rehabilitation. A 2005 study reported the presence of unilateral spatial neglect to be a significant predictor of length of stay (Gillen et al., 2005). In that study, patients with right-sided stroke and unilateral spatial neglect were matched for severity of functional deficits (FIM scores) at admission to rehabilitation with patients with right-sided stroke and no unilateral spatial neglect. It was determined that among patients with similar functional deficits, the presence of unilateral spatial neglect was associated with longer lengths of stay and slower rates of improvement (Gillen et al., 2005).

The presence of unilateral spatial neglect has been identified as a significant predictor of functional dependence in ADLs (Appelros et al., 2002; Katz et al., 1999) and poorer performance in IADLs at six months (Katz et al., 1999) and one year post discharge from rehabilitation (Jehkonen et al., 2000). The presence of unilateral spatial neglect explained 73% of the total variance in IADL at a three-month follow up, 64% at six months and 61% at one-year in 57 subjects post stroke (Jehkonen et al., 2000). Appelros et al. (2003) reported unilateral spatial neglect to be a significant predictor of both mortality (OR=2.7) and dependency (OR=4.0) one year after the stroke event. In addition, substantial proportions of individuals (79 – 82%) with neglect require home assistance following discharge (Appelros et al., 2003; Katz et al., 1999) or may be discharged to nursing home care (Appelros et al., 2003; Paolucci et al., 2001).

5.9 Screening and Assessment Tests for Unilateral Neglect

Screening and assessment tests for neglect can be performed via pen and paper test and by observation of behavioural/activity, or a combination of both. It is important to note that a single test may detect a specific type of neglect, thus a battery of tests are often more sensitive that single test.

Category	Rationale	Individual Assessment Tools
Visuospatial Processing & Neglect	These outcome measures assessed visuospatial processing and orientation to examine neglect severity	• Albert's Test • Auditory Subjective Median Plane (Midline) • Baking Tray Task • Balloons Test • Barrage test • Behavioural Inattention Test (BIT)

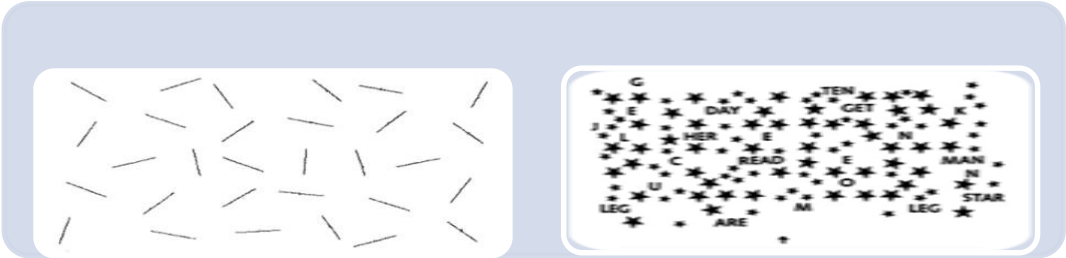
		• Bell's Test • Catherine Bergego Scale • Center of Cancellation • Clock Drawing Test • Coin Sorting • Comb and Razor Test • Cued Detection Task (Posner Cueing Task) • Dichotic Listening Task • Extinction Task • Fluff Test • Functional Neglect Index • Grey Scales • Hand Judgement Test • Harrington-Flocks Visual Screener • Joint Position Sense Test (JPST) • Judgement of Drawing of Two Houses • King Devick Test (Subtests 1,2,3) • Landmark Test • Lane Tracking Task • Line Cancellation (Line Bisection) Test • Line Crossing Test • Mobility Assessment Course • Motor-Free Visual Perception Test (MVPT) • Munich Reading Texts • Neale Analysis of Reading Ability • Ogden Figure Copying Task • Orientation Lines Test • Ota's Task • Quadruplet Detection Task • Real Objects Test • Rey-Osterrieth Complex Figure Test • Rivermead Perceptual Assessment Battery • Semi-structured Scale for the Functional Evaluation of Hemi-attention • Sentence Reading Test • Single and Double-digit Cancellation • Subjective Neglect Questionnaire • Tangent Screen Exam • Target Cancellation • Testing Battery for Attentional Performance • Unawareness and Behavioural Neglect Index • Verbal Cancellation Test (Letter Cancelation) • Vienna Test System – Peripheral Perception • Visual Scanning Tasks • Visual Subjective Straight Ahead • Wundt- Jaslow Illusion Test

Learning and Memory	These outcomes measures assessed an individual's ability to explicitly and implicitly learn and recall information	• Corsi Vertical Span Test
Global Cognition	These outcome measures assessed an individual's overall cognitive processing capability factoring in multiple domains.	• Mini Mental Status Examination (MMSE) • Ravens Coloured Progressive Matrices • Wechsler Adult Intelligence Scale (WAIS)
Motor Rehabilitation	These outcome measures covered gross motor movements, as well as fine, dexterous movements when using the upper extremities.	• Action Research Arm Test (ARAT) • Box and Block Test (BBT) • Fugl-Meyer Assessment • Functional Test for the Hemiparetic Upper Extremity (FTHUE) • Motricity Index • Nine Hole Peg Test (9HPT) • Rivermead Mobility Index (RMI) • Wolf Motor Function Test
Stroke Severity	These outcome measures assessed the severity of one's stroke through a global assessment of a multitude of deficits a stroke survivor may experience.	• Canadian Neurological Scale (CNS) • National Institutes of Health Stroke Scale (NIHSS) • Modified Rankin Scale (MRS)
Activities of Daily Living	These outcome measures assessed performance and level of independence in various everyday tasks	• Activities of Daily Living Questionnaire • Barthel Index (BI) • Functional Independence Measure (FIM) • Help Index (Help Scale)

5.9.1 Visuospatial Processing & Neglect

Cancellation Test

Several versions of cancellation tests are available. These tests equire the patient to cancel/mark target items printed on a paper placed directly in front of them. Cancellation can either be: 1) single target items (no distractors): Line cancellation/crossing test; 2) target item with distractors: Bells Test, star cancellation, alphabet.



Line Cancellation @ Crossing Test

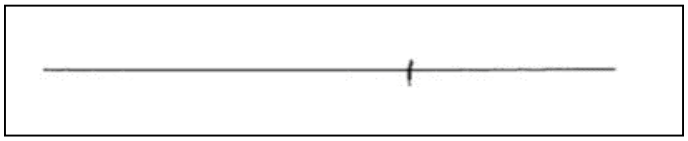
Composed of a page printed with black lines in random orientations.Patients are asked to cross out every black line.

Star Cancellation Test

The test consists of a page printed with 56 small stars, 52 large stars, 13 letters, and 10 short words. Patient is asked to cross out all the small stars

Line Cancellation (Line Bisection) Test (see Bell's Test. AKA Schenkenberg Test).
The line cancellation test is another version of a cancellation task used to detect the presence of neglect in stroke. Subjects are asked to cross out lines on a page filled with lines of various orientations. If lines are consistently crossed out closer to one side of each line than another, this can be interpreted as evidence of unilateral visual neglect. Any areas on the page where lines have failed to be crossed can also be used to evaluate neglect (Schenkenberg, Bradford & Ajax, 1980).

In the Line Bisection Test the patient is asked to find the midline on a number of horizontal lines.



Line Bisection Test

Questions	Answer
What does it measure?	Designed to detect the presence of unilateral spatial neglect.
What is the scale?	The LBT consists of 18 horizontal lines drawn on a single piece of paper. Patients are required to place a mark on each line that bisects it into two equal parts.
What are the key scores?	The test is scored by measuring the distance from the bisection mark to the actual center of the line. A deviation of 6mm or more is indicative of unilateral spatial neglect. USN may also be suggested if the patient omits two or more lines on one half of the page.
What are its strengths?	Simple and inexpensive measure of USN. Does not require formal training to administer.
What are its limitations?	The LBT may not be able to detect USN in as many as 40% of patients with severe USN (Ferber and Karnath 2001). The LBT should only be used as a screening tool as positive results could be indicative of other syndromes, such as hemianopia (Ferber and Karnath 2001).

Behavioural Inattention Test (BIT)

The BIT screens for unilateral visual neglect. It involves conventional testing (6 subtests) and 9 behavioral tests. The BIT is a battery of tests intended to evaluate the presence and severity of visual neglect. It consists of two subtests, a 'conventional subtest' and a 'behavioural subtest'. The conventional subtest consists of 6 items (eg. Line crossing, letter cancellation, etc…). The behavioural subtest consists of 9-items that are functional activities as opposed to standardized neglect tests (eg. telephone dialing, map navigation etc…). A maximum score for the BIT, the conventional subtest and the behavioural subtest are 227, 146 and 81 respectively, with higher scores indicating more severe impairment. The scale proven to have good test- retest validity and accurately predicts poor functional outcomes in stroke (Jehkonen et al. 2000; Wilson et al. 1987).

Behavioural Inattention Test

Questions	Answer
What does it measure?	Screens for unilateral visual neglect and provides information relevant to its treatment (Halligan et al. 1991).
What is the scale?	The BIT is divided into two major sections, each of which has its own set of subtests. The conventional section (BITC) is comprised of the following 6 subtests: line crossing, letter cancellation, star cancellation, figure and shape copying, line bisection, and representational drawing. The behavioural section (BITB) is comprised of the following 9 subtests: pre-scanning, phone dialing, menu reading, article reading, telling and setting the time, coin sorting, address and sentence copying, map navigation, and card sorting.
What are the key scores?	The BIT yields a total score out of 227 with higher scores indicating greater degrees of neglect. Cutoffs have been established for the total BIT as well as for each of the subsections with scores exceeding the cutoffs leading to a diagnosis of neglect. The cutoff for the total BIT is 196 out of 227, 129 out of 146 for the BITC, and 67 out of 81 for the BITB (reported in Menon and Korner-Bitensky, 2004).
What are its strengths?	The BIT is a comprehensive battery that provides a detailed and ecologically valid assessment of patient functioning (Halligan et al. 1991). A parallel form of the test is available, which allows for re-testing with minimal concern for practice effects. The behavioural subtests can be used to help therapists target tasks that should be given particular attention during treatment.
What are its limitations?	The BIT is both more time consuming and more expensive than most non-battery tests of neglect. Requiring 40 minutes for completion, the BIT is more taxing on patients than individual tests of neglect.

Comb and Razor Test

The Comb and Razor Test is a clinical test for personal neglect (neglect of personal space), in which the participant is given a comb and a razor (or powder compact case for women) and instructed to comb their hair or shave/apply makeup on their face. The number of strokes within 30 seconds are categorized into left, ambiguous or right strokes. The score is most often calculated based on the percent bias of strokes to a particular side. Scores fall anywhere between -1 (total left neglect) and +1 (total right neglect). The test has proven to be highly reliable and be able to distinguish between different known groups of participants (right or left-brain stroke, healthy individuals, extra personal neglect) (Beschin et al. 1997).

Catherine Bergego Scale
Catherine Bergego Scale involves direct observation of spontaneous (i.e., self-initiated) behaviors in 10 everyday activities. The CBS is a 10-item measure of functioning in everyday tasks used to assess unilateral neglect in stroke patients and anosognosia. A rater will score the patient on a 4-point scale (0 = no neglect, 3 = severe neglect) for each of the items, for example "Forgets to groom or shave left part of his/her face" (Item 1). There is a total score of 30, with higher scores corresponding to greater levels of impairment. The scale has proven to be both reliable and valid in assessing neglect and anosognosia (Azouvi et al. 2003; Azouvi 1996).

Clock-drawing Test for Visual Neglect
Performance on the CDT is most related to functions subserved by the right hemisphere (Suhr et al. 1998) and when used with other assessments may help to create a more complete picture of cognitive function. However, performance of the clock drawing task may be affected by other conditions prevalent in rehabilitation settings such as visual neglect, hemiparesis and motor dyscoordination (Ruchinskas & Curyto 2003). The reported sensitivity of the CDT when used to detect neglect appears poor (55.3%, Maeshima et al. 2001; 42%, Agrell et al. 1997) when compared to other assessments for neglect including cancellation tests, Albert's test and line bisection. Although visual neglect can be apparent on Clock Drawing Test, it is not sensitive in diagnosing visual neglect and is influenced by other cognitive problems such as executive function.

Motor-Free Visual Perception Test (MVPT)
The MVPT is a measure of visual- perceptual ability independent of motor ability. Spatial relationships, visual discrimination, figure-ground, visual closure and visual memory are assessed. A total raw score is obtained based on the number of correct responses and standard score, percentile rank and age-equivalent score are generated. In the current version (MVPT-4), the test contains 45 items. The MVPT exhibits acceptable construct, content and criterion validity as well as good test-retest reliability and internal consistency (Brown & Peres, 2018).

Rey-Osterrieth Complex Figure Test
The ROCFT is a measure of visuo-spatial abilities and visual memory. The test requires the subject to copy a complex geometrical figure and, after an interval, reproduce the figure from memory without forewarning. The most used method of scoring the test is the Osterrieth method, a scoring system that provides a 36-point summary score based to the presence and accuracy of 18 units of the figure. The test has been shown to have excellent interrater reliability and good discriminant validity (Salvadori et al. 2018).

5.9.2 Motor Rehabilitation

Action Research Arm Test (ARAT)
The ARAT is a commonly used observational measure to quantify upper extremity motor rehabilitation after stroke. It consists of 4 subtests: grasp, grip, pinch and gross motor. It is scored on a scale from 0 (no movement) to 3 (normal movement). ARAT has been shown to have good predictive validity in mild to moderate stroke without severe cognitive impairment as well as excellent test-retest and interrater reliability (Chen et al. 2012; Platz et al. 2005).

Box and Block Test (BBT)

The BBT is a measure of gross unilateral manual dexterity in stroke survivors. This measure consists of 1 functional task. This task involves a patient moving as many wooden blocks as possible from one end of a partitioned box to the other, in a span of 60 seconds. Patients are scored based on the number of blocks theytransfer (the higher the blocks transferred, the better the outcome). The measure has been shown to have good reliability and validity. (Higgins et al. 2005; Platz et al. 2005).

Fugl-Meyer Assessment

The FMA is one of the most commonly used measures of motor impairment post-stroke (Gladstone et al. 2002). The five domains of the assessment include motor rehabilitation, sensory function (maximum score of 24), balance (maximum score of 14), joint range of motion (maximum score of 44), and joint pain (maximum score of 44).The domain of motor rehabilitation can be divided into upper extremity (maximum score of 66) and lower extremity (maximum score of 34) subscales. Each of the subscales or domains can be administered individually to stand on their own. This assessment has demonstrated excellent Inter/intra-rater reliability, internal consistency, and criterion validity (Duncan et al. 1983; Lin et al. 2004; Malouin et al. 1994).

Nine Hole Peg Test (9HPT)

The 9HPT is a measure of overall manual dexterity in stroke survivors. The measure consists of 1 functional task. Patients are asked to take 9 pegs out of a container and insert them into the pegboard. Once all 9 pegs are inserted, they are then taken out of the pegs as quickly as possible and placed back in the container. Patients are scored on how quickly they can insert and take out the pins, so the faster the time, the better the outcome. This measure has been shown to have good reliability and concurrent validity (da Silva et al. 2017).

Wolf Motor Function Test

The Wolf Motor Function Test is a measure that quantifies upper extremity motor ability in stroke survivors. The measure consists of 17 tasks (e.g. lifting arm up using only shoulder abduction, picking up a pencil, picking up a paperclip). These tasks are then subdivided into 3 areas: functional tasks, measures of strength, and quality of movement. Patients are scored on a 6-point scale (1=cannot complete task, 6=completes task as well as the unaffected side. This measure has been shown to have good reliability and validity (Wolf et al. 2005; Wolf et al. 2001).

5.9.3 Stroke Severity

Canadian Neurological Scale (CNS)

The CNS is a measure used to assess neurological status of acute phase stroke patients. Ten clinical domains including motor rehabilitations, both weakness and response of arm, face and legs are measured along with mentation (speech, orientation and level of consciousness). The scale has demonstrated reliability and concurrent validity (Cote et al. 1989; Cote et al. 1986).

National Institutes of Health Stroke Scale

The NIHSS is a measure of somatosensory function in stroke patients during the acute phase of stroke. This measure contains 11 items and 2 of the 11 items are passive range of motion (PROM) assessments delivered by a clinician to the upper and lower extremity of the patient. The other 9 items are visual exams conducted by the clinician (e.g. gaze, facial palsy dysarthria, level of consciousness). Each item is then scored on a 3-point scale (0=normal, 2=minimal function/awareness). This measure has been shown to have good reliability and validity (Heldner et al. 2013; Weimar et al. 2004).

Modified Rankin Scale (MRS)
The MRS is a measure of functional independence for stroke survivors. The measure contains 1 item. This item is an interview that lasts approximately 30-45 minutes and is done by a trained clinician. The clinician asks the patient questions about their overall health, their ease in carrying out ADLs (cooking, eating, dressing) and other factors about their life. At the end of the interview the patient is assessed on a 6-point scale (0=bedridden, needs assistance with basic ADLs, 5=functioning at the same level as prior to stroke). This measure has been shown to have good reliability and validity (Quinn et al. 2009; Wilson et al. 2002).

5.10 Treatments of Spatial Neglect

5.10.1 Remedial Versus Compensatory Approach

Treatments of neglect can be divided into a compensatory or remedial approach:

Remedial
Remedial training aims for direct restoration of function. It focuses on training the patient to voluntarily compensate for their deficits. The Remedial approach requires full cooperation from the patient; the patient must be aware of the deficit. Top down focus on disability and not impairment. Example is visual scanning or visual/mental imagery where the patient is aware they have a deficit and is taught to actively compensate for that deficit.

Compensatory Approach
Compensatory approaches involve adapting the external environment. Bottom-up focus to increase a patient's perception of space. Commonly uses sensory stimulation. This approach does not require the patient to be aware of the deficit. Here the focus is on the level of impairment, e.g. altered perception.
Examples:

- Prisms adaptation
- Limb activation therapy
- Feedback training
- Neck muscle vibration
- Trunk rotation
- Eyepatching and Hemispatial Glasses
- Caloric Stimulation
- Optokinetic Stimulation
- TENS and Neck Vibration

Remedial Treatments in Unilateral Spatial Neglect

5.10.2 Visual Scanning

Patients with neglect often don't visually scan their whole environment, thus paying no attention to their left-sided space. Visual scanning involves teaching patients to look to left side in a consistent manner. It has been reported that individuals with neglect do not visually scan their whole environment (Weinberg et al. 1977), paying no attention to their affected side (Ladavas et al. 1994). Visuoperceptual or

visuospatial training, including training of visual scanning, attempts to improve the deficits of visual attention associated with neglect (Pierce & Buxbaum 2002). Cicerone et al. (2000) noted that the research literature concerning remediation of visuospatial deficits encompassed two basic approaches. One group of studies addressed the remediation of basic abilities and behaviour, such as visual scanning or visual perception, while the second focussed on the remediation of functional or constructional activities requiring spatial ability. By teaching behavioural skills such as visual scanning, the patient can re-learn to scan and explore the affected hemifield to a greater degree.

Highlighted Study

Weinberg J, Diller L, Gordon WA, Gerstman LJ, Lieberman A, Lakin P, Hodges G, Ezrachi O. Training sensory awareness and spatial organization in people with right brain damage. Arch Phys Med Rehabil 1979; 60:491-496.		
53 RH stroke patients >4 weeks post onset randomly assigned to either 20 hours/4 weeks of specific neglect training (NT) vs 20 hours OT/PT over 4 weeks. Severe NT group improved on 24 of 26 psychology test scores; Mild NT > control on 3 of 26 scores while severe NT > control on 15 of 26 scores.		

Highlighted Study

Paolucci S, Antonucci G, Guariglia C, Magnotti L, Pizzamiglio L, Zoccolotti P. Facilitatory effect of neglect rehabilitation on the recovery of left hemiplegic stroke patients: a cross-over study. J Neurol 1996; 243:308-314.		
Cross-over RCT (6) N_{start}=59 N_{end}=51 TPS=Subacute	E: Neglect Specific Training C: General Cognitive Treatment Duration: 1hr/d, 5d/wk for 8wk	• Rivermead Mobility Index (+exp) • Barthel Index (+exp) • Canadian Neurological Scale (-) • Letter Cancellation Test (+exp) • Albert's Barrage Test (-) • Wundt-Jastrow Area Illusion Test (+exp) • Sentence Reading Test (+exp)
59 right hemispheric stroke patients onset 2-6 months randomized to neglect Rx 5 hours/week x 8 weeks and then general cognitive Rx 3 hours/week x 8 weeks in cross-over design.		

Highlighted Study

Chan DY, Man DW. Unilateral neglect in stroke: A comparative study. Topics in Geriatric Rehabilitation. 2013 Apr 1;29(2):126-34.		
RCT (6) N_{Start}=40 N_{End}=40 TPS=Acute	E: Visual Scanning Training + Conventional Rehabilitation C: Conventional Rehabilitation Only Duration: 45min/d, 3d/wk for 4wk	• Catherine Bergego Scale (+exp) • Mini Mental State Examination (-) • Modified Barthel Index (-) • Behavioural Inattention Test (-) • Conventional Subtest (-)
Chan and Man (2013) found significantly greater reductions of unilateral neglect in the visual scanning group and a significant improvement in activities of daily living. The authors also observed a generalization effect where strategies used during visual scanning (eg. identifying an anchor on the left-hand side at all times) led to improvements in self-care tasks.		

Overall, the impact of visual scanning procedures on neglect has tended to be positive. Two studies compared a visual scanning program to no treatment and found visual scanning to significantly improve performance on tasks assessing visual perception (Antonucci et al. 1995, Niemeier et al. 2001). Similar

results were also observed in seven studies that contrasted visual scanning therapy to a form of conventional rehabilitation therapy.

In addition to measuring the impact of treatment on perceptual ability, six studies (five of which were RCTs) assessed the impact of visual scanning training on functional ability. In all six, participation in the treatment condition was associated with improved functional ability. However, it is unclear whether treatment effects are sustained.

Levels of Evidence for Visual Scanning Training

Intervention	Visualspatial Processing & Neglect	Global Cognition	Motor Rehab	Stroke Severity	ADLs
Visual Scanning Training	1a 5 RCTs	1b 2 RCTs	1b 1 RCT	1b 1 RCT	1a 4 RCTs

Conclusions
The literature is mixed regarding visual scanning training for improving neglect.
Visual scanning training may not be beneficial for improving activities of daily living.

5.10.3 Computer-Based Scanning in Neglect

Computer versions of tasks associated with visual scanning have been developed and their use evaluated. Computer training offers a means to supplement costly therapy with massed practice.

Highlighted Study

Robertson IH, Gray JM, Pentland B, Waite LJ. Microcomputer based rehabilitation for unilateral left visual neglect: A randomized controlled trial. Arch Phys Med Rehabil 1990; 71:663-638.		
RCT (6) N_{start}=36 N_{end}=32 TPS=Chronic	E: Computer Scanning + Attentional Training C: Recreational Computing Duration: 45min/d, 3d/wk for 4wk	• Behavioural Inattention Test (-) • Wechsler Adult Intelligence Scale (-) • Neale Reading Test (-) • Letter Cancellation Test (-) • Rey-Osterreith Test (-)
36 stroke patients with unilateral left VF neglect randomized to computer scanning and attention training (mean 15.5 hours) or recreational computing (mean 11.4 hours). No significant difference noted between 2 groups on any outcome measure.		

Levels of Evidence for Computer-Based Visual Scanning

Intervention	Visualspatial Processing & Neglect	Global Cognition	Motor Rehab	ADLs
Computer-Based Rehabilitation	1a 2 RCTs	1b 1 RCT	1b 1 RCT	1b 1 RCT

Conclusions
Computer-based visual scanning therapy for neglect appears to be effective in improving visual perception.

5.10.4 Virtual Reality Therapy for Neglect

There are several studies of virtual reality – promising but to date has been very expensive. Nintendo Wii and other gaming systems offers a potentially cheap alternative and is gaining in popularity on rehab units. Overall, most studies that used computer-based or virtual reality techniques for neglect treatment reported a positive effect on patients' awareness of the neglected space. Most of the interventions included made use of visual perception therapies; however, two studies also assessed the effectiveness of auditory alertness training for neglect (DeGutis & Van Vleet 2010, Van Vleet et al. 2014).

Levels of Evidence for Virtual Reality Therapy for Neglect

Intervention	Visualspatial Processing & Neglect	Learning and Memory	Global Cognition	Motor Rehab	Stroke Severity	ADLs

Conclusion
Virtual reality treatment for neglect appears to be effective in improving visual perception.

Compensatory Approach in Unilateral Spatial Neglect

5.10.5 Prisms Adaptation for Neglect

Prisms affect spatial representation by causing an optical deviation of the visual field. Prisms tend to shift the visual field input and increase visual fields by 5-10 degrees. Outside of visual field when looking straight ahead but when gaze is shifted to the affected side increases visual field. Prisms affect spatial representation by causing an optical deviation of the visual field to either the left or the right. One of the most common low vision interventions for stroke induced hemianopia is the incorporation of binocular sector prisms in the person's habitual spectacle lenses. These may be Fresnel membrane lenses or prisms that are cemented onto the lens surface. The prism is located so that it remains outside the residual field of view when the person if looking straight ahead. When gaze is shifted in the direction of the non-seeing hemi-field, the prismatic effect gives a more peripheral view to the side (6 - 9 deg.) than would otherwise be possible without a larger magnitude eye movement.

Highlighted Study

Rossi PW, Kheyfets S, Reding MJ. Fresnel prisms improve visual perception in stroke patients with homonymous hemianopia or unilateral visual neglect. Neurology 1990; 40(10):1597-1599.

RCT (4) N_{start}=39 N_{end}=35 TPS=Subacute	E: Prismatic Adaptation Treatment (8.5°, 15-diopter) C: No Treatment Duration: 4wks	• Barthel Index (-) • Motor-free Visual Perceptual Test (+exp) • Line Bisection Test (+exp) • Line Cancellation Test (+exp) • Tangent Screen Examination (+exp) • Harrington Flocks Visual Screener (+exp)
39 stroke patients with homonymous hemianopsia or unilateral spatial neglect randomly assigned to receive 4 weeks of treatment with Fresnel prisms or to control group. At baseline, both groups had similar MVPT response behavioural scores in the affected visual field (53.2 vs. 47.7). By the end of 4 weeks, experimental group improved significantly (p<0.01) relative to baseline and control group. Patients in the prism group also made significant improvements on the Line Bisection Test, the Line Cancellation Task, the Harrington Flocks Visual Field Screener, and the Tangent Screen Examination.		

Overall, a general positive effect of treatment is observed with prism adaptation in patients with neglect and homonymous hemianopsia (Rossi et al. 1990). In two RCTs, the authors found no differences in measures of neglect between patients using rightward shifted goggles compared to neutral goggles (Mancuso et al. 2012, Turton et al. 2010). However, these studies only used a prismatic shift of 5° and 6° while other successful prismatic interventions generally used a shift of 10° or greater (Barrett et al. 2012). Most of the included studies incorporated target pointing during prism adaptation and used a concurrent adaptation protocol, allowing the patient to view their limb during the reaching movement and make changes before completing the movement (Làdavas et al. 2011). Two recent studies, similar in methodology, showed different results.

Levels of Evidence for Prism Adaptation in Neglect

Intervention	Visualspatial Processing & Neglect	Learning and Memory	ADLs
Prism Glasses	**1a** **10 RCTs**	**2** **1 RCT**	**1b** **1 RCT**

<u>Conclusion</u>
Prismatic adaptation with a significant rightward shift appears to be beneficial for neglect; however, the long-term effect is unclear.
The literature is mixed regarding prism adaptation training for improving neglect.

5.10.6 Limb Activation Strategies

Limb activation is based on the idea that any movement of the contralesional side may function as a motor stimulus activating the right hemisphere and improving neglect. It is intended to increase orientation and attention to neglected hemi-space. A motor or externally-applied sensory stimulus to the affected side attempts to "activate" the right hemisphere. It includes limb activation (better studied) as well as application of a sensory stimulus (lesser studied).

Activation strategies are intended to increase orientation and attention to the neglected hemi-space. A stimulus, either a motor stimulus or externally applied sensory stimulus, to the affected side is thought

to "activate" the right hemisphere. The mechanism by which this might improve neglect is still under debate. The activation may be a general activation of the right hemisphere (Robertson et al. 1994), which improves attention control in the neglected space (Bailey et al. 2002).

Highlighted Study

Kalra L, Perez I, Gupta S, Wittink M. The influence of visual neglect on stroke rehabilitation. Stroke 1997; 28:1386-1391.		
RCT (7) N_{start}=50 N_{end}=46 TPS=Acute	E: Spatiomotor Cueing of Affected Limb in Deficit Hemispace C: Conventional Therapy Duration: 45min/d, 1d/wk for 12wk	Rivermead Perceptual Assessment Battery: • Cancellation (+exp) • Body Image (+exp) • Picture Matching (-) • Object Matching (-) • Size Recognition (-) • Series (-) • Missing Article (-) • Sequencing-pictures (-) • Right/Left Copying (-) • Word Colour Matching (-) • 3-dimensional Copying (-) • Figure Ground Discrimination (-) • Animal Halves (-)
50 stroke patients with visual neglect were randomized to spatiomotor cueing during motor activity (integrating attentional and motor functions using limb activation approach) vs. conventional therapy (aimed at restoring normal tone, movement patterns and motor activity). Intervention group had significantly shorter length of hospital stay (42 vs. 66 days, p=0.001), less time in physiotherapy and improved neglect scores at 12 weeks.		

Highlighted Study

Robertson IH, McMillan TM, MacLeod E, Edgeworth J, Brock D. Rehabilitation by limb activation training reduces left-sided motor impairment in unilateral neglect patients: A single-blind randomized control trial. Neuropsychological Rehabilitation 2002; 12:439-454.		
RCT (6) N_{start}=40 N_{end}=36 TPS=Subacute	E: Limb Activation Treatment + Perceptual Training C: Perceptual Training Duration: 45min/d, 3d/wk for 4wk	• Motricity Index (+exp) • Barthel Index (-) • Catherine Bergego Scale (-)
Improvement up to 24 months in LA+PT with little improvement in PT group.		

Levels of Evidence for Limb Activation in Neglect

Intervention	Visualspatial Processing & Neglect	Motor Rehab	ADLs
Limb Activation	**1a** **3 RCTs**	**1b** **1 RCT**	**1b** **1 RCT**

Conclusions

Limb activation may not be beneficial for improving neglect.

5.10.7 Sensory Feedback Strategies for Neglect

Feedback strategies are intended to improve awareness and attention to neglected space. This includes auditory and visual feedback. Sensory stimulation makes patients aware of his/her neglect behaviors and may assist in learning ways to remediate neglect.

Highlighted Study

Fong KNK, Yang NYH, Chan MKL, Chan DYL, Lau AFC, Chan DYW, . . . Chan CCH. Combined effects of sensory cueing and limb activation on unilateral neglect in subacute left hemiplegic stroke patients: a randomized controlled pilot study. *Clinical Rehabilitation* 2013; 27(7):628-637		
RCT (9) N_{Start}=40 N_{End}=35 TPS=Subacute	E: Conventional Rehabilitation + Cued Arm Movements C: Conventional Rehabilitation + Instructions to Move as Much As Possible Duration: 3hr/d, 5d/wk for 3wk	Behavioural Inattention Test Conventional Subtest: • Cancellation Tasks (-) • Drawing Tasks (+exp) Fugl-Meyer Assessment - Upper Extremity • Motor Subscore (-) • Hand Subscore (-) • Functional Test for Hemiplegic Upper Extremity (-) • Functional Independence Measure- Motor Subscale (-)
The authors compared a cued limb activation protocol to instructions to move as much as possible and found rightward bias to be significantly alleviated with cued activation. Although this suggests improvements in the patients' awareness of their hemiplegic field, the authors failed to find the same benefit for visual target detection and functional ability when compared to the control intervention.		

Highlighted Study

Polanowska K, Seniow J, Paprot E, Lesniak M, Czlonkowska A. Left-hand somatosensory stimulation combined with visual scanning training in rehabilitation for post-stroke hemineglect: a randomised, double-blind study. Neuropsychol Rehabil 2009; 19(3):364-382.		
RCT (7) N_{Start}=40 N_{End}=35 TPS=Subacute	E: Computerized visual scanning training + electrical somatosensory stimulation C: Computerized visual scanning training + sham stimulation Duration: 30min/d, 2d/wk for 6wks	• Barthel Index (-) • Functional Independence Measure (-) • Visual scanning accuracy (+exp) • Visual scanning range (+exp)
A single, recent RCT examined the impact of supplementing visual scanning training with electrical somatosensory stimulation applied to the left hand of patients with left-sided visual neglect (Polanowska et al. 2009). While all study participants demonstrated significant gains over the course of the 1-month-long treatment, individuals who received the supplementary stimulation demonstrated greater improvement on measures of neglect. Unfortunately, there was no similar improvement in functional ability associated with treatment allocation.		

Levels of Evidence for Sensory Stimulation

Intervention	Visualspatial Processing & Neglect	Learning and Memory	Global Cognition	Motor Rehab	Stroke Severity	ADLs

Conclusions
The use of external sensory stimulation in the treatment of neglect may be beneficial, although evidence is limited.
Electrical somatosensory stimulation may be a useful supplement to visual scanning training.
Visuomotor feedback strategies appear to be beneficial in the treatment of neglect.

5.10.8 Mirror Therapy

Highlighted Study

Pandian J, Arora R, Kaur P, Vishwambaran D, Arima H. Mirror therapy in unilateral neglect after stroke (MUST trial). Neurology 2014; 83(11):1012-1017.		
RCT (8) N_{Start}=48 N_{End}=46 TPS=Acute	E: Mirror Training C: Sham Mirror Training Duration: 1.5hr/d, 5d/wk for 4wk	• Star Cancellation Test (+exp) • Line Bisection Test (+exp) • Picture Identification Task (+exp) • Functional Independence Measure: 1mo (-); 3mo (+); 6mo (+) • Modified Rankin Scale: 1mo (-); 3mo (+); 6mo (+)
This RCT investigated the effectiveness of mirror therapy for visual neglect. The authors used a sham mirror therapy condition as a comparison and found significantly greater improvements in measures of neglect and disability associated with mirror therapy.		

Provision of visual or visuomotor feedback appears to have a beneficial effect on the performance of various neglect behaviours. There is strong evidence feedback strategies are beneficial in treatment of neglect. More study required to establish the degree to which treatment effects generalize to other behaviors and to determine the durability of effect.

Levels of Evidence for Mirror Training

Intervention	**Visualspatial Processing & Neglect**
Mirror Therapy	**1b** **1 RCT**

Conclusion
Visuomotor feedback strategies appear to be beneficial in the treatment of neglect.
Mirror training may be beneficial for improving neglect.

5.10.9 Eye Patching and Hemispatial Glasses

Eye patching of the eye ipsilateral to lesion (right eye for left neglect) causes the patient to attend more to the unpatched side. Smania et al. (2013) reviewed 13 intervention studies which involved right or left monocular eye-patching for individuals who previously had a stroke and had hemi-spatial neglect. This review included five case-series/case-control studies, two single-case studies and six randomized controlled trials. This review concluded that eye-patching is a promising procedure in rehabilitation for those with hemi-spatial neglect (Smania et al. 2013).

Highlighted Study

Tsang MH, Sze KH, Fong KN. Occupational therapy treatment with right half-field eyepatching for patients with subacute stroke and unilateral neglect: a randomised controlled trial. Disabil Rehabil 2009; 31(8):630-637.		
RCT (7) N_{start}=35 N_{end}=34 TPS=Acute	E: Conventional Occupational Therapy + Right Half-field Eye Patching C: Occupational Therapy Duration: 3hr/d, 5d/wk for 4wk	• Behavioural Inattention Test - Conventional Subtest (+exp) • Functional Independence Measure (-)

There is limited evidence that monocular, opaque patching may not improve visual neglect (Beis et al. 1999; Walker et al. 1996). There is conflicting evidence bilateral half-field eye patches or right half-field eye patches for left visual neglect improves visual neglect and functional ability (Ianes et al. 2012; Tsang et al. 2009; Zeloni et al. 2002; Machner et al. 2014). Eye-patching is a promising intervention for neglect because of its high feasibility and low cost (Smania et al. 2013).

Levels of Evidence for Eye Patching and Hemispatial Glasses

Intervention	Visualspatial Processing & Neglect	Motor Rehab	Stroke Severity	ADLs
Eye Patching	**1b** **1 RCT**	**1b** **1 RCT**	**2** **1 RCT**	**1b** **3 RCTs**

Conclusions

Eye patching and hemispatial glasses may not be beneficial for neglect, stroke severity, motor rehabilitation.

They may be beneficial for activities of daily living.

5.10.10 Other Treatments

Caloric Stimulation

There is little evidence regarding the effectiveness of caloric stimulation as a treatment intervention for visual spatial neglect post stroke.

Conclusion

The effectiveness of caloric stimulation as part of a treatment intervention for unilateral spatial neglect has not been well studied.

Galvanic Vestibular Stimulation

Galvanic vestibular stimulation (GVS) is a variant of transcranial direct current stimulation (tDCS). It is a non-invasive neuromodulation technique that involves placing electrodes directly over the vestibular nerve (which is responsible for the patient's sense of balance) and sending electrical signals through the skull (Krewer et al. 2013a). Spatial perception and exploration is a multisensory task requiring the integration of signals from visual, auditory, proprioceptive and vestibular cortices (Barra et al., 2010). If neglect is assumed to be an error in the perceptual integration and transformation of this information, manipulating input (vestibular) could ameliorate the impact of neglect.

Levels of Evidence for Galvanic Vestibular Stimulation

Intervention	Visualspatial Processing & Neglect
Galvanic Vestibular Stimulation	1a 5 RCTs

<u>Conclusions</u>
Galvanic vestibular stimulation (GVS) may not be beneficial for improving neglect.
There does not appear to be a difference in efficacy between left or right GVS, and high or low volume GVS.

Optokinetic Stimulation

Optokinetic stimulation (OKS) uses a visual stimulus moving linearly from right to left to induce the optokinetic reflex and nystagmus in the contralesional direction (Pierce & Buxbaum 2002). By inducing the slow phase of nystagmus, a patient is 'forced' to spend more time focusing in the neglected hemifield. Like vestibular stimulation, optokinetic stimulation is also believed to function by modulating sensory input to the representation of personal space, and egocentric reference frames (Karnath 1996)

Levels of Evidence for Optokinetic Stimulation

Intervention	Visualspatial Processing & Neglect	Stroke Severity	ADLs
Optokinetic Stimulation	1b 1 RCT	2 1 RCT	2 1 RCT

<u>Conclusions</u>
The literature is mixed regarding optokinetic stimulation training for improving neglect. Although optokinetic stimulation appears to have a positive effect on neglect, it is uncertain whether the addition of optokinetic stimulation to a program of rehabilitation for neglect would be of benefit.

Trunk Rotation Therapy

It has been proposed that the orientation of the trunk midline in space functions as the dividing line between our personal representation of left versus right space and acts as an anchor for the calculation of body position (Karnath et al. 1991). Karnath et al. (1993) demonstrated that turning only the trunk of the patient to the left such that both right and left stimuli were projected to the right side of the trunk could compensate for deficits in reaction times to stimuli in the left visual field.

Levels of Evidence for Trunk Rotation Therapy

Intervention	Visualspatial Processing & Neglect	ADLs
Trunk Rotation Therapy	1b 1 RCT	1b 1 RCT

Conclusion
The literature is mixed concerning trunk rotation therapy for improving neglect and activities of daily living.

Neck Vibration Therapy

Neck muscle vibration is thought to improve neglect by creating a kinaesthetic illusion, whereby a spot of light will appear to move in the opposite direction of stimulation (Leplaideur et al., 2016). It is non-invasive, has no side-effects and is easy to apply (Schindler et al. 2002). This somatosensory stimulation can also increase awareness of the neglected hemifield, providing a cue of sorts to attend more to that side of the body.

Levels of Evidence of Neck Muscle Vibration

Intervention	Visualspatial Processing & Neglect	ADLs
Neck Muscle Vibration	2 1 RCT	2 1 RCT

Conclusion
The literature is mixed concerning visual exploration with neck muscle vibration for improving activities of daily living.

Transcutaneous Electrical Nerve Stimulation (TENS)

Transcutaneous electrical nerve stimulation (TENS) involves the application of electrical current through surface electrodes on the skin to facilitate activation of nerves (Teoli et al. 2019). The application of afferent electrical stimulation at the sensory level may help to enhance neuroplasticity of the brain, through increased activation and recruitment of cortical networks involved in information processing of

the contralesional hemifield. It is an alternative form of somatosensory stimulation, whereby the stimulation on the neglected side will also increase attention to the neglected side.

Levels of Evidence for TENS

Intervention	Visualspatial Processing & Neglect	Global Cognition	ADLs
TENS	1a 3 RCTs	2 1 RCT	1b 1 RCT

Conclusion
TENS may be beneficial for improving neglect.

5.10.11 Repetitive Transcranial Magnetic Stimulation

rTMS is commonly used to treat spatial neglect (Utz et al. 2011). Studies demonstrated a positive treatment effect associated with rTMS, with several RCTs finding improvement in neglect symptoms and performance of activities of daily living when compared to sham rTMS. Kim et al. (2013) found that both high-frequency and low-frequency rTMS were effective in improving neglect and performance on activities of daily living, with no significant difference in effectiveness between high and low frequency rTMS. There is moderate evidence that transcranial direct current stimulation is associated with improvement on tests of neglect although lesser quality studies suggest otherwise.

Highlighted Study

Yang NY, Fong KN, Li-Tsang CW, Zhou D. Effects of repetitive transcranial magnetic stimulation combined with sensory cueing on unilateral neglect in subacute patients with right hemispheric stroke: a randomized controlled study. Clinical rehabilitation. 2017 Sep;31(9):1154-63.		
RCT (7) N_{start}=60 N_{end}=60 TPS=Subacute	E1: rTMS Alone E2: rTMS + Sensory Cueing C: Sham rTMS Duration: 3hr/d, 5d/wk for 2wk	E1/E2 vs C Behavioural Inattention Test • Cancellation (+exp_2) • Drawing (-) • Bergego Scale (-) • Fugl-Meyer Assessment (-) • Action Research Arm Test (-) • Modified Barthel Index (-) E1 vs E2 • Behavioural Inattention Test (-) • Bergego Scale (-) • Fugl-Meyer Assessment (-) • Action Research Arm Test (-) • Modified Barthel Index (-)

Levels of Evidence for rTMS for Neglect

Intervention	Visualspatial Processing & Neglect	Motor Rehab	ADLs
rTMS	1a 5 RCTs	1a 3 RCTs	1b 1 RCT

Conclusions
The literature is mixed regarding rTMS for improving neglect and motor rehabilitation.
rTMS may not be beneficial for improving activities of daily living.

5.10.12 Theta-Burst Stimulation

Theta Burst Stimulation (TBS) is an emerging treatment modality that is a patterned form of rTMS where stimulation pulses are delivered in triplets or bursts at a high frequency (50Hz), and in a short interval (200ms), intending to mimic naturally occurring theta brain oscillations (Schwippel et al. 2019). TBS can also be used to adjust interhemispheric rivalry after a stroke through the delivery of continuous TBS (cTBS) to reduce cortical excitability in the contralesional hemisphere (600 pulses over 40 seconds); or intermittent TBS (iTBS) to increase cortical excitability in the ipsilesional hemisphere (600 pulses over 190 seconds) (Schwippel et al. 2019; Cotoi et al. 2019).

Highlighted Study

Koch G, Bonni S, Giacobbe V, Bucchi G, Basile B, Lupo F, Versace V, Bozzali M, Caltagirone C. Theta-burst stimulation of the left hemisphere accelerates recovery of hemispatial neglect. Neurology. 2012 Jan 3;78(1):24-30.		
RCT (9) N_{start}=20 N_{end}=18 TPS=Subacute	E: Continuous TBS + Conventional Therapy C: Sham TBS + Conventional Therapy Duration: 45min/d, 5d/wk for 2wk	• Behavioural Inattention Test (+exp)

Levels of Evidence for TBS

Intervention	Visualspatial Processing & Neglect
Theta Burst Stimulation	1a 6 RCTs

Conclusions
TBS may be beneficial for improving neglect.

5.10.13 Transcranial Direct Current Stimulation

Another form of non-invasive brain stimulation is transcranial direct-current stimulation (tDCS). Anodal stimulation is performed over the affected hemisphere and increases cortical excitability, while cathodal

stimulation is performed over the unaffected hemisphere and decreases cortical excitability (Alonso-Alonso et al. 2007). Additionally, tDCS can be applied on both hemispheres concurrently, this is known as dual tDCS. In contrast to transcranial magnetic stimulation, tDCS does not induce action potentials, but instead modulates the resting membrane potential of the neurons (Alonso-Alonso et al. 2007).

Highlighted Study

Ko MH, Han SH, Park SH, Seo JH, Kim YH. Improvement of visual scanning after DC brain polarization of parietal cortex in stroke patients with spatial neglect. Neuroscience letters. 2008 Dec 26;448(2):171-4.		
Cross-over RCT (8) N_{start}=15 N_{end}=15 TPS=Subacute	E: Active tDCS C: Sham Stimulation Duration: 20min, 48hr washout period	• Line Bisection Test (+exp) • Shape Cancellation Test (+exp) • Letter Cancellation Test (-)

Levels of Evidence for tDCS

Intervention	Visualspatial Processing & Neglect
Transcranial Direct Current Stimulation	**1b** **1 RCT**

Conclusion
tDCS may be beneficial for improving neglect.

5.10.14 Dopaminergic Medications

Marshall & Gotthelf (1979), as cited in (Pierce & Buxbaum 2002), reported that a reduced level of dopamine, a neurotransmitter, has been identified as playing a role in the arousal and orientation to stimuli.

Highlighted Study

Gorgoraptis N, Mah YH, Machner B, Singh-Curry V, Malhotra P, Hadji-Michael M, Cohen D, Simister R, Nair A, Kulinskaya E, Ward N. The effects of the dopamine agonist rotigotine on hemispatial neglect following stroke. Brain. 2012 Aug 1;135(8):2478-91.		
RCT (9) N_{Start}=16 N_{End}=16 TPS=Chronic	E: Rotigotine (9.0mg skin patch) C: Placebo Duration: (rotigone), 24hr, 3x during 6wk	• Mesulam Cancellation Task (+exp) • Bell's Cancellation Test (-) • Line Bisection Test (-) • Touch Screen Visual Search Task (-) • Visual Vigilance and Salience Task (-) • Corsi Vertical Span Test (-) • Motricity Index (-) • Nine-hole Peg Test (-) • Box and Blocks Test (-)

Levels of Evidence for Dopaminergic Drugs

Intervention	Visualspatial Processing & Neglect	Learning and Memory	Motor Rehab
Dopamine	1b 1 RCT	1b 1 RCT	1b 1 RCT

Conclusion
Dopaminergic medication may not be beneficial for improving neglect, learning and memory, and motor rehabilitation.

5.11 Rehabilitation for Aphasia

5.11.1 Definition of Aphasia

The AHCPR Post-Stroke Rehabilitation Clinical Practice Guidelines defines aphasia as "the loss of ability to communicate orally, through signs, or in writing, or the inability to understand such communications" (Klein 1995). Darley (1982) noted that aphasia is generally described as an impairment of language as a result of focal brain damage to the language dominant cerebral hemisphere. This serves to distinguish aphasia from the language and cognitive-communication problems associated with non-language dominant hemisphere damage, dementia and traumatic brain injury (Orange & Kertesz 1998). Expression of language is the most often affected.

5.11.2 Aphasia: Relation to Handedness

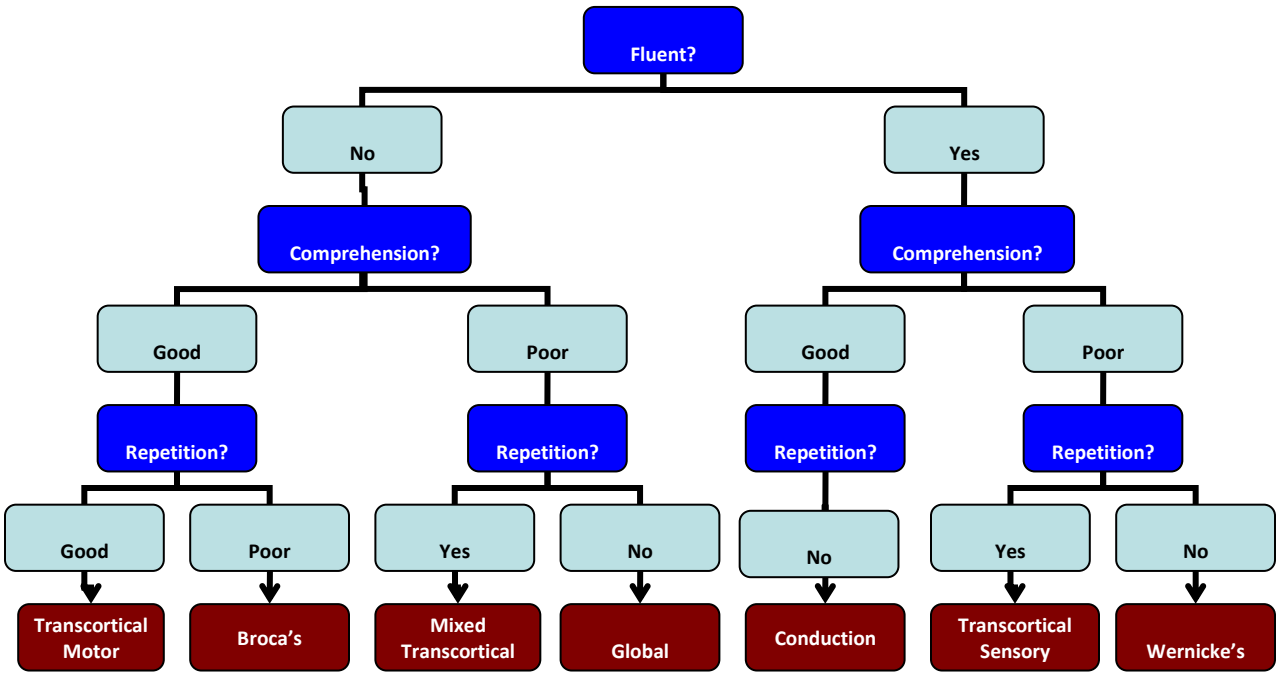
93% of the population is right hand dominant.

- Right hand dominant individuals – 99% use left hemisphere for language.
- Left hand dominant individuals– 70% use left hemisphere, 15% use right hemisphere and 15% use both hemispheres for language function.

5.11.3 Classification of Aphasia

Table 1. Boston Classification System - Characteristic Features of Aphasia

Type	Fluency	Comprehension	Repetition
Broca's	Nonfluent	Good	Poor
Transcortical motor	Nonfluent	Good	Good
Global	Nonfluent	Poor	Poor
Wernicke's	Fluent	Poor	Poor
Transcortical sensory	Fluent	Poor	Good
Anomic	Fluent	Good	Good
Conduction	Fluent	Good	Poor



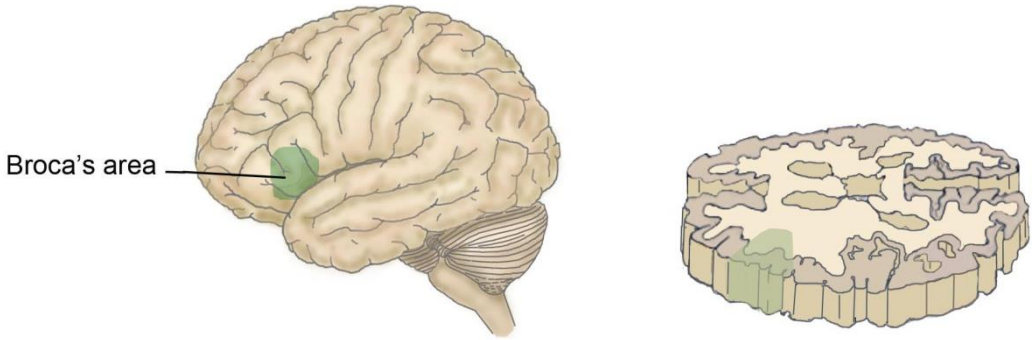
Paraphasias

Paraphasias are incorrect substitutions of words or parts of words. These can be:

- **Literal or phonemic paraphasias:** similar sounds (e.g., "sound" for "found" or "fen" for "pen").
- **Verbal or semantic paraphasias:** word substituted for another from same semantic class (e.g., "fork" for "spoon" or "pen" for "pencil").

Broca's Aphasia

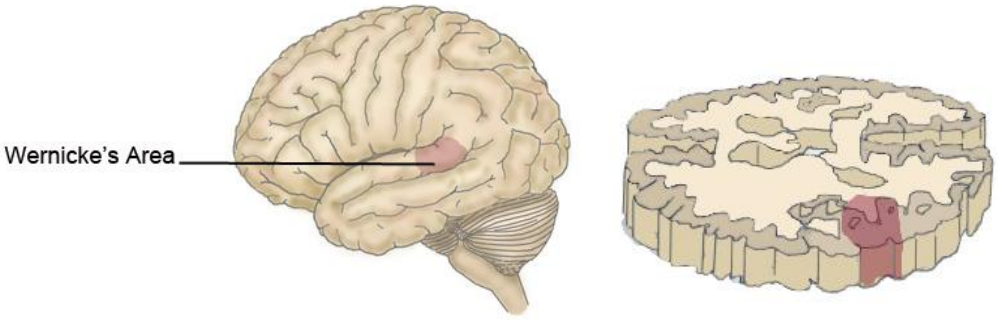
Broca's aphasia is also refered to as an expressive or motor aphasia. It tends to involve the posterior-inferior frontal lobe stroke characterized by nonfluent, effortful speech (sometimes referred to as telegraphic speech) with preserved comprehension and poor repetition. Patients with Broca's aphasia have problems with verbal output and their speech is nonfluent, hesitant, labored, with articulatory errors and paraphasias; speaking vocabulary and confrontation naming is severely impaired; understanding remains intact. Writing is similarly affected while reading is generally intact.



Anomic Aphasia
An anomic aphasia is a mild motor aphasia. Anomic aphasia is characterized by **w**ord-finding difficulties or mild articulatory errors (often called a verbal apraxia).

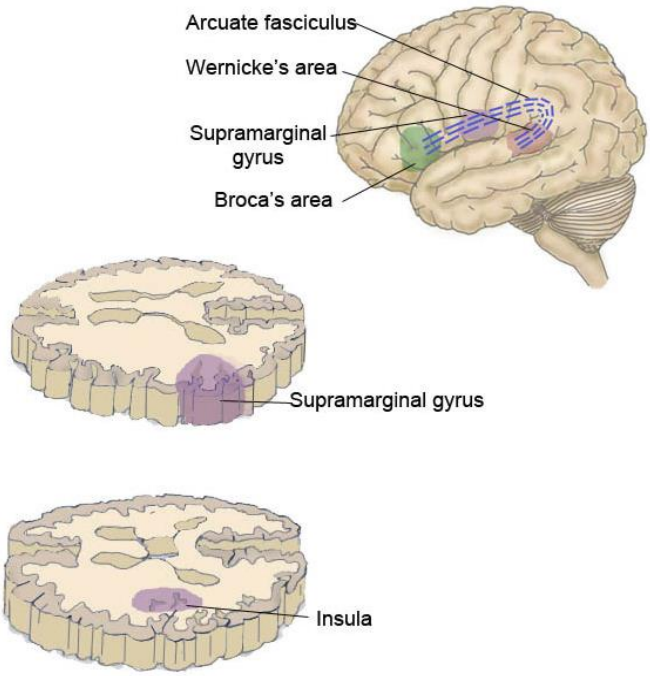
Transcortical Motor Aphasia
The stroke is located in the frontal lobe, anterior or superior to Broca's area or in the subcortical region deep to Broca's area. It is characterized by being nonfluent (reduced rate of speech and limited language output) with good comprehension and good repetition.

Wernicke's Aphasia
Wernicke's aphasia is a sensory aphasia. There is a problem with input or understanding of language. Wernicke's aphasia is a fluent speech with a severe comprehension deficit, poor repetition and often unintelligible jargon; reading is similarly affected. The stroke is localized to the posterior part of superior (first) temporal gyrus. Wernicke's aphasia is associated with marked paraphasias and neologisms.



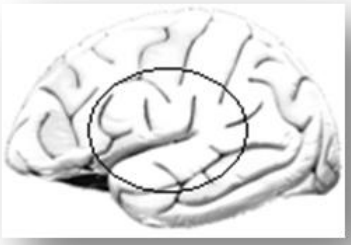
Transcortical Sensory Aphasia
Transcortical sensory aphasia is generally associated with a watershed stroke isolating the perisylvian speech structures (Broca's and Wernicke's areas) from the posterior brain. It is characterized by fluent speech (neologisms), poor comprehension and good repetition (possibly echolalia).

Conduction Aphasia
Conduction aphasa occurs with a stroke of the parietal operculum (arcuate fasciculus) or insula or deep to the supramarginalgyrus characterized by disproportional impairment in repeating spoken language. These patients use literal paraphasias with "targeting" of words (until getting the right one).



Global Aphasia

Global aphasia is a motor and sensory aphasia. In patients with this type of aphasia the problem is with both input (understanding of language) and output (verbal and writing) of language. There is no communication even with gestures and no speech or only stereotypical repetitive utterances. Both reading and writing are affected. These patients are often not good rehabilitation candidates because of difficulty with understanding, learning and following commands. This type of aphaisa is associated with a stroke generally involve the entire MCA region with moderate to severe impairment of language of all language function.



5.11.4 Natural History and Impact of Aphasia

It has been reported that aphasia is one of the most common consequences of stroke in both the acute and chronic phases. Acutely, it is estimated that from 21 – 38% of stroke patients are aphasic (Berthier 2005). A recent report based on data from the Ontario Stroke Audit (Ontario, Canada) estimated that 35% of individuals with stroke have symptoms of aphasia at the time of discharge from inpatient care (Dickey et al. 2010).

Global aphasia is the most common type in the acute period affecting as many as 25-32% of aphasic patients, while other classic aphasias described within the Boston system of classification are seen less frequently (Godefroy et al. 2002, Laska et al. 2001, Pedersen et al. 2004). The frequency of unclassified or mixed aphasias that cannot be assigned to a classic category is more difficult to determine. Godefroy et al. (2002) reported approximately 25% of patients as having non-classified aphasias, comprised mostly of disorders similar to anomic aphasia in addition to some other impairments. In that study, the presence of non-classified aphasia was significantly associated with a history of previous stroke. Initial stroke severity and lesion volume have been associated with initial severity of aphasia (Ferro et al. 1999, Laska et al. 2001, Pedersen et al. 2004).

For many, aphasia improves during the first year following the stroke event. A review by Ferro et al. (1999) reported that approximately 40% of acutely aphasic patients experience complete or almost complete recovery by one year post stroke. Similarly, Maas et al. (2012) found that 86% of stroke patients presenting with aphasia symptoms in an emergency setting experienced partial improvement within six months, 74% of whom had completely resolved. Most longitudinal studies have identified that the greatest amount of spontaneous recovery occurs in the first 3 months following stroke. After this, the rate of recovery slows and little additional spontaneous recovery can be expected after the first 12 months (Ferro et al. 1999). Pedersen et al. (2004) reported that during these first 12 months, aphasia of all types (even global aphasia) tended to evolve to a less severe form. While 61% of aphasic patients in the Copenhagen Aphasia Study still experienced aphasia one year post stroke, it was usually of a milder form.

Similarly, Bakheit et al. (2007b) demonstrated that patients with all types of aphasia experienced significant improvement in the first 6 months post-stroke when treated with conventional speech and language therapy as part of a comprehensive rehabilitation program. Improvements were greatest in the first 4 weeks, and then slowed to a lesser though still significant rate. Further, individuals diagnosed with Broca's aphasia demonstrated the greatest gains despite greater initial impairment. In general, patients with Broca's aphasia made greater gains in terms of scores on the Western Aphasia Battery (WAB) than patients with global aphasia, who in turn demonstrated greater improvement than those with Wernicke's, anomic or conduction aphasia. However, it should be noted that patients with anomic and conduction aphasia demonstrated better WAB scores at baseline and so did not require as much improvement in order to return to normal speech and language abilities as patients with Broca's or Wernicke's aphasias. Bakheit et al. (2007a) also cite previous literature that suggests severe and non-fluent aphasia progresses through phases of moderate aphasia such as conduction to less severe aphasia such as anomic aphasia before a full recovery.

The most powerful predictor of recovery may be the initial severity of aphasia such that greater severity is associated with poorer recovery (Berthier 2005, Ferro et al. 1999, Laska et al. 2001, Laska et al. 2011, Pedersen et al. 2004). Lazar et al. (2010) reported that more than 80% of recovery could be predicted based on initial severity of aphasia. In addition, the authors suggested that the relationship between recovery and initial impairment is proportional. Based on 21 stroke patients with mild to moderate aphasia and composite scores from 3 subtests of the Western Aphasia Battery (comprehension,

repetition and naming), the authors demonstrated that patients improved by 73% of maximum potential recovery (defined as maximum potential language score minus their initial WAB score) during the first 90 days post stroke. The authors suggested that this may be attributable to mechanisms of spontaneous recovery common to all domains of function.

5.12 Assessment and Aphasia Outcomes

Category	Rationale	Individual Assessment Tools
Discourse	These outcome measures assessed aspects of speech such as content and grammar, as well as the overall ability for giving instructions, storytelling or description.	• Content Units • Sabadel Story Retelling Task • Conversational Rating • Cookie Theft Picture Description • Discourse Quality • Discourse Quantity, Word and Utterance Count • Information Index • Speech Content Analysis
Naming	These outcome measures assessed an individual's ability to retrieve and name certain objects. This includes fluency, convergent naming, divergent naming and confrontation naming.	• Controlled Oral Work Association Test • Action Communication Test • Boston Naming Test • Object and Action Naming Battery • Picture Naming and Category Test • FAS Phonemic Fluency Task • Letter Fluency • Naming Tests (Fluency Tests) • Semantic Fluency Test • Verbal Fluency Test
Verbal Fluency	These outcome measures assessed the overall fluency of verbal expression. This includes aspects of speech such as prosody, the spontaneity of production or vocabulary and phase length.	• Mean Phrase Length • Mean Vocal Reaction Time • Melodic Intonation Therapy Task • Spontaneous Speech
Social Communication	These outcome measures assess the more social aspects of communication, such as social appropriateness and turn-taking.	• Amsterdam-Nijmegen Everyday Language Test • Functional Communication Profile • Communication Effectiveness Index • Informant's Rating • Communication Outcomes After Stroke Scale • Communicative Activity Log • Functional Communication Therapy Planner • Measure of Participation in Conversation • Speech Questionnaire

Repetition aaa	These outcome measures assess the ability for an individual to repeat a given word, phrase or text.	• Phonological Measures – repetition • Standardized Language Test
Writing	These outcome measures are designed to assess the ability of an individual to produce written language.	• Written Language
General Comprehension	These outcome measures assess an individual's ability to comprehend speech and/or language in multiple modalities.	• Gesture Comprehension • Semantic Association Test • Body-Part Identification • Discrimination Tasks
Reading Comprehension	These outcome measures specifically assess comprehension of written language and alphanumeric symbols.	• Reading Comprehension Battery for Aphasia
Auditory Comprehension	These outcome measures specifically assess comprehension of heard speech sounds.	• Complex Ideation • Miscellaneous Commands • Peabody Picture Vocabulary • Token Test • Phonological Measures – lexical decision
Global speech and Language	These outcome measures are generally comprehensive aphasia batteries that examine multiple aspects of speech and language. Should the study report specific subscales of these batteries, they will be counted towards their corresponding category above.	• Aachen Aphasia Test • American Speech-Language Hearing Association Functional Assessment of Communication Skills • Aphasia Severity Rating Scale • Boston Diagnostic Aphasia Examination • Communicative Activities in Daily Living • Comprehensive Aphasia Test • Concise Chinese Aphasia Test • Hemispheric Stroke Scale- Language • Montreal-Toulouse Aphasia Battery (MT-86) • Persian Language Test • Porch Index of Communicative Ability • Psycholinguistic Assessment of Language Processing in Aphasia • Reinvang's Aphasia Test • Rivermead Perception Assessment Battery • Spreen-Benton Test • Test Lillois de Communication • Western Aphasia Battery
Apraxia	These outcome measures assess apraxia impairment.	• Ideomotor Apraxia • Apraxia Battery for Adults

Activities of Daily Living	These outcome measures assessed performance and level of independence in various everyday tasks.	• Barthel Index (BI) • Functional Independence Measure (FIM) • Kuriansky Performance Test • Therapy Outcome Measure – activity

5.12.1 Discourse

Speech Content Analysis
Speech Content Analysis is a method of analysing speech based on a standardized rule set for scoring. Although the exact analysis may differ from study to study, all have the same basic principles. Speech is generally recorded, and the rated. There will be different variables, like significant words (verbs, nouns, adjectives etc…), content units (grammatical and semantic unit eg), pauses and other relevant aspects of speech production (Sabe et al., 1995).

5.12.2 Naming

Boston Naming Test
The Boston Naming Test is used as an assessment of the ability to retrieve words, and is commonly used in patients with aphasia (Roth 2011). 60 line drawings of various difficulty are presented and patients are asked to identify and name objects depicted (Ellis et al. 1992). This assessment has demonstrated good validity and reliability (Pedraza et al. 2011).

Naming Tests (Fluency Tests)
These tests can take many different forms but evaluate a patient's ability to demonstrate proper speech production and fluency. Patients do this by naming various objects and/or words. Common examples include naming items in picture form, naming words that fall into a specific category (eg. animals), or naming words that begin with a specific letter. Results are then analyzed by a trained clinician (Rabbit 2004).

Semantic Fluency Test
The Semantic Fluency Test is a cognitive assessment in which patients are instructed to produce as many words as possible from a given category (ex. countries of the world) within a set amount of time (usually 60 seconds). The patient is then rated on two distinct categories: speed and level of fluency (Lezak et al. 2004).

5.12.3 Verbal Fluency

Spontaneous Speech
Spontaneous Speech is a subtest of the Aachen Aphasia test, and the Western Battery Aphasia. It involves a semi-structured interview that is often recorded and rated afterwards. Spontaneous speech is assessed on 6 scales (production, articulation and prosody, sentence structure, word finding, sound structure and comprehension). All subscales are rated on a scale from 0-5, with smaller scores indicating greater levels of impairment (Miller, Willmes & De Bleser, 2000).

5.12.4 Social Communication

Amsterdam-Nijmegen Everyday Language Test
This is a measure of verbal communication in patients with aphasia. It assesses how understandable and intelligible verbal communication is. It contains 10 items, each of which relates to an everyday life situation in which an individual would need to speak. The situation Is briefly described, and the question of 'What do you say?" is posed to participant. Their verbal responses are scored based on a standardized rating scheme. It has shown good reliability, stability and ecological validity (Blomert et al. 1994).

Functional Communication Profile
The Functional Communication Profile is a measure of a patient's communication abilities, mode of communication, and degree of independence. Subtests include sensory/motor, attentiveness, receptive language, expressive language, pragmatic/social language, speech, voice, oral, fluency, non-oral communication.

5.12.5 Writing

Written Language
This is a component of many comprehensive aphasia batteries. Although the exact methodology may differ between types of written language tests, subjects are generally required to write down some requested information, a description or story and/or writing what is dictated to them.

5.12.6 Auditory Comprehension

Token Test
The Token Test is an assessment of auditory comprehension in patients with aphasia. This test is crucial for discovering subtle auditory comprehension deficits. It consists of 20 plastic tokens of two sizes (large and small), two shapes (square and round) and five colours. These items are then laid in front of a patient and they are then instructed to point to specific ones by a clinician. For example, the clinician could say: "point to a large token and then a square". The patient is then evaluated on how quickly and accurately they carried out this request (Coupar et al. 1976).

5.12.7 Global Speech and Language

Aachen Aphasia Test (AAT)
The AAT is a speech rating scale that includes 6 subscales. Spontaneous language, the Token Test, repetition, written language, naming, and comprehension. Each subscale is made up of multiple subtests, each examining various aspects of language comprehension, processing and production. The test originally developed in german has been translated to multiple different languages, ad has shown good validity and reliability (Miller, Willmes & De Bleser, 2000).

American Speech-Language Hearing Association Functional Assessment of Communication Skills
This is a measure of how speech, language, hearing, or cognitive deficits influence performance on activities of daily living (Frattali et al. 1995). The test includes 2 distinct scales, The Scale of Communication Independence and The Scale of Qualitative Dimensions of Communication. The first contains four

assessments (social communication, communication of basic needs, reading, writing and number concepts, and daily planning), all of which are made up of multiple items, scored on a 7-point Likert scale. The second scale contains 4 assessments (adequacy, appropriateness, promptness and communication sharing) that are graded on a 5-point Likert scale. The measure has shown good reliability, consistency and validity in multiple languages (Muò et al., 2015).

Boston Diagnostic Aphasia Examination
The Boston Diagnostic Aphasia Examination is a measure of aphasia and evaluates perceptual modalities, processing functions, as well as response modalities. The exam is made up of 8 subdomains (fluency, auditory comprehension, naming, oral reading, automatic speech, reading comprehension and writing) all of which contain multiple subtests. This assessment has demonstrated good construct validity in patients with aphasia (Fong et al. 2019).

Communicative Activities in Daily Living
The Communicative Activities in Daily Living is an assessment of functional communication skills in which 50 items are used to assess seven areas of communication ability (Holland 1980). These include reading, writing, and using numbers; social interactions; contextual communication; nonverbal communication; sequential relationships; humor, metaphor, absurdity; and internet basics (Holland 1980).

Porch Index of Communicative Ability
The Posche Index of Communicative Ability is a measure of comprehension, verbal expression, writing, and spelling. The patient is assessed on a 16-point scale (1=no awareness of task and no response, 16=complete/full awareness of the task and complex/thoughtful response) (Meikle et al. 1979).

The Rivermead Perception Assessment Battery
The Rivermead Perception Assessment Battery is an assessment of visual perceptual ability and includes 16 subtests (Picture Matching, Object Matching, Size Recognition, Series, Missing Article, Sequencing-Pictures, Right/Left Copying Words, Colour Matching, Right/Left Copying Shapes, Cube Copying, Three-Dimensional Copying, Cancellation, Figure-Ground Discrimination, Animal Halves, Body-Image Self-Identification and Body Image). A trained clinician then compiles all the results and evaluates the patient

Western Aphasia Battery
The Western Aphasia Battery is an assessment of linguistic and nonlinguistic skills of individuals with aphasia. It characterizes strengths and weaknesses in fluency, comprehension, repetition, and naming (Pritchard & Dipper 2018). This measure has three composite scores consisting of the language quotient, the cortical quotient, and the aphasia quotient (Shewan & Kertesz 1980). This measure has been demonstrated to be valid, with excellent reliability (Shewan & Kertesz 1980).

5.13 Therapy of Aphasia Post-Stroke

Many studies of speech and language therapy post-stroke. Robey (1998), in a meta-analysis, found SLT had a significant impact acutely and a lesser but still significant impact chronically. However, many of the studies were of poor quality – small samples and not randomized trials. Cochrane review (Kelly et al. 2010) noted that few significant differences were noted in SLT vs no SLT comparisons although there was a consistent trend in favour of speech and language therapy.

One of the most influential language studies by Lincoln et al. (1984) was negative for SLP treatment and led to a nihilist attitude toward speech language therapy for many years.

Highlighted Study

Lincoln NB, Mulley GP, Jones AC, McGuirk E, Lendrem W, Mitchell JR. Effectiveness of speech therapy for aphasic stroke patients: a randomised controlled trial. The Lancet. 1984 Jun 2;323(8388):1197-200.		
RCT (6) N_{Start}=327 N_{End}= 161 TPS= Subacute	E: Hospital or Home Language Therapy C: No Therapy Duration: 1hr, 2x/wk, 6mo	• Porch Index of Communicative Ability (-) • Boston Diagnostic Aphasia Examination (-) • Functional Communication Profile (-)

Non-Pharmacological Interventions for Aphasia

5.13.1 Speech Language Therapy

Speech and language therapy for aphasia rehabilitation can take on many different forms, but the underlying principles remain relatively the same. Because of the different types of aphasia and varying levels of severity, treatment is often individualized. Depending on the nature of their deficits, certain tactics can be employed, and certain aspects of language and speech focused on more intensely. Some can be very structured 'lessons' with tasks and instruction, whereas others can consist of a more unstructured, conversational therapy. Many involve some form of auditory stimulation, where phonemes, words or sentences are played to patient. They also may be taught to follow commands that are relevant to their day to day activities. Many will also facilitate the production of speech through repetition, semantic associations and cueing strategies. Many general speech and language therapies also encourage communication through all forms (eg. gesture, writing) so as to provide the patient with the tools for functional communication.

Highlighted Study

Höeg Dembrower KE, von Heijne A, Laska AC, Laurencikas E. Patients with aphasia and an infarct in Wernicke's area benefit from early intensive speech and language therapy. Aphasiology. 2017 Jan 2;31(1):122-8.		
RCT (5) N_{Start}=118 N_{End}=90 TPS=Acute	E: Early Intensive Speech and Language Therapy (LET) C: No Therapy Duration: 45min/d, 5d/wk. 3wks	• Amsterdam-Nijmegen Everyday Language Test (+exp)

Highlighted Study

Bowen A, Hesketh A, Patchick E, Young A, Davies L, Vail A, Long A, Watkins C, Wilkinson M, Pearl G, Ralph ML. Clinical effectiveness, cost-effectiveness and service users' perceptions of early, well-resourced communication therapy following a stroke: a randomised controlled trial (the ACT NoW Study). InNIHR Health Technology Assessment programme: Executive Summaries 2012. NIHR Journals Library.		
RCT (7) N_{Start}=170 N_{End}=153 TPS=Acute	E: Enhanced Communication Therapy C: Attentional Control Duration: 3x/wk, 16wks	• Therapy Outcome Measure: Activity Subscale (-) • Communication Outcomes After Stroke Scale (-)

Levels of Evidence for General Speech and Language Therapy

Intervention	Discourse	Naming	Verbal Fluency	Social Commun-ication	Writing	General Compre-hension	Reading Compre-hension	Auditory Compre-hension	Global Speech & Language	ADLs
General Speech and Language Therapy	2 3 RCTs	2 3 RCTs	2 2 RCTs	1a 4 RCTs	2 1 RCT	2 2 RCTs	2 1 RCT	2 3 RCTs	1a 3 RCTs	1b 1 RCT

Conclusions

General speech and language therapy may improve writing in stroke survivors with aphasia.

Speech and language therapy may not be beneficial for global speech and language or social communication, in addition to activities of daily living.

5.13.2 Intensity of SLT on Aphasia

The most effective means of treating aphasia post stroke has yet to be determined, and studies investigating the efficacy of speech and language therapy for patients suffering aphasia post stroke have yielded conflicting results. One possible explanation for the observed heterogeneity of findings across studies is a difference in intensity of therapy. The recent Cochrane update (Kelly et al. 2010) reported that intensive therapy was associated with improved outcome when compared to conventional treatment; however, more participants withdrew from intensive therapy conditions than conventional.

Bhogal et al. (2003) identified 8 RCTs comparing intensity of SLT delivered by trained therapist vs. non-SLT control. 4 RCTs showed a positive impact of speech and language therapy and 4 did not. The association of therapy intensity and therapy effectiveness was examined. Positive RCTs provided a mean of 8.8 hours per week for an average of 11.2 weeks; Total therapy hours were 98.4 hours. Negative trials provided a mean of 2 hours per week for an average of 22.9 weeks; Total therapy hours were 43.6 hours. More intensive therapy over a shorter period of time was efficacious while less intensive therapy over a longer period of time was not.

Kelly et al. (2010) in the Cochrane review found that intensive SLT was associated with improved written and receptive language and in overall measures of severity when compared to conventional SLT. However, two recent RCTs (Bakheit et al. 2007; Martins et al. 2013) suggest that there is strong evidence that intensive language therapy may not improve performance on comprehensive language assessments or communicative ability when compared to standard language therapy; however, the benefit of high-intensity therapy in those who can tolerate it is not yet known. There is moderate evidence that 19.3 hours of speech therapy program may improve performance on comprehensive language assessments compared to standard therapy (6.9 hours).

Highlighted Study

Bakheit AM, Shaw S, Barrett L, Wood J, Carrington S, Griffiths S, Searle K, Koutsi F. A prospective, randomized, parallel group, controlled study of the effect of intensity of speech and language therapy on early recovery from poststroke aphasia. Clinical Rehabilitation. 2007 Oct;21(10):885-94.		
RCT (8) N_{Start}=116 N_{End}= 105 TPS=Acute	E: Intensive Speech Therapy (5hrs/wk) C1: Standard Speech Therapy (2hrs/wk) C2: National Health Service Standard Therapy (2hrs/wk) Duration: 12wks	E vs C1 • Western Aphasia Battery (-) C1 vs C2 • Western Aphasia Battery (+con1)

Conclusions

Moderate intensity language therapy may not be more effective in treating aphasia when compared to less intensive therapy; however, the benefit of high intensity language therapy in those that can tolerate it is not yet known.

5.13.3 Word-Retrieval Interventions

Word finding difficulty, also known as a lexical retrieval deficit, is a phenomenon whereby an individual can usually supply an accurate semantic representation of an object, but they are unable to verbally label that same object (Saito & Takeda, 2001). This deficit is the main feature of anomic aphasia however it is also a common problem in other types of aphasia. In all cases, this deficit can significantly impact the patient's verbal communication. It has been hypothesized that word-retrieval deficits stem from "an impaired access to the phonological form of the intended word" (Saito & Takeda, 2001). Therapies usually employ associative learning procedures including semantic and/or phonological cueing to aid lexical access and improve word retrieval abilities. Semantic cues require the patient to focus on the meaning of the word whereas phonological cues require the patient to understand the structure of the word (first syllable or its proper spelling). Most studies have administered picture-naming tasks which enable the patient to make a semantic connection with the word, thus if they are to see the picture again, they may be prompted to say the word.

Highlighted Study

Nouwens F, de Lau LM, Visch-Brink EG, Van de Sandt-Koenderman WM, Lingsma HF, Goosen S, Blom DM, Koudstaal PJ, Dippel DW. Efficacy of early cognitive-linguistic treatment for aphasia due to stroke: a randomised controlled trial (Rotterdam Aphasia Therapy Study-3). European Stroke Journal. 2017 Jun;2(2):126-36.		
RCT (8) N_{Start}=153 N_{End}=142 TPS=Acute	E: Early Intensive Semantic and Phonological Therapy C: No Language Therapy Duration 1hr/d, 4wks	• Amsterdam-Nijmegen Everyday Language Test (-) • The Token Test (-) • Boston Naming Test (-) • Semantic Association Test (-) • Comprehensive Aphasia Test (-) • Nonword Repetition an Auditory Lexical Decision from the Psycholinguistic Assessment of Language Processing in Aphasia (-) • Barthel Index (-)

Level of Evidence

	Discourse	Naming	Verbal Fluency	Social Commun-ication	Repet-ition	Writing	General Compre-hension	Reading Compre-hension	Auditory Compre-hension	Global Speech & Language	ADLs
Lexical Retrieval therapy	**1b 1 RCT**	**1a 2 RCTs**	**1b 1 RCT**	**1a 1 RCT**	**1a 1 RCT**	**1b 1 RCT**	**1b 1 RCT**	**1b 1 RCT**	**1a 2 RCTs**	**1a 2 RCTs**	**1b 1 RCT**

Conclusions

Lexical (word) retrieval therapy may not be beneficial for improving aphasia related outcomes post-stroke.

5.13.4 Trained Volunteers in Aphasia Training

Kelly et al. (2010) reported that speech therapy delivered by volunteers produced outcomes similar to those produced by therapy delivered by trained speech-language professionals. There is moderate evidence that volunteers can provide speech and language therapy and achieve similar outcomes in terms of comprehension and communicative ability when compared to speech language therapists. Trained volunteers may serve as an important supplement to scarce SLT resources.

Highlighted Study

Marshall RC, Wertz RT, Weiss DG, Aten JL, Brookshire RH, Garcia-Bunuel L, Holland AL, Kurtzke JF, LaPointe LL, Milianti FJ. Home treatment for aphasic patients by trained nonprofessionals. J Speech Hear Disord 1989; 54:462-470.		
Follow-up of Wertz et al. (1986) RCT (5) N_{Start} =121 N_{End} =103 TPS=Subacute	E1: Home Therapy with a Volunteer E2: Speech-language Pathologist Treatment E3: Treatment Deferred for 12wks Duration: 8-10hrs/wk, 12wks	E1 vs E2 • Porch Index of Communicative Ability (-) E1 vs E3 • Porch Index of Communicative Ability (-) E2 vs E3 • Porch Index of Communicative Ability (+exp2)
121 aphasic males 2-12 months post onset. Randomized to home therapy treatment given by a wife, friend or relative, treatment by SLP or treatment by SLP deferred for 12 weeks. Therapy provided 8-10 weeks x 12 weeks. At 12 weeks SLP Rx better than deferred but not significantly different from home therapy. Deferred group caught up after 12 more weeks. Trained volunteers can provide an effective adjunct to SLP treatment.		

Highlighted Study

David R, Enderby P, Bainton D. Treatment of acquired aphasia: speech therapists and volunteers compared. Journal of Neurology, Neurosurgery & Psychiatry. 1982 Nov 1;45(11):957-61.		
RCT (5) N_{Start} =155	E: Speech-language pathologist therapy C: Volunteer therapy	• Functional Communication Profile (-)

N_{End} =96 TPS=Acute	Duration: 30hrs over 15-20wks	

Level of Evidence

Intervention	Discourse	Global Speech & Language
Volunteer Facilitated Speech and Language Therapy	**2** **1 RCT**	**1b** **3 RCTs**

Conclusions

Volunteer facilitated speech and language therapy may not be more beneficial than speech language pathology delivered therapy for improving aphasia related outcomes post-stroke.
Volunteers can provide an effective adjunct to speech-language pathologists' treatment.

5.13.5 Group Therapy for Aphasia Post-Stroke

Group therapy for aphasic patients is a potential means to maximize limited language resources and thus encourage social interactions (Wertz et al. 1981; Elman & Bernstein-Ellis 1999). There is limited evidence that group aphasia therapy may improve communicative ability but not conversational ability, non-verbal reasoning

Highlighted Study

Wertz RT, Collins MJ, Weiss D, Kurtzke JF, Friden T, Brookshire RH, Pierce J, Holtzapple P, Hubbard DJ, Porch BE, West JA, Davis L, Matovitch V, Morley GK, Resurreccion E. Veterans Administration cooperative study on aphasia: a comparison of individual and group treatment. J Speech Hear Res 1981; 24:580-585.		
RCT (6) N_{Start}=67 N_{End}=34 TPS=Acute	E: Group therapy C: Individual therapy Duration: 8hrs/wk, 48wks	• Porch Index of Communicative Ability (-) • Token Test (-) • Word Fluency (-) • Conversational Rating (-) • Informant's Rating (-)
67 male aphasic stroke patients, 4 weeks post-onset. Randomized to 4 hours/week of individualized SLT vs. 4 hours/week of group therapy. Patients who received individualized therapy did better with writing.		

Evidence for Group Therapy for Aphasia

Intervention	Discourse	Naming	Social Commun-ication	Auditory Compre-hension	Global Speech & Language
Social Interaction	**1b** **1 RCT**	**1b** **1 RCT**	**1b** **1 RCT**	**1b** **1 RCT**	**1b** **3 RCTs**

Conclusion

Group therapies may not be more beneficial than individual therapies for improving aphasia related outcomes post-stroke.
There is mixed evidence that group therapies offer more benefit than recreational social activities.

5.13.6 Training Conversation / Communication Partners

Conversation is important in social participation and plays an important role in many social functions such as establishing and maintaining relationships, sharing ideas and opinions, and making plans. Training conversation or communication partners within the aphasic's social setting can promote opportunities for restored access to conversation. A systematic review by Simmons-Mackie et al. (2010) noted that communication partner training is effective in improving communication activities and/or participation of the communication partner. Communication partner training is also probably effective in improving communication activities and/or participation of persons with chronic aphasia when they are interacting with trained communication partners. There is moderate evidence that training communication partners may result in improved participation in conversation and improved conversational skills of persons with aphasia and their communication partners.

Highlighted Study

Kagan A, Black SE, Duchan JF, Simmons-Mackie N, Square P. Training volunteers as conversation partners using "supported conversation for adults with aphasia" (SCA): A controlled trial. Journal of_Speech, Language and Hearing Research 2001; 44:624-637.		
RCT (6) N_{Start}=40 N_{End}=40 TPS=Chronic	E: Conversation partners trained to acknowledge and reveal competence of aphasia participants C: Conversation partners exposed to an informative aphasia video presentation Duration: 1d workshop, 5.5hrs + 1.5hr hands-on session within 2wks	• Measure of Skill in Providing Supported Conversation for Adults with Aphasia (+exp) • Measure of Participation in Conversation for Adults with Aphasia (+exp)
40 volunteers randomly assigned to supported conversation training vs video regarding stories of aphasics and their families then assigned to stroke patients with moderate to severe aphasia. SCA trained volunteers associated with enhanced conversation skills for both trained partner and aphasic individual (moderate evidence). Limited evidence SCA trained conversation partners may result in improved access to conversation and increased social participation.		

<u>Conclusion</u>
Training communication partners may result in improved participation in conversation and improved conversational skills of persons with aphasia and their communication partners

5.13.7 Computer-Based Treatment

Computer-based aphasia therapy is appealing as a means of massed practice increasing intensity of therapy (Doesborgh et al. 2004; Katz & Wertz 1997). There is limited evidence that computer-based aphasia therapy results in improved language skills and may improve functional communication.

Highlighted Study

Katz RC, Wertz RT. The efficacy of computer provided reading treatment for chronic aphasic adults. Journal of Speech, Language and Hearing Research 1997; 40:493-507.

RCT (5)
N_{Start}=63
N_{End}=55
TPS=Chronic
	E1: Computer Reading Treatment
	E2: Computer Stimulation Treatment
	C: No Treatment
	Duration: 3hrs/wk, 26wks
		<u>E1 vs E2</u>
		• Western Aphasia Battery – Overall (+exp1), Spontaneous Speech (-), Comprehension (-), Repetition (+exp1), Naming (-)
		• Porch Index of Communicative Ability – Overall (+exp1), Auditory (-), Verbal (+exp1), Pantomime (-), Reading (-), Writing (-)
		<u>E1 vs C</u>
		• Western Aphasia Battery – Overall (+exp1)
		  • Spontaneous Speech (-)
		  • Comprehension (-)
		  • Repetition (+exp1)
		  • Naming (-)
		• Porch Index of Communicative Ability – Overall (+exp1)
		  • Auditory (-)
		  • Verbal (+exp1)
		  • Pantomime (+exp1)
		  • Reading (-)
		  • Writing (-)
		<u>E2 vs C</u>
		• Western Aphasia Battery – Overall (-), Spontaneous Speech (-), Comprehension (-), Repetition (+exp1), Naming (-)
		• Porch Index of Communicative Ability – Overall (-)
		  • Auditory (-)
		  • Verbal (-)
		  • Pantomime (+exp2)
		  • Reading (-)
		  • Writing (-)

RCT examined 55 aphasic patients at least 1 year post-stroke onset. Received 3 hours/week x 6 months of computer reading, computer stimulation or control. Computer reading > stimulation > control.		

Varley R, Cowell PE, Dyson L, Inglis L, Roper A, Whiteside SP. Self-administered computer therapy for apraxia of speech: two-period randomized control trial with crossover. Stroke. 2016 Mar;47(3):822-8.		
Crossover RCT (6) N_{Start} =50 N_{End} =44 TPS=Chronic	E: Computer Speech Therapy C: Visuospatial Sham Condition Duration: 20min/d, 6wks, 4wk washout period	• Naming (+exp) • Repetition (+exp)

Levels of Evidence for Computer-Based Therapies

Intervention	Discourse	Verbal Fluency	Repet-ition	Writing	General Compre-hension	Reading Compre-hension	Auditory Compre-hension	Global Speech & Language
Computer based therapies	1b 2 RCTs	2 1 RCT	1b 2 RCTs	2 1 RCT	2 1 RCT	2 1 RCT	2 1 RCT	1b 1 RCT

Conclusion
The literature is mixed regarding computer-based therapies ability to improve naming.
Computer-based therapy may be beneficial for repetition.

5.13.8 Telerehabilitation and Speech Language Therapy

Although increased intensity of speech-language therapy (SLT) has been associated with improved outcome, delivery of such services may be complicated by issues of increased demand, available resources and equitable access to services. While "in-person" services are the gold standard of care, other options for service delivery should be considered. One such option is telerehabilitation or telecare, in which services are provided at a distance even though the definition for 'telerehabilitation' varies across studies assessing the efficacy of speech and language therapies remotely. Online platforms such as video-conferencing or interactive computer-based programs may be used to assess, deliver interventions and monitor function in a timely fashion (Theodoros et al. 2008). Other telecommunication methods (e.g. telephone calls) are often considered telerehabilitation and used to connect the patient to the health care professional to conduct assessments remotely; however, these methods do not provide live face-to-face communication.

Two previous reviews have identified a number of studies examining the use of telerehabilitation for the provision of communication services in a variety of populations including stroke (Hill & Theodoros 2002, Reynolds et al. 2009). The majority of studies included in both of these reviews present positive findings with regard to the use of telehealth. However, in both reviews, the authors note that the research suffers from a number of significant shortcomings that need to be addressed. Studies tend to be very small of single group or case series design. Twenty-two of the 28 studies identified for inclusion by Reynolds et al. (2009) were classified as preliminary studies only (i.e. pilot studies, case studies, conference presentations). Studies tend to lack important information necessary for replication (e.g. information about characteristics of participants and about the technology and procedures employed). Outcome assessment was variable and measures used were not necessarily accompanied by appropriate reliability and validity information. A majority of studies identified in previous reviews have examined the use of telehealth technologies for evaluation and consultation.

Conclusions
Remote assessment of language following stroke may be as effective as face-to-face assessment of stroke outcomes among individuals with aphasia.
Remotely administered language therapy may be an effective alternative to face-to-face therapy.

5.13.9 Music Therapy

Music and speech production are thought to have shared neural pathways (Tomanino 2012). Singing also reduces the rate at which words are articulated and, as such, dependence on the left hemisphere is reduced (Marchina 2010). Similarly, lengthening of syllables provides the ability to distinguish phonemes as well as allows the stringing of words to enhance fluency (Marchina 2010). Furthermore, rhythmic tapping that is often associated with music based therapy may engage the right hemisphere sensorimotor network, providing an impulse for verbal production and encourage auditory-motor coupling (Marchina 2010).

There are music-based therapies that may be used when treating aphasia. The most prominent is Melodic Intonation Therapy (MIT). This therapy encompasses the two main components of music based therapy: melodic intonation (singing) and rhythmic tapping while words, and eventually phrases, are repeated (Marchina 2010). Other approaches to this type of therapy involve other musical elements such as melody, rhythm, dynamics, tempo, and meter (Hurkmans 2012). These components of music may be provided as therapies encompassing the singing of familiar songs, musically assisted speech, dynamically cued singing, rhythmic speech cueing, or oral motor exercises (Tomanino 2012).

Highlighted Study

Van der Meulen et al. 2014		
Cross-over RCT (6) N_{Start}=25 N_{End}=24 TPS=Subacute	E: Intensive melodic intonation therapy C: Standard language therapy Duration: 5h/wk for 6wks	• Aachen Aphasic Test: Repetition. (+exp); Naming (-) • Repetition task: Overall score (+exp); Untrained items (+exp); Trained items (+exp) • Amsterdam Nijmegen Everyday Language Test (-)
In a cross-over comparison of MIT with standard language therapy, van der Meulen et al. (2014) found significant differences between interventions in repetition ability, but not in the naming subtest of the Aachen Aphasia Test or the Amsterdam Nijmegen Everyday Language Test.		

Highlighted Study

Conklyn D, Novak E, Boissy A, Bethoux F, Chemali K. The effects of modified melodic intonation therapy on nonfluent aphasia: A pilot study. Journal of Speech, Language, and Hearing Research. 2012.		

RCT (5)
N_{Start}=32
N_{End}=30
TPS= Acute
	E: Modified Melodic Intonation Therapy
	C: No Language Therapy
	Duration: 10-15min, 3 sessions
		• Western Aphasia Battery
		  • Total Score (-)
		  • Responsiveness (+exp)
		  • Repetition (-)

This RCT compared MIT to a no language treatment control. After administering the intervention for only two sessions, they observed significant improvements in favour of the MIT group on the responsiveness subtest of the Western Aphasia Battery and the adjusted total of responsiveness and repetition. Although MIT appears to be an effective treatment, the main contributing components of the intervention have not been clearly determined.		

Level of Evidence for Music-Based Speech Language Therapy

Intervention	**Discourse**	**Naming**	**Verbal Fluency**	**Social Commun-ication**	**Repet-ition**	**Auditory Compre-hension**	**Global Speech & Language**	**Apraxia**
Music therapy	**1b** **2 RCTs**	**1b** **2 RCTs**	**1a** **3 RCTs**	**1a** **2 RCTs**	**1b** **1 RCT**	**2** **1 RCT**	**1b** **2 RCTs**	**1b** **1 RCT**

Conclusion

Music-based speech language therapies, such as melodic intonation therapy may be beneficial in improving verbal fluency, but not social communication, discourse, or global speech and language; however, there is limited evidence which suggests it may be no better than standard language therapy.

5.13.10 Constraint-Induced (CI) Aphasia Therapy

Chronic aphasic patients use communication channels that are most accessible and which require the least amount of effort, such as gesturing and drawing, or using communicative utterances that they know they can produce with ease.

Constraint Induced aphasia therapy is based on 3 principles:

1. Intensive practice for short intervals.
2. Constraints are used to force the patient to perform actions that are being avoided.
3. Therapy focuses on action relevant to everyday life.

There is evidence for the effectiveness of constraint-induced aphasia therapy on language function and everyday communication in individuals with chronic aphasia suggests that it may be as effective as conventional aphasia therapy.

Highlighted Study

Sickert A, Anders LC, Münte TF, Sailer M. Constraint-induced aphasia therapy following sub-acute stroke: a single-blind, randomised clinical trial of a modified therapy schedule. Journal of Neurology, Neurosurgery & Psychiatry. 2014 Jan 1;85(1):51-5.		
RCT (7) N_{Start}=100 N_{End}=100 TPS= Subacute	E: Constraint Induced Therapy C: Usual Care Duration: 2hrs/d, 15d over 3wks	• Aachener Aphasia Test (-) • Communicative Activity Log (-)

Levels of Evidence for Constraint Induced Aphasia Therapy

Intervention	Discourse	Naming	Social Commun-ication	Repet-ition	Writing	General Compre-hension	Auditory Compre-hension	Global Speech & Language
Constraint Induced Aphasia Therapy	1b 1 RCT	1a 3 RCTs	1a 3 RCTs	1b 1 RCT	1b 1 RCT	1b 1 RCT	1a 2 RCTs	1a 4 RCTs

Conclusions

Constraint induced aphasia therapy may be beneficial for improving repetition and writing.
Constraint induced aphasia therapy may not be beneficial for improving global speech and language and social communication.
The literature is mixed concerning constraint induced aphasia therapy's ability to improve auditory comprehension.
Evidence for the effectiveness of constraint-induced aphasia therapy on language function and everyday communication in individuals with chronic aphasia suggests that it may be as effective as conventional aphasia therapy.

5.13.11 Repetitive Transcranial Magnetic Stimulation (rTMS)

Transcranial magnetic stimulation is a non-invasive procedure that uses a rapidly fluctuating magnetic field to "create electrical currents in discrete areas of the brain" (Martin et al. 2004). In stroke patients with nonfluent aphasia, functional MRI studies have revealed unusually high levels of right-sided cortical activation during language tasks (Martin et al. 2004, Naeser et al. 2004, Naeser et al. 2005, Rosen et al. 2000). While the potential importance of activation of the right frontal cortex in language recovery cannot be dismissed (Rosen et al. 2000), it has also been suggested that this unusually high level of activation is not necessarily associated with improved language performance, but rather may be a maladaptive strategy that hinders aphasia recovery in non-fluent patients (Martin et al. 2004, Naeser et al. 2004, Rosen et al. 2000). Recent studies have examined the effectiveness of the application of slow rTMS to reduce excitability in right-sided Broca's homologue in improving naming function in patients with nonfluent aphasia.

Highlighted Study

Tsai PY, Wang CP, Ko JS, Chung YM, Chang YW, Wang JX. The persistent and broadly modulating effect of inhibitory rTMS in nonfluent aphasic patients: a sham-controlled, double-blind study. Neurorehabilitation and neural repair. 2014 Oct;28(8):779-87.		
RCT (9) N_{Start}=56 N_{End}=53 TPS= Subacute	E: Inhibitory rTMS (10min) + Conventional Speech Rehabilitation (1hr) C: Sham rTMS + Conventional Speech Rehabilitation Duration: 10d	• Concise Chinese Aphasia Test ○ Conversation (+exp) ○ Description (+exp) ○ Expression (+exp) ○ Repetition (+exp) • Picture Naming Test ○ Naming Accuracy (+exp) ○ Naming Reaction Time (+exp)

Levels of Evidence for rTMS

Intervention	Discourse	Naming	Verbal Fluency	Social Commun-ication	Repet-ition	General Compre-hension	Auditory Compre-hension	Global Speech & Language	ADLs
Low Frequency rTMS	1a 3 RCTs	1a 7 RCTs	1a 3 RCTs	1a 3 RCTs	1a 5 RCTs	1b 1 RCT	1a 3 RCTs	1a 7 RCTs	1b 1 RCT

Conclusion

Inhibitory rTMS may be beneficial for improving discourse, naming, verbal fluency, social communication and global speech and language.

5.13.12 Transcranial Direct Current Stimulation

Like transcranial magnetic stimulation, transcranial direct current stimulation (tDCS) is used to provoke changes in excitability in the brain. The polarity of the current flow determines whether excitability is increased (anodal tDCS) or decreased (cathodal tDCS) (Floel et al. 2008). In healthy adults, application of

anodal tDCS over Wernicke's area has been associated with improved acquisition of novel vocabulary (Floel et al. 2008), suggesting that this technique may be useful in the rehabilitation of language.

Recently published RCTs found statistically significant differences between real and sham tDCS interventions on language performance outcomes or naming accuracy on nouns, verbs, words and sentences (Shah-Basak et al. 2015). Despite their higher methodological quality rating, the sample sizes of these studies are very small, and the results of these studies conflict with findings from cross-over RCTs given a lower quality rating, and a single cross-over prospective controlled trial. The latter suggests that tDCS may be no more effective than a conventional sponge-based tDCS intervention or word retrieval therapy on naming accuracy and response time.

Additionally, a Cochrane Systematic Review (Elsner et al. 2015) of twelve randomized controlled trials reported no difference between the use of anodal or cathodal tDCS versus control or sham tDCS for the improvement of language impairment post-stroke, and also concluded that existing evidence was deemed to be of low-quality and remained unclear about the effectiveness of tDCS on enhancing speech-language therapy outcomes.

Highlighted Study

Spielmann K, van de Sandt-Koenderman WM, Heijenbrok-Kal MH, Ribbers GM. Transcranial direct current stimulation does not improve language outcome in subacute poststroke aphasia. Stroke. 2018 Apr;49(4):1018-20.		
RCT (9) N_{Start}=58 N_{End}=56 TPS=Subacute	E: Anodal tDCS C: Sham-tDCS Duration: 5d/wk, 2wks of intervention, separated by 2wks	• Boston Naming Test (-) • Naming Performance of Trained Items (-) • Naming Performance on Untrained Items (-) • Aphasia Severity Rating Scale (-) • The Amsterdam Nijmegen Everyday Language Test (-)

Highlighted Study

Polanowska KE, Leśniak M, Seniów JB, Członkowska A. No effects of anodal transcranial direct stimulation on language abilities in early rehabilitation of post-stroke aphasic patients. Neurologia i neurochirurgia polska. 2013;47(5):414-22.		
RCT (8) N_{Start}=40 N_{End}=37	E: Anodal tDCS over left Broca's area (10min) + Language therapy (45min) C: Sham tDCS + Language therapy Duration: 5d/wk, for 3wks	• Naming (-) • Comprehension (-) • Repetition (-)

Levels of Evidence for tDCS

Intervention	Discourse	Naming	Verbal Fluency	Social Commun-ication	Repet-ition	General Compre-hension	Global Speech & Language
tDCS	1b 1 RCT	1a 5 RCTs	1b 1 RCT	1b 1 RCT	1b 1 RCT	1b 1 RCT	1b 1 RCT

Conclusions
Excitatory tDCS may not be beneficial for improving naming post-stroke.
The addition of tDCS to traditional aphasia therapies may improve remediation of language deficits other than naming.
Further research is needed to fully understand the current conflicting results of tDCS compared to sham-tDCS treatment.

Drug Therapy for Post-Stroke Aphasia

5.13.13 Piracetam

Piracetam is a γ-aminobutyrate derivative, a pharmacological agent with a potential effect on cognition and memory. Piracetam is thought to improve learning and memory by facilitating release of acetylcholine and excitatory amino acids, with increases in blood flow and energy metabolism (Kessler et al. 2000).

Highlighted Study

Enderby P, Broeckx J, Hospers W, Schildermans F, Deberdt W. Effect of piracetam on recovery and rehabilitation after stroke: a double-blind, placebo-controlled study. Clinical neuropharmacology. 1994 Aug;17(4):320-31.		
RCT (6) N_{Start}=158 N_{End}=137 TPS=Subacute	E: Piracetam Treatment (4.8g/d) C: Placebo Duration: 12wks	• Aachen Aphasia Test (+exp) • Barthel Index (-) • Rivermead Perception Assessment Battery (-) • Kuriansky Performance Test (-)

Levels of Evidence for Piracetam

Interventions	Discourse	Naming	Social Commun-ication	Repet-ition	Writing	General Compre-hension	Auditory Compre-hension	Global Speech & Language	ADLs
Piracetam	1b 1 RCT	1a 2 RCTs	1b 1 RCT	1b 1 RCT	1a 2 RCTs	1a 2 RCTs	1a 2 RCTs	1a 2 RCTs	1b 1 RCT

Conclusion
Piracetam may not be beneficial for improving aphasia related outcomes post-stroke.

5.13.14 Bromocriptine

Bromocriptine is a dopaminomimetic ergot derivative with D2-type receptor antagonist properties that is primarily regarded as a dopamine agonist.

Highlighted Study

Ashtary F, Janghorbani M, Chitsaz A, Reisi M, Bahrami A. A randomized, double-blind trial of bromocriptine efficacy in nonfluent aphasia after stroke. Neurology. 2006 Mar 28;66(6):914-6.		
RCT (7) N_{Start}=38 N_{End}=38 TPS=Subacute	E: Bromocriptine Treatment (2.5mg/d to 10mg/d) C: Placebo Duration: 16wks	• Persian Language Test (-)

Conclusion
Bromocriptine does not appear to be better than placebo in improving aphasia disorders.

5.13.15 Levodopa

Levodopa is a metabolic precursor of dopamine. Dopamine is involved in a variety of actions or mechanisms many of which may be influential in learning and executive function (Knecht et al. 2004, Seniow et al. 2009). In normal adults, the use of levodopa as an adjunct to massed training of an artificial vocabulary was associated with the speed, success and retention of novel word learning (Knecht et al. 2004).

Highlighted Study

Seniów J, Litwin M, Litwin T, Leśniak M, Członkowska A. New approach to the rehabilitation of post-stroke focal cognitive syndrome: Effect of levodopa combined with speech and language therapy on functional recovery from aphasia. Journal of the neurological sciences. 2009 Aug 15;283(1-2):214-8.		
RCT (7) N_{Start}=40 N_{End}=39 TPS=Subacute	E: Levodopa (100mg) + Speech-language Therapy (45min) C: Placebo + Speech-language Therapy Duration: 5x/wk, 3wks	• Boston Diagnostic Aphasia Examination • Animal naming (+exp) • Repetition (+exp) • Word Discrimination (-) • Commands (-) • Complex Ideational Material (-); • Visual Confrontation Naming (-) • Body Part Naming (-) • Body Part Identification (-)

Conclusion
There appears to be little effectiveness of levodopa as an adjunct to speech and language therapy.

Levels of Evidence for Bromocriptine and Levadopa

Interventions	Discourse	Naming	Social Commun-ication	Repet-ition	General Compre-hension	Auditory Compre-hension	Global Speech & Language
Bromocriptine or Levodopa	**1a 2 RCTs**	**1a 5 RCTs**	**2 1 RCT**	**1b 1 RCT**	**1b 1 RCT**	**1b 1 RCT**	**1a 2 RCTs**

5.13.16 Amphetamines

The amphetamines belong to the general group of sympathomimetic amines. Effective doses can enhance performance and wakefulness, decrease feelings of fatigue, increased alertness and mood (euphoria) in humans. Methylphenidate, an amphetamine, blocks the reuptake of serotonin and norepinephrine, and has dopaminergic activity as well.

Highlighted Study

Walker-Batson D, Curtis S, Natarajan R, Ford J, Dronkers N, Salmeron E, Lai J, Unwin DH. A double-blind, placebo-controlled study of the use of amphetamine in the treatment of aphasia. STROKE-DALLAS-. 2001 Sep 1;32(9):2093-6.		
RCT (7) N_{Start}=25 N_{End}=21 TPS=Acute/Subacute	E: Dextroamphetamine (10mg) + Speech Language Therapy (1hr) C: Placebo + Speech Language Therapy Duration: 10 sessions	• Porch Index of Communicative Ability (+exp)

Level of Evidence for Amphetamines

Intervention	Global Speech & Language
Amphetamines	1a 2 RCTs

Conclusion

Dextroamphetamine appears to improve aphasia recovery when combined with language therapy based on 2 small RCTs.

5.13.17 Donepezil

Donepezil is a selective acetylcholinesterase inhibitor used to stabilize cognitive deficits in individuals with mild to moderate dementia. Use of donepezil in patients with mild to moderate vascular cognitive impairment has been associated with significant improvements in cognitive and global function, including improvements in the performance of activities of daily living (Passmore et al. 2005). The results of an open-label, 20-week pilot study (Berthier et al. 2003) suggested that patients with chronic post stroke aphasia experienced improvement in language function following treatment.

Highlighted Study

Berthier ML, Green C, Higueras C, Fernandez I, Hinojosa J, Martín MC. A randomized, placebo-controlled study of donepezil in poststroke aphasia. Neurology. 2006 Nov 14;67(9):1687-9.		

RCT (7)
N_{Start}=26
N_{End}=26
TPS=Chronic
	E: Donepezil Treatment
	C: Placebo Treatment
	Duration: 4wks titration starting at 5mg, 12 wks at 10mg
		• Western Aphasia Battery (+exp)
		• Psycholinguistic Assessments of Language Processing in Aphasia
		  • Picture Naming (+exp)
		  • Non-word Repetition (-)
		  • Word Repetition (-)
		  • Spoken Word-picture Matching (-)

		• Spoken Sentence-picture Matching (-) • Auditory Lexical Decision (-) • Auditory Phonemic Discrimination-word Pairs (-) • Communicative Activity Log (-)

Levels of Evidence for Donepezil

Intervention	Discourse	Social Commun-ication	Repetition	General Compre-hension	Auditory Compre-hension	Global Speech & Language
Donepezil	1b 1 RCT	1b 1 RCT	1b 1 RCT	1b 1 RCT	1b 1 RCT	1b 1 RCT

Conclusions

Acetylcholinesterase inhibitors may be beneficial for improving naming, but not social communication, repetition, general and auditory comprehension, and global speech and language.

5.13.18 Memantine

Memantine is an antagonist of the N-methyl-D-aspartate (NMDA) receptor. Its use has been evaluated among patients with Alzheimer's dementia and those with vascular dementia.

Highlighted Study

Barbancho MA, Berthier ML, Navas-Sánchez P, Dávila G, Green-Heredia C, García-Alberca JM, Ruiz-Cruces R, López-González MV, Dawid-Milner MS, Pulvermüller F, Lara JP. Bilateral brain reorganization with memantine and constraint-induced aphasia therapy in chronic post-stroke aphasia: An ERP study. Brain and language. 2015 Jun 1;145:1-0.		
RCT (8) N_{Start}=28 N_{End}=27 TPS=Chronic	E: Memantine Treatment (10mg/d) + Constraint Induced Aphasia Treatment C: Placebo Treatment + Constraint Induced Aphasia Treatment Duration: 16wks on drug, then 2wks language training on drug (3hr/d, 5d/wk):	• Western Aphasia Battery (+exp)

Highlighted Study

Berthier ML, Green C, Lara JP, Higueras C, Barbancho MA, Dávila G, Pulvermüller F. Memantine and constraint-induced aphasia therapy in chronic poststroke aphasia. Annals of Neurology: Official Journal of the American Neurological Association and the Child Neurology Society. 2009 May;65(5):577-85.		

RCT (8)
N_{Start}=28
N_{End}=27
TPS=Chronic
	E: Memantine Treatment (20mg/d) + Constraint Induced Aphasia Treatment
	C: Placebo Treatment+ Constraint Induced Aphasia Treatment
	Duration: 16wks on drug, then 2wks language training on drug
		• Western Aphasia Battery
		  • Aphasia Quotient (+exp)
		  • Naming (+exp)
		  • Spontaneous Speech (+exp)
		  • Auditory Comprehension (+exp)
		  • Repetition (-)

		• Communicative Activity Log (+exp)

Levels of Evidence for Memantine

Intervention	Discourse	Naming	Social Commun-ication	Repetition	Auditory Compre-hension	Global Speech & Language
Memantine	1b 1 RCT	1b 1 RCT	1b 1 RCT	1b 1 RCT	1b 1 RCT	1b 1 RCT

Conclusion

Memantine may be beneficial for improving discourse, naming, social communication auditory comprehension and global speech and language, but not repetition.

5.14 Cognitive Rehabilitation for Apraxia

5.14.1 Apraxia

Apraxia is a disorder of voluntary movement where one cannot execute willed purposeful activity despite the presence of adequate mobility, strength, sensation, coordination, and comprehension. Apraxia occurs in up to 30% of strokes in acute phase. Apraixa is thought to result from loss of motor engrams or a disconnection between praxis system (Greene 2005). Anatomy correlations include:

- Left parietal or frontal premotor area are most commonly associated with apraxia.
- Orobuccal apraxia usually associated with insular and left inferior frontal lesion.
- Other areas: right parietal lobe, temporal and even subcortical regions.

While it has been suggested that the presence of apraxia can lead to severe disabilities in activities of daily living (Bjorneby & Reinvang 1985; Saeki et al. 1995; Sundet et al. 1988; Foundas et al. 1995; Rothi & Heilman 1997), results of the Copenhagen Study suggest that this is not necessarily the case. When the influence of manual and oral apraxia on functional outcome (represented by performance on the Barthel Index) was examined, taking initial Barthel Index scores, initial stroke severity and history of prior stroke, comorbidity, gender, age and handedness into account, no significant independent relationship could be found between apraxia and functional outcome. Unsal-Delialioglu et al. (2008) demonstrated that patients with apraxia may experience significant gains in function over the course of rehabilitation, although admission and discharge FIM scores may be significantly lower than their non-apraxic counterparts (Unsal-Delialioglu et al. 2008).

While apraxia usually improves over time, spatiotemporal errors in imitation or tool use may persist (Maher & Ochipa 1997). Basso and colleagues (1987) (as cited by van Heugten et al. (2000)) investigated the recovery from ideomotor apraxia (IMA) in acute stroke patients and attempted to identify predictive variables of IMA. They observed that recovery was related to the site of lesion in that patients with anterior lesions demonstrated better recovery. Recovery was not related to age, education, sex, type of aphasia and the initial severity or the size of the lesion.

5.14.2 Types of Apraxia

Praxis requires:

- **Conceptual system for action- semantic knowledge of tool functions and actions** (eg. the purpose of a screwdriver).
- **Production system for action -actual** sensorimotor action programs needed to carry out tasks (e.g. ability to move a limb in the correct direction).

Subdivisions of apraxia can be confusing. Many classifications on apraxia have been proposed. Traditional subdivisions of apraxia, particularly ideomotor and ideational apraxia are often used in an inconsistent manner (Greene 2005).

Classification of Apraxia (Mendez et al. 2012)

Ideomotor Apraxia – Parietal Variant: Disruption of movement formulas in the inferior parietal lobule with impaired pantomime, imitation and gesture recognition.

Ideomotor Apraxia –Disconnection Variant: Disruption of motor programs in the supplemental motor or interhemispheric connections with impaired pantomime, imitation of gestures and spatiotemporal errors. Movement formulas are preserved so patients are able to recognize and identify gestures.

Dissociation Apraxia – Errors when the movement is evoked by stimuli in one specific modality I.e., disconnection between lingual areas and movement formulas resulting in impaired pantomime but normal imitation of gestures or object use. Other types include verbal dissociation apraxia and visual dissociation apraxia.

Conceptual Apraxia – Errors in content of action, i.e., tool identification, use, object knowledge. Unable to point to name or identify a tool with its function is discussed or recall the actions associated with a specific tool or object.

Limb-Kinetic Apraxia – Inability to perform precise coordinated individual finger movements.

Ideational Apraxia – Can perform separate component tasks but cannot coordinate all steps for an integrated sequence

Constructional and Dressing Apraxia – Not true apraxias. Usually involvement of right parietal lobe lesion impacting on visual spatial function

5.14.3 Testing for Apraxia

There are various methods to test for apraxia. It is important to test all input modalities.

Test to Measure Upper Limb Apraxia (TULIA)
Test to Measure Upper Limb Apraxia (TULIA) is one method of determining upper limb apraxia through the qualitative and quantitative assessment of gesture production. In contrast to previous publications on apraxic assessment, the reliability and validity of TULIA was thoroughly investigated (Vanbellingen et al. 2010). The TULIA consists of subtests for the imitation and pantomime of non-symbolic ("put your index

finger on top of your nose"), intransitive ("wave goodbye") and transitive ("show me how to use a hammer") gestures. Discrimination (differentiating between well- and poorly-performed tasks) and recognition (indicating which object corresponds to a pantomimed gesture) tasks are also often tested for a full apraxia evaluation (Vanbellingen et al. 2010).

Mendez et al. (2012) outlined the following tests:

Ideomotor intransitive actions: (Alternate sides)
Pantomime: Ask to perform tasks like salute, wave goodbye, the peace sign.
Imitation: Ask to copy examiners actions - examiner gestures salute, peace sign.
Gesture Knowledge: Patient asked to identify the function or purpose of the action demonstrated.

Ideomotor transitive actions: (Alternate sides)
Pantomime: Ask to perform tasks like comb hair, brush teeth, use hammer.
Imitation: Ask to copy examiners action – examiner gestures combing hair, brushing teeth
Gesture Knowledge: Patient asked to identify the function or purpose of the action performed by the examiner.
Conceptual Knowledge: Patient asked to identify, demonstrate use or explain use of a tool shown by the examiner.

Ideational Apraxia: (Sequential Actions)
Pantomime: Examiner ask patient to show how they would prepare a letter for mailing, a sandwich with imaginary objects.
This process of performing transitive and intransitive actions continues in assessment of trunk, Lower limb and orofacial apraxia.

5.14.4 Treatment of Apraxia

A recent review of the literature identified studies describing 10 treatment approaches; multiple cues, error reduction, six-stage task hierarchy, conductive education, strategy training, transitive/intransitive gesture training, rehabilitative treatment and errorless completion + exploration training (Buxbaum et al. 2008). Most of the reports identified are single-case, or single-case series. Only two of these treatment approaches have been investigated using randomized controlled trials and are described below. Please note that "rehabilitative treatment" is sufficiently similar to gesture training to be included with it for the purposes of the present review.

Highlighted Study

Donkervoort M, Dekker J, Stehmann-Saris FC, Deelman BG. Efficacy of strategy training in left hemisphere stroke patients with apraxia: A randomized clinical trial. Neuropsychological Rehabilitation 2001; 11(5):549-566.		
RCT (8) N_{Start}=113 N_{End}=102 TPS=Subacute	E: Strategy Training to Compensate for Apraxia + Usual Occupational Therapy C: Usual Occupational Therapy Only Duration: 8wks	• Barthel Index (+exp)

113 patients with apraxia due to LH stroke randomly assigned to strategy training (involving use of compensatory strategies) integrated into usual OT vs usual OT. At 8 weeks treatment group improved more than controls on ADLs and Barthel Index scores. At 20 weeks no differences noted between groups.

Highlighted Study

Geusgens C, van Heugten C, Donkervoort M, van den Ende E, Jolles J, van den Heuvel W. Transfer of training effects in stroke patients with apraxia: an exploratory study. Neuropsychological rehabilitation. 2006 Apr 1;16(2):213-29.		
RCT (8) N_{Start}=113 N_{End}=102 TPS=Subacute	E: Strategy Training to Compensate for Apraxia + Usual Occupational Therapy C: Usual Occupational Therapy Only Duration: 8wks	• ADL Functioning (+exp)

Level of Evidence for Apraxia Therapy

Interventions	**General Comprehension**	**Apraxia**	**ADLs**
Apraxia Training	**2** **1 RCT**	**2** **1 RCT**	**1a** **2 RCTs**

<u>Conclusions</u>

Apraxia strategy training may be beneficial for improving activities of daily living.

Gesture training for apraxia may be beneficial for improving general comprehension, apraxia and activities of daily living.

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Bakheit A, Shaw S, Carrington S, Griffiths S. The rate and extent of improvement with therapy from the different types of aphasia in the first year after stroke. *Clin.Rehabil. 2007b;21:941-949.*

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