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Aphasia and reperfusion therapies in hyper-acute settings: A scoping review

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Abstract

Purpose: Reperfusion therapies are medical treatments that restore blood flow either by surgical removal of a blood clot or with medications that dissolve clots. The introduction of reperfusion therapies has the potential to change the presentation of aphasia following acute ischaemic stroke (AIS). This scoping study will explore the relationship between aphasia and reperfusion therapies from a speech-language pathology perspective.

Method: A systematic literature search was performed on studies published up until October 2016. Relevant studies that reported on aphasia and reperfusion therapy were assessed for quality and the relationship between the two.

Results: Overall, 27 studies were identified, these studies were heterogeneous in nature. Despite speech-language pathologists filling a central role in management of aphasia, only seven of these studies mentioned involvement of speech-language pathologists, with minimal information about the precise nature of the involvement of speech-language pathology services.

Conclusion: Based on this scoping review, reperfusion therapy appears to be impacting on the presentation of aphasia. A prospective study into reperfusion therapy and aphasia is required to inform speech-language pathologists on this patient population.

Keywords: *aphasia*; *thrombolysis*; *thrombectomy*; *ischaemic stroke*

Introduction

Acute ischaemic stroke (AIS), a blood clot in the brain, makes up more than 80% of the strokes in Western countries (Zhang et al., 2014). Stroke is associated with significant long-term disability and is the most common cause of aphasia (Miller, Hartwell, & Lewandowski, 2012). Aphasia is present in 21–38% of acute stroke patients (Pedersen, Jørgensen, Nakayama, Raaschou, & Olsen, 1995) with studies indicating that language is still impaired in over half of the patients 12–18 months after stroke (Denier et al., 2016). Changes in medical treatments provided in the hyper-acute setting (within the first 24 hours of arrival to hospital) can potentially change the presentation of post-stroke symptoms, such as aphasia. When these hyper-acute medical treatments are utilised, early restoration of blood flow can be achieved, resulting in reductions in the size, pattern, and nature of infarcts following AIS (Martins et al., 2016).

A National Institute of Neurological Disorders and Stroke (NINDS, 1995) trial initiated a shift towards hyper-acute medical treatments for AIS that restore blood flow to the brain. Hyper-acute treatments known as reperfusion therapies, included intravenous (IV), intra-arterial (IA) or combined IV–IA thrombolysis, and mechanical thrombectomy (Alonso de Lecinana et al., 2014; Layton, White, Cloft, Kallmes, & Manno, 2006; Nguyen et al., 2011). The conclusion drawn from the NINDS (1995) trial was that despite an increased incidence of symptomatic intracerebral haemorrhage, treatment with IV thrombolysis within three hours of onset improved clinical outcomes at three months following AIS.

Reperfusion therapies target areas of hypo-perfusion, which are areas of reduced blood flow (Robinson, Zaheer, & Mistri, 2011). Hypo-perfusion causes hypoxia (reduced oxygenation) and temporary loss of function to an area of the brain. This area of temporary loss of function is referred to as the penumbra. The penumbra surrounds an area of cell death called the "core". If blood flow is restored quickly to the penumbra, permanent damage can be minimised, and clinical outcomes may be improved,

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leading to the recovery of function (Zhang et al., 2014). It is therefore important that reperfusion therapies are provided as soon as possible. Globally, the percentage of patients receiving the most common type of reperfusion, IV recombinant tissue-type plasminogen activator (rtPA), varies from 1–12% across countries; 7% in Australia (The National Stroke Foundation, 2015), 11–12% in the UK (Royal College of Physicians, 2015), 9% in Qatar, 5.1% in the USA, 8.6% in Sweden (Hoffmeister et al., 2016). Quain et al. (2008) suggested that the percentage of patients treated by reperfusion therapies could increase to up to 20%, a number that individual specialised stroke units with thrombolysis protocols have successfully achieved.

IV alteplase, a form of rtPA, has become the emerging standard of care for patients with AIS who present to the emergency department. IV alteplase must be administered within 4.5 hours of onset of symptoms (Denier et al., 2016). Current eligibility criteria for IV alteplase include: arrival with 4.5 hours of stroke onset, National Institutes of Health Stroke Scale (NIHSS) of >4, CT with no signs of haemorrhage, patients' age is >18 years old. Exclusion criteria for IV alteplase include: uncertainty about time of onset, hypertension, septic embolus, and recent use of blood thinning medication such as heparin. If used within the recommended guidelines, IV alteplase is associated with a significant net reduction in death and disability in those treated with IV alteplase compared with those treated with placebo (52.4% versus 45.2%, respectively; OR, 1.34; 95% CI, 1.02–1.76; $p = .04$) despite a small but significant increase in the risk of intracerebral haemorrhage (ICH) (2.4% versus 0.2%, $p = .008$) (Robinson et al., 2011).

Another form of reperfusion therapy involves delivering alteplase via arteries rather than veins. Crijnen et al. (2016) recently reported intra-arterial treatment (IAT) with retrievable stents for patients with AIS improves functional outcome at 90 days. The main advantage of IAT reperfusion therapy, over IV alteplase, is that it allows direct delivery of a highly concentrated thrombolytic drug to the clot (Nguyen et al., 2011). Another benefit is IAT reduces the risk of systemic side effects (i.e., allergic reaction, by minimising the use of chemical thrombolytics, this decreases the risk of ICH, and reduces the risk of increased blood brain barrier permeability and oedema) and can be delivered up to six hours post-stroke. IAT is not as prevalent, however, as it is a costly therapy requiring expensive devices, highly trained proceduralists, periprocedural support from interventional teams including anaesthesiology and close post procedure monitoring (Leppert, Campbell, Simpson, & Burke, 2015).

For patients who are ineligible for IV rtPA or IAT, due to possible interactions with medications or pre-existing medical conditions, mechanical thrombectomy is an alternative stroke therapy (Zhang et al., 2014). Mechanical thrombectomy involves the insertion of a catheter into effected blood vessel. Once at the blood clot, a stent is used to remove the blood clot instead of dissolving it. Clinical experience with mechanical thrombectomy is limited, expensive and requires specialised unit with extensive training. Despite the introduction of reperfusion therapies, in acute stroke management, many patients still require inpatient rehabilitation and treatment from speech-language pathologists for aphasia (Meyer et al., 2012). Speech-language pathologists are needed to rehabilitate patients post stroke, often to target dysphagia, dysarthria, apraxia and/or aphasia.

Patients with aphasia can experience expressive and/or receptive language impairments for several months or years following stroke; often leading to difficulty in investing in rehabilitation and understanding therapist's instructions, depression, social drawback, decreased professional activities, and altogether a lower quality of life (Power et al., 2015). Given the prevalence of aphasia following stroke and the increasing use of reperfusion therapies in acute stroke management, there is a high likelihood that speech-language pathologists will increasingly manage patients with aphasia who have received reperfusion therapies as part of their stroke management in acute and rehabilitation settings. The aim of this scoping review is to investigate the relationship between the introduction of reperfusion therapies and aphasia.

Method

A scoping review method was adopted to explore the depth of evidence regarding the relationship between reperfusion therapies and aphasia. Scoping reviews are a relatively recent addition to healthcare literature and represent an increasingly popular approach to reviewing literature (Davis, Drey, & Gould, 2009). Scoping reviews are particularly relevant to disciplines with emerging evidence, such as rehabilitation science, in which the paucity of randomised controlled trials makes it difficult for researchers to undertake systematic reviews (Levac, Colquhoun, & O'Brien, 2010). Unlike systematic reviews, which use narrow questions and a predetermined level of acceptable quality of studies; scoping reviews use a broad question and include all relevant studies. Scoping reviews differ from narrative or literature reviews in that the scoping process requires analysis of common data presented in the source literature and reinterpretation of hypotheses using the combined data (Levac et al., 2010).

A scoping review provides an appropriate method to systematically evaluate a heterogeneous area of research to identify gaps in the existing literature by allowing variation in methods between studies selected to be included (Armstrong, Hall, Doyle, & Waters, et al., 2011). As per the scoping review process, developed by Arksey and O'Malley (2005) and Levac et al. (2010), all the literature within a defined set is summarised, regardless of its quality, to examine the range of studies that exist.

Literature search

A systematic literature search was performed on studies published up until October 2016 on Web of science, Medline, CINAHL, Cochrane database of systematic reviews and EMBASE. Search terms included for reperfusion therapy (thrombolysis; tissue plasminogen activator; alteplase; arterial thrombolysis; fibrinolytic agent; urokinase; thrombectomy); combined it with a communication term (aphasia; cognitive communication; language impairment); and medical diagnosis (stroke; middle cerebral artery occlusion; brain infarction; brain ischemia).

Inclusion and exclusion criteria

The studies included in this scoping review met the following criteria: (1) individuals who have experienced an ischaemic stroke; (2) studies that identify the use of thrombolysis and/or thrombectomy and the presence of aphasia; (3) studies published in English.

The studies excluded from this scoping review met the following criteria: (1) individuals under the age of 18; (2) studies that primarily discussed thrombolysis and/or thrombectomy for cardiac clots; (3) studies on mimic strokes; (4) studies on brain tumours and other neurological issues; (5) studies that briefly mention aphasia in introduction but not in results ("minimal aphasia"); (6) studies that briefly mention thrombolysis without providing outcomes ("minimal thrombolysis").

Data analysis

The studies were graded using a critical review form developed by McMaster University Occupational Therapy Evidence-Based Practice Research Group (Law et al., 1998). The critical review form was used to provide each study with a score out of 14. Each question was assigned a value of one for "yes" and zero for "no". Each study was assessed according to its: 1) Study purpose and inclusion of background literature; 2) sample, including description of the patient sample and drop outs; 3) outcome measures; 4) description of the intervention used; 5) reporting of results; and 6) conclusion. The designs of the studies were categorised but not included in the scoring. Two assessors reviewed each study and any differences in scores were discussed until a consensus was reached.

Result

The literature search initially revealed 302 studies, which after screening for title and abstract, was reduced to 43 studies for full text analysis. An additional thirty-eight studies were identified in the reference sections. A flowchart of the literature search and selection process can be seen in Figure 1. Twenty-seven studies met the criteria for inclusion and were assessed. Eleven of the studies reviewed were retrospective studies that utilised data collected from databases. These databases were established with the intent to monitor and improve management of acute stroke care. The 11 studies used data collected from three large prospective studies or eight regional databases that were not designed for in-depth investigation of aphasia. These databases were established by medical facilities to collect baseline demographic and stroke-related data, such as the Erlangen Stroke and Thrombolysis Database or the Careggi Hospital Acute Stroke Registry (Kohrmann et al., 2009; Nesi, Lucente, Nencini, Fancellu, & Inzitari, 2014).

Study characteristics

Studies included in the current review were heterogeneous in nature. For example, as presented in Table I, the number of participants ranged from 1 to 1007; the ages of participants, ranged from 28–82; percentage of females included in studies (excluding single case studies) ranged from 25–52%; and length of follow-up varied from 24 hours to one year following reperfusion therapy.

Outcome measures

Aphasia was most commonly assessed using the NIHSS, the NIHSS is a quantitative measure of stroke-related neurological deficits, it includes assessment of: level of consciousness, speech and language function, neglect, visual fields, eye movements, facial symmetry, motor strength, sensation and coordination (Kasner et al., 2003). Due to the broad scope of areas assessed by the NIHSS, a diagnosis of aphasia is based on picture naming, picture description (the Cookie theft) and sentence reading if based on item 9 (best language) with a maximum score of three. Items 1b (LOC questions) add questions about the month and age, and item 1c (LOC commands) add one-stage commands. As noted in Table I, additional language assessments used included the Language Screening Test (LAST) (Denier et al., 2016); the Western Aphasia Battery (WAB) (Finch et al., 2014); the French version of the Boston Diagnostic Aphasia Examination (BDAE) (Jacquin et al., 2014); the Lisbon Aphasia Assessment Battery (BAAL) (Martins et al., 2016); and the Basel–Minnesota test (Engelter et al., 2006). The study by de Oliveira and Damasceno (2011) diagnosed aphasia with a collection of informal language tasks described as spontaneous narrative, fluency, yes/no and three stage command, naming six objects and ideomotor praxis. In 11 of the studies, follow-up was assessed with the modified Rankin Scale (mRS) (Table I). The mRS is a seven-point scale that progresses from 0 (no symptoms) to 6 (death) with varying levels of disability (Lubeck et al., 2016).

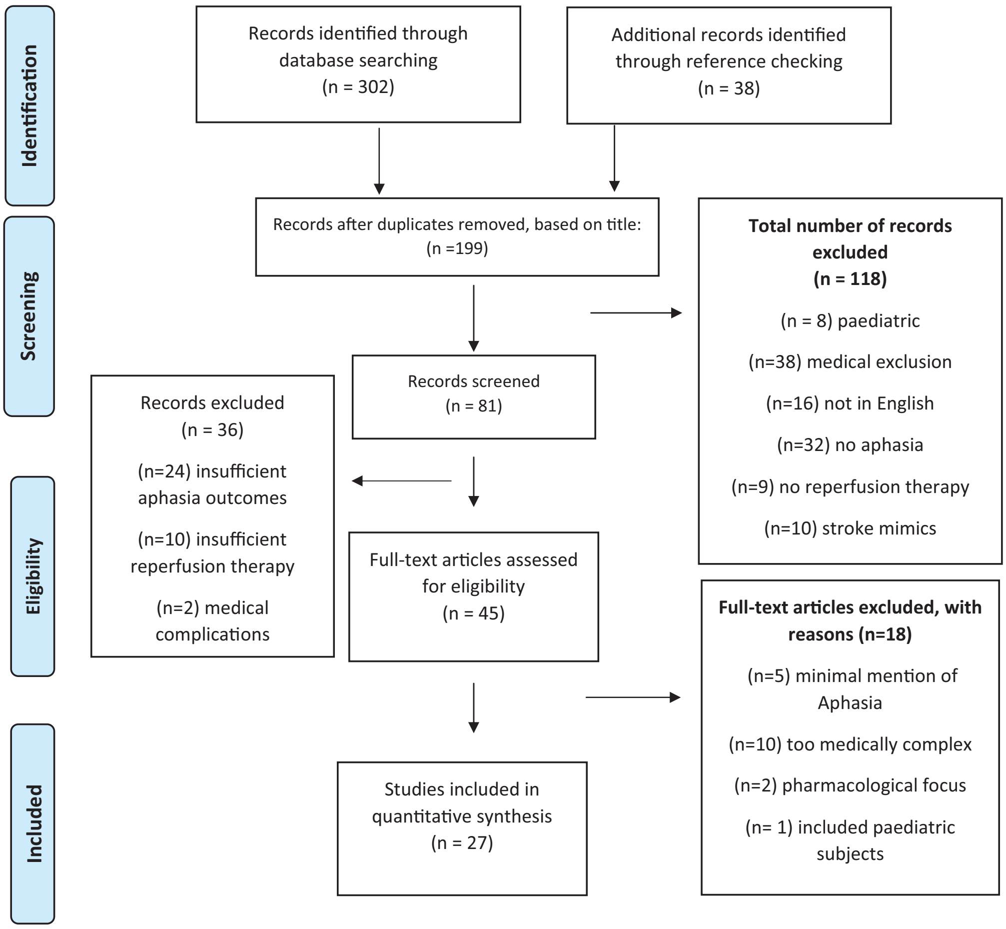

Figure 1. The screening process. The method used to refine results from database searches and select studies to review for quantitative synthesis.

Medical imaging was an additional measure of impairment, with one or a combination of computed tomography (CT), magnetic resonance (MR) or of transcranial Doppler (TCD) performed at baseline, prior to reperfusion therapy in 25 of the studies. Twenty-three of the studies screened functional impairment with the NIHSS as per the national stroke guidelines. A repeat imaging scan was also completed at follow-up in 16 of the 25 studies, however, the same method of imaging was not always used making pre-post comparisons difficult. Three studies used imaging alone as their method of assessment (Table I).

Core concepts

The literature revealed two core concepts between the relationship between aphasia and thrombolysis and/or thrombectomy (1) Studies that examined isolated aphasia as a predictor for the need to treat patients with reperfusion therapy regardless of the NIHSS score (Kohrmann et al., 2009; Lundstrom, Zini, Wahlgren, & Ahmed, 2015; Nesi et al., 2014) and (2) Studies that established aphasia as a lasting symptom of stroke following the use of endovascular therapies. These two core concepts will now be explored in this scoping review.

Core concept one: aphasia as a predictor

Thirteen of the 27 studies reviewed (Table I) discussed the relationship between aphasia and the need for reperfusion therapy (44 case studies, 8 cohort studies and 1 cross-sectional study). Nesi et al. (2014) suggested that aphasia, as a presenting symptom, strongly predicted negative outcomes in ischaemic stroke patients. Global aphasia can predict a poor prognosis in acute ischaemic stroke (de Oliveira & Damasceno, 2011).

Engelter et al. (2006) and Kohrmann et al. (2009) identified that patients presenting with aphasia as a symptom were significantly more likely to receive reperfusion therapy. Four of the studies (Cho, Hermier, & Nighoghossian, 2010; Denier et al., 2016; Lundstrom et al., 2015; Mazza et al., 2012) concluded that patients with aphasia, in the absence of physical symptoms, should still receive reperfusion therapy even if the patient presents with a low NIHSS. Cho et al. (2010) commented that the natural course of aphasia leaves patients at risk of severe deterioration, while Denier et al. (2016) concluded that the diagnosis of aphasia alone on early assessment independently predicted a worse outcome. Mazza et al. (2012) indicated that the presentation of aphasia alone resulted in a low NIHSS score, and suggested that there should be a

Table I. General characteristics of the studies.

First author (year)	Sample size	Study type	Average age (±SD)	Sex% female	Baseline assessment tools	Follow-up assessment (time)	% Treated with reperfusion therapy (type)	% With aphasia	Summary
Core Concept 1: "Aphasia as a predictor" studies									
Al-Khaled (2014)	1007	Cohort	71.5 (12.2)	52	NIHSS mRS CT scan	CT (24 hr)	100 (rtPA)	56%	After rt-PA predictors for poor outcomes include age, aphasia, reduced LOC and hypertension.
Cho (2010)	2	Case study	51	0	MRI NIHSS	NIHSS (24 hr)	100% (rt-PA)	100%	Patients with aphasia and a low NIHSS benefit from thrombolysis.
Denier (2016)	100	Cohort	70.4 (13.8)	52	NIHSS Language composite score LAST CT or MRI	NIHSS (24 hr, 7 days for all) Language composite score LAST CT or MRI (24 hrs)	25% (rtPA)	100%	Suggests that the efficacy of thrombolysis in stroke patients with mild strokes/'isolated aphasia'.
Engelter (2006)	269	Cross sectional	Aphasic 80 (45–98) Non-aphasic 75 (37–96)	Aphasic 66% Non-aphasic 54%	NIHSS Basel–Minnesota test Extracranial and transcranial Doppler or CT or MRI or digital subtraction angiogram.	–	11% of those who presented with aphasia (rtPA)	30%	The presence of aphasia was associated with a higher likelihood of thrombolysis. (OR, 3.5; 95% CI, 1.12 to 10.96)
Kohrmann (2009)	32	Cohort	69.5	25	NIHSS CT	mRS 90 days MRI or CT (24-26 hours)	100% (rt-PA)	66%	Excluding patients from thrombolysis solely based on specific NIHSS is not justified.
Kremer (2014)	243	Cohort	60 (30)	43%	NIHSS CT	mRS (3 months) CT (24 hr)	100% (rt-PA)	28.4%	Supports the use of no lower NIHSS limit for IVT.
Leishangthem (2014)	1	Case study	82	100	NIHSS DynaCT	NIHSS (24 hr) MRI (24 hr) mRS (3 months)	100% (mechanical post rtPA)	100%	A subset of appropriately triaged patients may benefit from treatment with IAT mechanical thrombectomy devices.
Lundstrom (2015)	663	Cohort	71 (62–78)	45.3	Language composite score (NIHSS) CT/MRI	NIHSS (7 days) mRS (3 months) CT/MRI (22–36 hrs)	100% (rt-PA)	100%	Half of the patients with aphasia alone, treated with IV rtPA recovered fully within 7 days and 72% had an excellent outcome at 3 months.
Maas (2012)	669 (0m) 166 (D/C) 102 (6m)	Cohort	Discharge group 68.2 yrs 6m group 67.7 yrs	Discharge = 50% six months = 46.1%	NIHSS mRS CT	NIHSS (at discharge and 6 m follow up) mRS CT	Discharge: 28.3% 6m:29.4%	100%	Given the excellent prognosis for language recovery in mild stroke, the net benefit of thrombolysis in such cases is uncertain.
Mazza (2012)	1	Case study	41	100	NIHSS CT ABCD* MRI	TEE (24 hrs) CT (24 hrs)	100% (rtPA)	100%	Eligibility criteria for rt-PA not met, patient received IV rtPA over one hour and at the end of rt-PA infusion aphasia completely disappeared.

(continued)

Table I. Continued

First author (year)	Sample size	Study type	Average age (±SD)	Sex% female	Baseline assessment tools	Follow-up assessment (time)	% Treated with reperfusion therapy (type)	% With aphasia	Summary
Nesi (2014)	128	Cohort^	66	28	NIHSS	NIHSS (3 months post) mRS	36.7% (rtPA)	17.2%	Patients rated as mild at the first evaluation were unexpectedly seriously impaired 3 months after the stroke. Aphasia at onset was a strong predictor of such a negative outcome.
de Oliveira and Damasceno(2011)	37	Cohort	63.96 (11.3)	40.6	A collection of language tasks CT and/or MRI	Survival	1.6%	89.2%	Global aphasia associated with poor prognosis and a high rate of thrombolysis.
Pelletier (2010)	1	Case study	35	100	CT	MRI (24 hr)	100% (rtPA)	100%	A paradoxical stroke related to *PFO* that was thrombolysed for both conditions with a “neurological dose” of rtPA.
Core concept 2: “Aphasia as a persisting symptom” studies									
Chan (2008)	1	Case study	32	0	CT MRI NIHSS	CT (48 hr) MRA (8 hr) mRS (3 months)	100 (mech.)	100	Three months following stroke, the patient had moderately severe expressive aphasia but was mobilising independently with normal upper right and lower limb strength.
Crijnen (2016)	126 Assigned to IAT 162 to usual care	Randomised control trial	Intervention 65 (56–76) control 65.6 (58–76)	Intervention 40.5% control 35.2%	NIHSS CT	NIHSS (24 hr; 7 days)	Total 88.2% intervention 88.9% control 87.7%	100	IAT resulted in better early recovery from aphasia than usual care alone. The early effect of IAT on aphasia is smaller than the effect on motor deficits.
Denier (2015)	338	Cross sectional	68.9 ± 15.2	45	Composite language (NIHSS) MRI or CT	Composite language (24 hr; 7D) MRI or CT 24 hr	100 (rtPA)	40.5	Aphasia due to ischaemic stroke is considered to have a low likelihood of recovery even following rtPA.
Felberg (2002)	53	Cohort	68 ± 17 years for dramatic-recovery group versus 70 ± 15 years for non–dramatic-recovery group	–	NIHSS TCD	NIHSS (24h) mRS (1.6–1.7 months) TCD (Infusion end)	100% (rtPA)	13.2	Certain deficits ranked late in the infusion and often had only a partial improvement. These included facial motor strength and aphasia.
Finch (2014)	4	Single case design	64.25	25	NIHSS WAB CT	WAB (90 days)	100 (rtPA)	100	Using a standardised tests for motor deficits and aphasia, a reliable change in assessment scores over the three month time frame was observed only in the two participants with severe functional limitations and only for lower limb function.

(continued)

Table I. Continued

First author (year)	Sample size	Study type	Average age (±SD)	Sex% female	Baseline assessment tools	Follow-up assessment (time)	% Treated with reperfusion therapy (type)	% With aphasia	Summary
Hinman (2013)	1	Case study	28	0	NIHSS MRI	MCA (24 hr) NIHSS (10 days) mRS (10 days)	100 (rtPA then mech.)	100	Combined reperfusion therapies can yield revascularisation and good clinical outcomes. Discharged to acute rehabilitation 10 days after admission with residual right hemiparesis and mild transcortical motor aphasia.
Jacquin (2014)	75	Cohort^	67 ± 13.9	41.3	NIHSS French BDAE CT or MRI	NIHSS (7D) French BDAE (6months)	49.3 (rtPA)	75	Demonstrates that beyond its favourable effect on motor recovery, IV rtPA in AIS is an effective treatmentto improve recovery from Aphasia.
Kremer (2013)	50	Cohort	70 (30–90)	42	CT NIHSS	CT (24 hrs) NIHSS (24 hr) mrS (3 months)	100 (rtPA)	100	One-third of patients with aphasia improved, while two-thirds remained unchanged within 24 h after IV rtPA. Aphasia at 24 h was correlated to a higher morbidity according to the mRS at 3 months.
Layton (2006)	1	Case study	78	100	CT	MRI (48 hrs)	100 (mech.)	100	At the time of discharge, the patient had regained mobility on their right side and improved their language deficit from global aphasia to a moderate expressive aphasia.
Martins (2016)	228	Cohort	67.32	42.5	NIHSS CT or MRI	BAAL (D5-9) NIHSS (D7 ± 2)	100 (rtPA)	100	Approximately half of them showed mild improvement, one-fifth improved dramatically. Almost a third of the cases remained unchanged or worsened.
Saarinen (2015)	1	Case study	38	0	NIHSS CT and CT angiogram	CT (24 hrs) mRS (3 months)	100 (rtPA)	100	At the three-month follow-up, the patient had moderate disability caused by aphasia.
Santos (2014)	1	Case study	34	0	NIHSS CT	MRI (315mins) NIHSS (28D)	100 (rtPA then mech.)	100	Clinical evolution was favourable; however, the patient remained aphasic, with preserved comprehension.
Stapf (2000)	1	Case study	70	100	CT	MRI (48 hrs)	100 (IAT)	100	Speech skills improved from global aphasia to a syndrome of mixed transcortical aphasia, with a mild right sensory impairment and a moderate right facial paresis. No further motor deficit.
Tassi (2013)	1	Case study	28	100	NIHSS MRI	NIHSS (24h) MRI (24 hr)	100 (rtPA)	100	Persisting only with a slight "motory" aphasia.

National Institutes of Health Stroke Scale (NIHSS); NIHSS subtests 1b, 1c and 9 (language composite);recombinant tissue-type plasminogen activator (rt-PA); computed tomographic (CT); Magnetic resonance imaging (MRI/MRA); mechanical thrombectomy (mech) modified Rankin Scale (mRS); language screening test (LAST); Age, blood pressure, clinical features, duration (ABCD); Level of consciousness (LOC); acute ischaemic stroke (AIS); intravenous thrombolysis (IVT); intra-arterial thrombolysis (IAT); Western Aphasia Battery (WAB); Boston Diagnostic Aphasia Examination (BDAE); transcranial Doppler (TCD). "^" based on 'retrospectively extracted data from large prospective studies'.

more personalised case by case approach to administering reperfusion therapy. Multiple authors agreed that reperfusion therapy should be based on individual circumstances, rather than strict adherence to guidelines (Cho, Hermier, & Nigjoghossian, 2010; Denier et al., 2016; Pelletier, Bugeaud, Ibrahim, Morency, & Kouz, 2010). Leishangthem and Satti (2014) also highlighted the importance of using the right type of reperfusion therapy for the patient, as in their case study, the patient's aphasia did not improve after IV rtPA, however, the patient made a full recovery following a subsequent mechanical thrombectomy.

There has been some suggestion that patients with aphasia due to a minor stroke may receive less benefit from reperfusion therapies. Kremer et al. (2014) and Maas et al. (2012) proposed arguments against using isolated aphasia as an indication for reperfusion therapy. Both study arguments were based on a clinically suspected dissociation between a good early outcome from aphasia in minor strokes relative to recovery of other neurological deficits; as opposed to a better recovery from other neurological deficits than from aphasia in patients with severe strokes.

Core concept two: aphasia as an ongoing symptom post reperfusion therapy

Fourteen of the 27 studies, summarised in Table I, discussed aphasia as a persisting symptom following reperfusion therapy. When comparing mobility outcomes to aphasia outcomes, four of these studies have reported that mobility outcomes greatly improve, whereas aphasia appears to remain persistent in isolation, following IV and mechanical reperfusion therapy (Crijnen et al., 2016; Layton et al., 2006; Santos et al., 2014; Tassi et al., 2013).

Two case studies, one reported by Chan, Cordato, Kehdi, Schlaphoff, & McDougall (2008) the other by Saarinen, Sillanpaa, & Kantola (2015) described similar patients with a baselines that included dense hemiplegia, global aphasia and a marked facial droop. In both case studies, the patients received mechanical reperfusion therapy. Each case study reported almost complete resolution of symptoms, with aphasia as the sole remaining symptom.

Reperfusion therapy does appear to improve the severity of aphasia during the first week to 3 months post-stroke when studies compare patients who have been thrombolysed with non-thrombolysed patients. For example, Crijnen et al. (2016) compared 126 patients who received IAT with 162 controls. When language scores were measured at 24 hours and 1 week, it was noted that IAT resulted in better early recovery of aphasia, however, the effect of IAT was smaller than the effect on motor deficits at both points in time. A case study by Finch et al. (2014) found that of the four patients who received reperfusion therapy, in the form of IV rtPA, three of the four still required speech-language pathology services three months' post, for treatment of aphasia (2 mild aphasia, 2 severe aphasia).

Larger studies designed to identify trends in neurological recovery post reperfusion therapy also noted that certain deficits often had only a partial improvement, these included facial motor strength, aphasia and dysarthria (Felberg et al., 2002). Kremer et al. (2013) noted that early ischaemic changes were not a predictor of improvement in aphasia in patients receiving IV reperfusion therapy rtPA in the hyper-acute phase. Furthermore, two-thirds of those diagnosed with aphasia remained unchanged, prompting Kremer et al. (2013) to recommend a close follow-up of language functions at the acute stage.

The role of speech-language pathology

Speech-language pathology involvement was noted in seven of the 27 studies (Table II). Kremer et al. (2013) reported that 31 of the 50 patients in their study were seen by a speech-language pathologist to confirm the diagnosis of aphasia. In the study by Jacquin et al. (2014), for patients to be included in the study aphasia had to be clinically diagnosed by a speech-language pathologist. Jacquin et al. (2014) noted that the severity of aphasia during the first week and at 3 months following AIS stroke was milder in the patients that received thrombolysis. The authors also noted that patients treated with thrombolysis initially presented with a greater frequency of conduction and mild atypical aphasia. In their large multicentre study Engelter et al. (2006) also only included patients who had their aphasia diagnosed by a speech-language pathologist.

None of the 27 studies described the speech-language pathology intervention in detail, although this was not unexpected considering the studies were primarily written from a medical perspective. Only three of the seven studies (Denier et al., 2015; Finch et al., 2014; Jacquin et al., 2014) mentioned speech-language pathology management beyond administering assessments. Denier et al. (2015) reported patients with aphasia received daily speech and language therapy from baseline to discharge when appropriate. Finch et al. (2014) reported all four patients were assessed by a speech-language pathologist, with three of the four patients requiring speech-language pathology at discharge. A case study by Layton et al. (2006) noted that their patient was discharged to a rehabilitation centre for further speech-language pathology intervention. At the time of discharge, she had regained mobility of her right side and improved her language deficit to a moderate expressive aphasia. Jacquin et al. (2014) also noted whether the patients were discharged to a rehabilitation centre, for speech-language pathology treatment alone or whether the patient received no follow-up.

Five of the 27 studies looked at improvements in aphasia three months post stroke (Finch et al., 2014; Kremer et al., 2014; Leishangthem & Satti, 2014;

Table II. Speech pathology involvement in current reperfusion studies targeting aphasia.

First Author (year)	Speech pathology involvement	Assessment	Diagnosis – terms used	Treatment	Outcome
Denier (2015)	Patients with aphasia received daily speech and language therapy from baseline to discharge when appropriate	Not completed by a SLP	Aphasia	One hour of therapy with a SLP	100% of the patients with aphasia showed improvements in language scores by D7 with 20% completely recovering.
Engelter (2006)	Involved in confirming the diagnosis of aphasia – initially made by a neurologist	Speech, language, swallowing, Basel–Minnesota test.	Mild, moderate, severe aphasia utilising the subscale of the Scandinavian Stroke Scale.	n/a	n/a
Finch (2014)	Detailed 4 case studies from admission to discharge from allied health perspective	WAB	Aphasia classified as receptive or expressive Aphasia	n/a	Three of the four patients required ongoing speech language therapy following discharge
Jacquin (2014)	SLP reviewed aphasia diagnosis on request, to confirm eligibility	BDAE	Acute aphasia: Mutism Fluent aphasia Nonfluent aphasia One week post stroke: Conduction, Wernicke's, Motor aphasia (Broca's), Global, Subcortical, Nonclassified	Patients received: 1. Rehabilitation centre (46% post rtPA vs. 13.2% non-rtPA) 2. Speech therapist alone (29.7% post rtPA vs. 36.8% non-rtPA) 3. No rehabilitation (24.3% post rtPA vs. 50% non-rtPA)	One week post stroke aphasia was less severe in the thrombolysed than in the nonthrombolysed patients. Three months post stroke, this significant relationship was not observed The frequency of conduction and mild atypical aphasia is greater after a thrombolysed than a nonthrombolysed stroke.
Kremer (2013)	SLP reviewed aphasia diagnosis on request, to confirm eligibility	Not mentioned	Aphasia	n/a	n/a
Layton (2006)	Provision of therapy for aphasia on discharge to rehabilitation centre	Not completed by a SLP	Global aphasia Expressive aphasia	Not mentioned	Nine days after the thrombectomy, the patient was discharged to a rehabilitation centre. At the time of discharge, she had regained mobility of her right side and improved her language deficit to a moderate expressive aphasia.
Martins (2016)	Assessed patients with persisting aphasia	Aphasia was diagnosed by the attending neurologist. Patients with persisting aphasia were evaluated by SLPs using the BAAL	Normal, mild to moderate, severe or mute/global aphasia	Patients did not commence speech and language therapy before D7	One-third of the patients recovered completely and another 40% presented some degree of language improvement.

Speech-language pathologist (SLP); Western Aphasia Battery (WAB); Boston Diagnostic Aphasia Examination (BDAE); day seven (D7); National Institutes of Health Stroke Scale (NIHSS); Lisbon Aphasia Assessment Battery (BAAL).

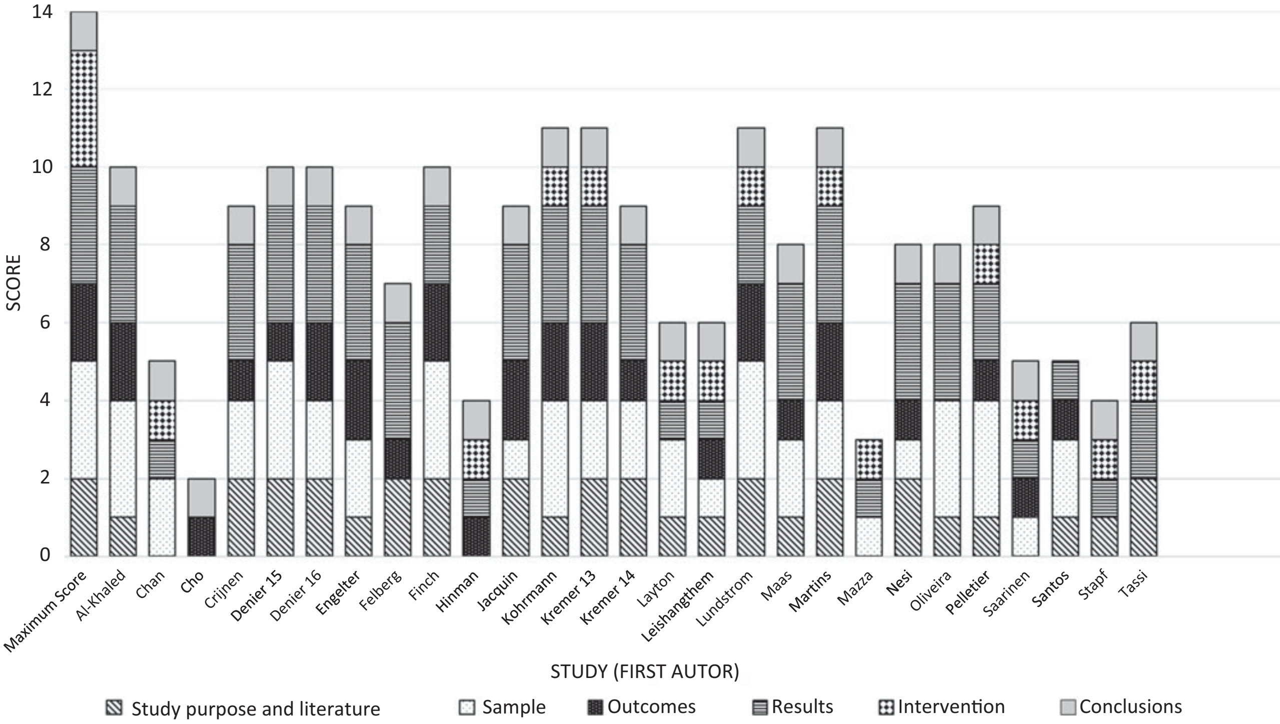

Figure 2. The McMasters critical review form (Law et al., 1998) was used to analyze the 27 studies. The data extracted from this analysis is presented here as a harvest plot. "Maximum Score" indicates maximum score per assessment criteria.

Lundstrom et al., 2015; Nesi et al., 2014). The rest of the studies look at aphasia until discharge from the acute setting.

Study quality

All 27 studies reviewed were analysed with the McMasters critical review form (Law et al., 1998). The data extracted from this analysis is presented as a harvest plot in Figure 2. None of the studies received the maximum score of 14, the highest score (11), was received by only four studies (Kohrmann et al., 2009; Kremer et al., 2013; Lundstrom et al., 2015; Martins et al., 2016). A strength of all studies were the conclusions, the conclusions were deemed appropriate in all but two studies, Mazza et al. (2012) and Saarinen et al. (2015). The next strength was the results section where all the studies reported the clinical importance of their study. However, their results were not always discussed in terms of statistical significance, which was largely because 11 of the studies were single case studies.

Twelve of the studies recorded outcomes by assessing aphasia with the NIHSS. However, Martins et al. (2016) reported that the NIHSS alone is insufficient for providing a diagnosis of aphasia. The NIHSS is considered a valid and commonly used stroke impairment scale that sums the scores from individual elements of neurological examination to provide an overall stroke impairment score, and is considered reliable in the setting of emergent stroke evaluation (Maas et al., 2012). However, when it comes to diagnosing aphasia, the NIHSS is a relatively crude instrument for language assessment, as the measure does not explore language comprehension or expression in detail.

Another strength of the reviewed studies was that all 27 of the studies reviewed had a clearly stated purpose, however, many were missing a thorough review of background literature.

Discussion

Since the USA Food and Drug Administration (FDA) approval in 1996, there has been a small, yet gradual increase in the utilisation of rtPA for treatment of AIS (Lubeck et al., 2016). Results from the NINDS (1995) Study Group demonstrated that rtPA improved functional outcome after ischaemic stroke when given within three hours of symptom onset. Research into reperfusion therapies has focussed to date on safety and efficacy along with functional improvement in general, we now need more detailed examination about its impact on the recovery of specific functions, such as communication. Consequently, this scoping review explored the relationship between aphasia and the emerging use of reperfusion therapy, with two core concepts emerging within the literature. The first concept was that aphasia could potentially predict the need for reperfusion therapy. The second concept was that aphasia was one of the last symptoms to resolve post reperfusion therapy. There was a lack of long-term follow-up with only two studies following-up aphasia scores six months post stroke (Jacquin et al., 2014; Maas et al., 2012). Since much of the research into the relationship between reperfusion therapies and aphasia has been conducted from a medical standpoint, the assessment used to diagnose aphasia in most of these studies, such as the NIHSS or composite assessments made up of NIHSS subtests, was not ideal for diagnosing aphasia. These three subtests provide a reliable yet insensitive measure of aphasia.

Aphasia and reperfusion therapy is an important area to research as aphasia not only causes functional disability but impairs quality of life. Speech-language pathology involvement within the emergency setting may be indicated, as aphasia alone appears to be an indicator of the need for reperfusion therapy, there may be a role for a quick and comprehensive aphasia assessment designed by speech-language pathologists, to use along with the NIHSS. A specific language screener like the LAST be completed prior to reperfusion therapy to compliment global stroke scales (Denier et al., 2015). The changing needs of this patient population in the rehabilitation setting also requires further research. Despite the success of reperfusion therapies, the studies reviewed in this scoping review indicate that this patient population may need to prioritise assessment and treatment by a speech-language pathologist, as aphasia appears to be a persisting symptom. Twenty-five of the 27 studies included in the review had ceased following up patients by three months post-stroke. The longest time between treatment with reperfusion therapy and follow up assessment was six months, only two studies included a six-month follow-up (Jacquin et al., 2014; Maas et al., 2012). Given the persisting nature of aphasia, there is a need for research into longer term outcomes (e.g. 12 months).

The majority of the studies reviewed in this scoping review were case studies or cohort studies, making up 40% and 44% of the studies included, respectively. The methodological quality of the studies varied greatly with scores ranging from two to eleven out of a possible fourteen on the critical review form developed by Law et al. (1998). This suggests room for longer more robust rigorous studies into aphasia and reperfusion. There was a distinct lack of cohesion between studies, with many of these studies identifying themselves as the first to look at the relationship between aphasia and thrombolysis without referring to the relevant earlier studies. Research into reperfusion therapy and how it is impacting on aphasia is progressing laterally, with several sites investigating similar questions, because more recent studies are not referring to older studies available, research is not progressing in a united manner. The goal of this scoping review is to bring the current literature together and identify the next step.

Limitations of this study include restricting the searches solely to papers published in English. Another limitation is the literature search was run twice and screened by one researcher.

Future research

As the use of reperfusion therapies becomes wide spread, speech-language pathologists are going to encounter this patient population more frequently. This scoping review has uncovered a number of areas for future research. One possible area of research is within the emergency department, investigating the current methods of diagnosing aphasia during the hyper-acute phase. Another is within the rehabilitation setting, looking at the natural progression of aphasia post thrombolysis and development of specialised treatment plans. Medical imaging could be conducted to see if there is an emerging pattern between the scans and presentation of aphasia. Twenty-five of the 27 studies included in the review had ceased following up patients by three months post-stroke. Given the persisting nature of aphasia, there is a need for research into longer term outcomes (e.g. 12 months).

Conclusion

In this scoping review, a total of 27 studies were examined to ascertain the current state of published literature on reperfusion therapies and aphasia. Assessment of the literature revealed two common themes: that a patient with AIS presenting with aphasia should be considered for reperfusion therapy and that aphasia is one of the last symptoms to remain post reperfusion therapy. This scoping review also identified a gap in the current literature, with only seven of the studies mentioning speech-language pathology, despite the key role speech-language pathologists play in assessing, diagnosing and treating aphasia. More research is required from a speech-language pathologist's perspective. Speech-language pathologists treating adults following AIS will benefit from additional information focussed on how the various forms of reperfusion therapies are impacting on the natural progression of aphasia, to ensure speech-language pathologists are effectively assessing and treating this patient population.

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No potential conflict of interest was reported by the authors.

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