Cognitive and Associated Communication Impairments Following Unilateral Acute Ischemic Stroke: Frequency, Predictors, and Clinical Outcomes

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Abstract

Background: Cognitive-communication disorders are preferentially associated with right hemisphere brain lesions and can be difficult to identify. **Objectives:** To identify predictors of cognitive-communication and overarching cognitive impairments in acute ischemic stroke (AIS). **Methods:** A prior MRI dataset of 72 AIS patients provided the basis for a voxel-based lesion-symptom mapping (VLSM) analysis of post-stroke aphasia and motor speech impairments. A chart review (N=32) of AIS patients was subsequently conducted to identify the frequency and predictors of cognitive and cognitive-communication impairments more comprehensively. **Results:** The VLSM analyses revealed involvement of the insula for aphasia and motor speech impairments. Frequencies of cognitive and cognitive-communication impairments were 62.5% and 34%, respectively. Predictors of cognitive impairments included left lesion laterality and stroke onset-to-arrival time. **Conclusion:** We identified the frequency and predictors of post-stroke cognitive and cognitive-communication impairments in acute stroke. There is a need for lesion mapping analyses in the future.

Résumé

Contexte: Les troubles cognitivo-linguistiques (TC-L) sont liés aux lésions cérébrales droites et sont difficiles à identifier. **Objectifs:** Identifier les indicateurs des TC-L après un accident vasculaire cérébrale ischémique aigu (AVC-IA) et des troubles cognitifs (TC). **Méthodes:** Un échantillon de 72 patients avec AVC-IA a permis une analyse cartographique lésion-symptôme basée sur les voxels (CL-SV) pour l'aphasie et les troubles de la parole (TP). Ensuite, une revue des dossiers (N=32, AVC-IA) a été réalisée pour identifier la fréquence et indicateurs des TC et TC-L. **Résultats:** Les analyses CL-SV ont démontré une association entre le cortex insulaire et l'aphasie et les TP. La fréquence des TC et TC-L était 62.5% and 34% respectivement. Les

indicateurs des TC comprenaient la latéralité gauche et le temps entre l'apparition des symptômes et l'arrivée à l'hôpital. **Conclusion:** Nous avons identifié la fréquence et indicateurs des TC et TC-L. Il reste une lacune scientifique concernant les analyses CL-SV.

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Legend

AAL	Automated Anatomical Labeling
ADC	Apparent Diffusion Coefficient
AIS	Acute Ischemic Stroke
Alpha FIM	Alpha Functional Independence Measure
AOS	Apraxia of Speech
BDAE	Boston Diagnostic Aphasia Examination
CADASIL	Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy
CCD	Cognitive-Communication Disorder
CI	Confidence Intervals
CLQT	Cognitive Linguistic Quick Test
CSBP	Canadian Stroke Best Practices
CT	Computed Tomography
DICOM	Digital Imaging and Communications in Medicine
DWI	Diffusion-Weighted Imaging
DW-MRI	Diffusion-Weighted Magnetic Resonance Imaging
ECG	Electrocardiogram
ESUS	Embolic Strokes of Unknown Source
EVT	Endovascular Therapy
FDR	False Discovery Rate
HIS	Health Information System

LHS	Left Hemisphere Stroke
MNI	Montreal Neurological Institute
MoCA	Montreal Cognitive Assessment
MR/MRI	Magnetic Resonance/Magnetic Resonance Imaging
NCCT	Non-Contrast Computerized Tomography
NIfTI	Neuroimaging Informatics Technology Initiative
NIHSS	National Institutes of Health Stroke Scale
OHRI	Ottawa Hospital Research Institute
OHSN-REB	Ottawa Health Science Network Research Ethics Board
OR	Odds Ratios
OT	Occupational Therapist
REB	Research Ethics Boards
RHD	Right Hemisphere Damage
RHS	Right Hemisphere Stroke
RIPA-2	Ross Information Processing Assessment (version 2)
rtPA	Recombinant Tissue Plasminogen Activator
SLP	Speech-Language Pathologist
TOH	The Ottawa Hospital
TWH	Toronto Western Hospital
VOI	Volume of Interest
VLSM	Voxel-Based Lesion Symptom Mapping
WAB	Western Aphasia Battery

Cognitive and Associated Communication Impairments Following Unilateral Acute Ischemic Stroke: Frequency, Predictors, and Clinical Outcomes

Stroke is a neurological disease characterized by a sudden onset of focal neurological deficits caused by vascular injury to the central nervous system including the brain, retina, and spinal cord (Sacco et al., 2013). Confirmatory symptoms are those lasting longer than 24 hours or identification of an infarct using neuroimaging and/or autopsy (Sacco et al., 2013). Stroke is categorized into two major types: ischemic and hemorrhagic, each differentiated based on how blood circulation is disrupted (Musuka et al., 2015). Ischemic stroke is the most common type accounting for approximately 85% of cases, while hemorrhagic stroke represents the remaining 15% (Musuka et al., 2015). Ischemic stroke occurs when blood circulation is disrupted as a result of vascular stenosis or occlusion, whereby a thrombolytic event may originate from the heart, artery, or in-situ small vessel disease (Hankey, 2017). Etiological subtypes of acute ischemic stroke include large-artery atherosclerosis, cardioembolism, small-vessel occlusion (also known as lacunar stroke), stroke of other determined etiology (such as non-atherosclerotic vascular causes, hypercoagulable states, or hematologic disorders), embolic strokes of unknown source (ESUS) (Hart et al., 2017), and stroke of undetermined etiology (Adams et al., 1993).

In contrast, hemorrhagic stroke occurs as a result of a blood vessel rupture that leads to bleeding and compression of surrounding brain tissue (American Heart Association, n.d.). There are two main categories of hemorrhagic stroke, one being intracerebral and the other subarachnoid hemorrhage (Sacco et al., 2013). Broadly speaking, symptoms of stroke can vary significantly based on etiology and lesion location. However, common symptoms often include unilateral weakness/numbness, speech difficulty, confusion, loss of vision, balance, or coordination (Hankey, 2017).

Risk Factors for Stroke

Stroke is a complex disease driven by a multitude of factors. Variables such as age, sex, ethnicity, and genetics are non-modifiable risk factors that contribute to disease onset and health outcomes (Boehme et al., 2017). Increasing age is a particularly strong risk factor as 95% of stroke cases are reported in adults who are 45 years of age or older among whom 66% are over the age of 65 (Allen & Bayraktutan, 2008). Additionally, the level of risk varies for men and women depending on their age. Overall, men are about 20% more likely to experience a stroke than women (Allen & Bayraktutan, 2008). However, across the adult population, women have equal or greater risk of stroke than men (Boehme et al., 2017). The elevated risk observed in young women may be attributed to issues related to pregnancy, postpartum recovery, and use of hormonal contraceptives thereby contributing to their increased susceptibility to stroke (Boehme et al., 2017). In age ranges above 65, risk of stroke shifts to being higher in men than women (Allen & Bayraktutan, 2008). Nevertheless, women experience a greater incidence of stroke with increasing age due to their longer life span (Government of Canada, 2016). Therefore, they may be disproportionately affected by stroke in terms of post-stroke disability and recurrence during their lifetime (Samai & Martin-Schild, 2015).

In addition to age, ethnicity is another important factor that contributes to risk of stroke. According to existing literature, the incidence of stroke and stroke-related mortality can differ significantly across different ethnic groups (Allen & Bayraktutan, 2008). For instance, a report from the United States shows that African Americans are twice more likely to experience a stroke and have higher stroke-related mortality rates in comparison to Caucasians (Boehme et al., 2017). Similarly, increased risk of stroke is observed in Hispanic and Latino Americans (Boehme et al., 2017) and Native Americans (Sanchez et al., 2021). This may be attributed to the

increased prevalence of cardiovascular risk factors such as hypertension, obesity, diabetes (McGruder et al., 2004), and atrial fibrillation in these minority groups (Sanchez et al., 2021). This disparity in stroke risk factors between ethnic groups may also be driven partly by certain barriers to healthcare such as income (Bravata et al., 2005), language differences (Clark et al., 2022), and geographical region (Hammond et al., 2022).

Additionally, genetic factors can also play a role in disease onset, especially in individuals with a family history of stroke. Moreover, stroke can also occur as a clinical presentation of certain genetic disorders such as Fabry disease, Moyamoya disease, cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) and sickle cell anemia (Barrett & Meschia, 2014). Similarly, genetic variations can contribute to the development of other risk factors for vascular disease such as hypertension, diabetes, and atrial fibrillation further compounding the risk of stroke in affected individuals (Boehme et al., 2017). Also, genetic heritability factors such as cardioembolism, large vessel disease, and small vessel disease may correlate with stroke subtypes (Bevan et al., 2012).

Modifiable risk factors are components of health that can be managed or altered to reduce the risk of stroke in vulnerable individuals. These may include pre-existing conditions such as hypertension, diabetes, hyperlipidemia, and atrial fibrillation (Allen & Bayraktutan, 2008). These are prominent risk factors that are known to contribute to stroke etiology including atherosclerotic disease and cardioembolism (Boehme et al., 2017). The presence of these health conditions contributes to elevating patient blood pressure and/or blood glucose levels which further increase their susceptibility to stroke (Grysiewicz et al., 2008). Likewise, lifestyle components such as diet, level of physical activity, alcohol consumption, smoking, substance use, and stress are other elements that can exacerbate the severity of stroke risk factors (such as

cardiovascular diseases) thereby increasing the likelihood of stroke (Boden-Albala & Sacco, 2000). To illustrate, diets with high sodium intake can lead to high blood pressure which in turns contribute to increase risk of hypertension (Boden-Albala & Sacco, 2000) and stroke mortality among overweight individuals (Grysiewicz et al., 2008). Similarly, diets lacking in folate, vitamin B12, and pyridoxine can lead to elevated levels of homocysteine which are associated with increased risk of vascular disease and stroke (Boden-Albala & Sacco, 2000). In contrast, lifestyle changes such as exercise can offer some protective effects against stroke in many individuals regardless of age, sex, or ethnicity (Grysiewicz et al., 2008). The benefits of exercise are associated with reduced risk of cardiovascular disease (Boden-Albala & Sacco, 2000), lower blood pressure and body weight, as well as decreased rates of diabetes (Boehme et al., 2017). Therefore, it is essential to consider the implications of different risk factors as part of stroke prevention strategies in order to help minimize risk of stroke in highly susceptible populations.

Acute Stroke Care

Stroke represents a medical emergency that requires rapid diagnosis and clinical evaluation in order to optimize patient chance of survival and recovery. This is crucial as the effectiveness of acute stroke interventions is time-sensitive based in terms of onset-to-arrival time. Thus, the primary goals of acute stroke care are to identify the stroke type and etiology, minimize health complications, promote early recovery, as well as provide palliative care if necessary (Boulanger et al., 2018). According to the Canadian Stroke Best Practices (CSBP) recommendations, patients who present with suspected stroke symptoms (i.e. sudden onset of focal neurological deficits) should receive immediate clinical evaluation as well as undergo neuroimaging through computed tomography (CT) or magnetic resonance imaging (MRI) to assess for the presence of stroke (Boulanger et al., 2018). Additionally, the primary purpose of

completing neuroimaging evaluation rapidly is to rule out the presence of hemorrhagic stroke and non-ischemic lesions that may exclude patients from receiving acute reperfusion therapies (Yew & Cheng, 2015).

Different types of neuroimaging modalities may be used to evaluate stroke patients depending on availability and stroke code protocol. In general, a non-contrast computerized tomography (NCCT) is the primary modality used to assess patients with suspected stroke symptoms due to its widespread availability across different stroke centers and fast acquisition time (Birenbaum et al., 2011). It is deemed to be a sufficient method to detect mass lesions, including brain mass or abscess, and acute hemorrhage (Yew & Cheng, 2015). Due to its sensitivity and fast processing time, this modality is often used to rule out the presence of hemorrhagic stroke which is crucial to help inform choice of acute interventions in cases of ischemic stroke (Birenbaum et al., 2011). Although, it is important to note that not all stroke cases can be detected by CT; thus the use of MRI may be required for diagnosis as it can provide better image resolution and has higher sensitivity than CT (Yew & Cheng, 2015). Diffusion-weighted magnetic resonance imaging (DWI or DW-MRI) is a form of MRI sequence that enables clinicians to examine the structural integrity of brain tissues and early infarcts in acute stroke (Yew & Cheng, 2015). This modality measures the diffusion of water in a tissue (Albers, 1998), where increased diffusion is evidenced as hyperintensities. In cases of acute ischemic stroke, the lesioned tissue would appear as an area of bright intensity on the DWI (Albers, 1998). These areas of hyperintensities seen on the DWI are then compared to a corresponding apparent diffusion coefficient (ADC) map to confirm the presence of acute ischemic stroke (Okorie et al., 2015). The ADC map is most confirmatory as it is not subject to artifacts or “shine through” that

may result from chronic lesions which allow physicians to firmly validate the presence of acute ischemia (Okorie et al., 2015).

In addition to neuroimaging procedures, the stroke care team should also complete an evaluation of the patient's airway, breathing, circulation, and overall neurological status as part of the initial assessment (Boulanger et al., 2018). This last item is usually assessed with a validated stroke scale such as the National Institutes of Health Stroke Scale (NIHSS), which provides an indicator of focal neurological deficits and stroke severity (Zeltzer, 2008). The NIHSS is composed of 11 items that are designed to measure a patient's level of consciousness, eye movement, vision, facial palsy, motor functions, limb ataxia, sensory loss, motor speech, and language (Zeltzer, 2008). The total score can range from 0 to 42 in which increasing scores indicate greater stroke severity (Zeltzer, 2008). Results from the NIHSS can be used to inform treatment decisions and provide a good indicator of a patient's neurological deterioration as well as recovery over the course of their hospital stay.

Currently, evidence-based treatment for acute ischemic stroke includes intravenous thrombolysis and endovascular therapy (EVT) (Boulanger et al., 2018). The effectiveness of these reperfusion therapies are time-limited in terms of stroke onset to arrival to hospital. For instance, intravenous thrombolysis with recombinant tissue plasminogen activator (rtPA) is only recommended for patients who arrive within 3 to 4.5 hours of stroke onset (Boulanger et al., 2018). EVT is typically considered for those who are diagnosed within a 6-hour window or up to 24 hours for specific patients with disabling symptoms and those with stroke on awakening (Boulanger et al., 2018). In addition to time, treatment eligibility may also be impacted by other factors such as advanced age, stroke severity, pre-existing conditions/risk factors, and/or medications (Boulanger et al., 2018).

Within the first 24 hours of symptom onset, the Canadian Stroke Best Practices (CSBP) also recommends that patients undergo vascular imaging (through CT or MR angiography), electrocardiogram (ECG), and receive comprehensive laboratory tests as part of standard protocol (Boulanger et al., 2018). Following these initial evaluations, patients are assessed by an interdisciplinary team of healthcare specialists such as neurologists, nurses, speech-language pathologists (SLP), occupational therapists (OT), physiotherapists, social workers, and other clinicians with expertise in stroke care (Boulanger et al., 2018). The goal is to identify the presence of post-stroke impairments and address any health complications (e.g., deterioration in status, responsiveness to therapy) that may arise during the acute phase (Boulanger et al., 2018). In general, assessments are carried out to evaluate swallowing functions, gross and fine motor skills, cognitive functions, nutritional needs and/or intake, bowel and bladder functions, and skin conditions (Boulanger et al., 2018).

Moreover, patient functional status is usually evaluated with a standardized tool such as the Alpha Functional Independence Measure (Alpha FIM) within the first two or three days of admission (Boulanger et al., 2018). This scale is made up of six outcome measures that can be divided into two categories: motor and cognitive ratings (Stillman et al., 2009). The motor component is assessed based on performance on tasks such as toilet transfer, bowel movement, walking, and bed transfer (for patients who could walk beyond 150 feet), or alternatively, eating and grooming (for those who could walk for less than 150 feet) (Lo et al., 2012; Stillman et al., 2009). As for the cognitive tasks, they are evaluated based on items such as expression and memory (Stillman et al., 2009). The total ratings from this instrument are used to evaluate stroke severity in which decreasing scores represent greater severity. For example, mild, moderate, and severe stroke are represented by scores above 80, 40 to 80, and below 40, respectively (Stillman

et al., 2009). Generally, the acute care phase is set to end at the time the patient is discharged from the acute care unit or by 30 days of hospitalization (Boulanger et al., 2018). At the end of this phase, results from the Alpha FIM and other clinical assessments can be used to inform plans of discharge and goals for rehabilitation (Boulanger et al., 2018), particularly those that relate to motor and cognitive functions. Within the realm of communication impairments, motor speech disorders, cognitive impairments, and cognitive-communication functions can be particularly debilitating.

Motor Speech Impairments

Following a stroke, various motor speech deficits may occur. Two types of motor speech impairments commonly observed in stroke patients are dysarthria and apraxia of speech (AOS) (Borthwick, 2012). Dysarthria is a motor speech disorder that is characterized by articulatory disruptions emerging from neuromuscular dysfunction in the execution of speech involving multiple subsystems: breathing, phonation, and articulation (Borthwick, 2012; Enderby, 2013). The incidence of dysarthria in acute stroke is close to half of all stroke patients (42% in Flowers et al., 2013).

Conversely, AOS is defined as an impairment in motor speech programming and planning (Borthwick, 2012). Patients with this disorder may exhibit difficulties in articulation and prosody, characterized by irregular speech rhythm and intonation, inconsistent articulation of repeated words, and/or difficulty initiating speech (Ogar et al., 2005). They may make arduous attempts to self-correct and often become frustrated, especially when only producing single syllables as a result of the deficit (H. Flowers, personal communication, June 05, 2022; Ogar et al, 2005). The frequency of AOS is low, hovering around 12 to 16% of patients (Flowers et al., 2013; Itabashi et al., 2016) and almost always coincides with aphasia (Borthwick, 2012). These

disorders differ from cognitive impairments in that they relate to neuromuscular control mechanisms rather than higher cognitive functions.

Cognitive Impairments

After a stroke event, it is common for patients to experience some disturbances in cognitive function, especially during the early stage of their recovery. Cognitive impairments are defined as a disruption in cognitive function impacting at least one cognitive domain such as language, learning and memory, social cognition, complex attention, executive function, and/or perceptual-motor function (Sachdev et al., 2014). Broadly speaking, the frequency of post-stroke cognitive deficits can vary based on lesion characteristics and stages of stroke recovery. For example, reports from Nys et al. (2005) showed that cognitive deficits were present in 48% of acute stroke patients in the first three weeks after stroke presentation. When assessed at follow-up visits, this number was reduced to 30.6% (Nys et al., 2005). Additionally, a previous study by Nys et al. (2007) also showed that cognitive impairments were more frequently observed in patients who had cortical stroke (approximately 74%) as compared to those with infratentorial or subcortical strokes whose frequencies hovered slightly above 40% in the acute stage. Cognitive impairments are also strongly associated with poor functional outcomes even with successful overall clinical recovery (Jokinen et al., 2015). At the acute stage, cognitive impairments are strong predictors of long-term cognitive decline, depression, and decreased independence for activities of daily living (Nys et al., 2007). A longitudinal study conducted by Douiri et al. (2013) also demonstrated that the prevalence of post-stroke cognitive deficits in patients with first-ever stroke could persist past three months, five years, and 14 years after the stroke event. Sociodemographic factors such as age, ethnicity, and socioeconomic status were also found to contribute to the variation of these deficits (Douiri et al., 2013). As cognitive impairments can

persist long after stroke recovery, it is important to identify and address these issues early on to mitigate their impact on patients' quality of life.

For instance, aphasia is a prominent cognitive impairment that is frequently observed in acute stroke patients. It is a communication impairment defined as an acquired language disorder that hinders a patient's ability to use and understand oral and written language due to a disruption in language processes in the language-dominant hemisphere of the brain (McNeil & Pratt, 2001). According to existing literature, the frequency of aphasia is close to one-third of all stroke patients in the acute stage (Flowers et al., 2016). The presence of this disorder can impact patient recovery as it is associated with longer length of stay (Flowers et al, 2016) and increased complications such as infection, myocardial infarction, and diminished neurological functions in the acute setting (Boehme et al., 2016).

Cognitive-Communication Disorder

Disturbances in cognitive functions involving different cognitive domains can also interfere with language processing thereby hindering a patient's communication abilities after stroke due to impairment in interpretation and pragmatic use of language (Togher et al., 2014). Cognitive-communication disorder (CCD) constitutes a specific term used by speech-language pathologists (SLP) referring to a subset of communication deficits that emerge due to underlying cognitive dysfunction following an acquired brain injury, such as stroke (Togher et al., 2014). This type of communication impairment differs from acquired language disorders (i.e. aphasia) and speech disorders (such as dysarthria and AOS) as it results directly from impacts from other cognitive domains (H. Flowers, personal communication, Sept 24, 2022). This is because microlinguistic processes of language often remain intact in CCD patients (Ferré & Joanette, 2016; Hewetson et al., 2017). These processes mainly refer to mechanisms involved in within-

phrase functions such as grammar, syntax, phonological encoding, and lexical retrieval (Barker et al., 2017). Language components are generally not impacted in patients with CCD as they retain their capacities to use and understand the structural aspects of language and can formulate and understand basic sentences accordingly (Togher et al., 2014). Instead, CCD mainly impacts the macro level of language processes which represent discourse and other between-sentence interpretive mechanisms (Barker et al., 2017). For example, affected mechanisms may include interpreting figurative language, social and emotional content of language, speaker perspectives in discourse, and/or narrative coherence (Joanette et al., 2013; Kimbarow, 2019), and such deficits are often preferentially associated with right hemisphere functions (Barker et al., 2017). Hence, CCD identification is often sought in stroke patients with right hemisphere damage (RHD) (Abusamra et al., 2009). Currently, the characterization of cognitive and communicative deficits resulting from RHD results from a small body of literature at present (Blake et al., 2002; Côté et al., 2007; Joanette et al., 2013). This issue was highlighted in an article by Blake and her colleagues (2002) who further commented on a lack of consistency in the type of terminology used to describe cognitive and communicative deficits in patients with RHD across and within healthcare disciplines. They pointed out that the range of terminology used to identify such deficits represents a barrier to improving effective clinical diagnosis and management of patients with RHD (Blake et al., 2002).

Current Challenges

At this time, identifying CCD in acute stroke patients can be a challenge due to the diverse clinical presentations of this disorder. To illustrate, common features of CCD may include: difficulties with turn-taking, topic maintenance, inferences, figurative language/metaphor, and perspective taking in social interactions (Joanette et al., 2013;

Kimbarow, 2019). Other examples may also include aprosodia, tangential speech, excessive fixation on details (i.e. unable to see the big picture), and forgetfulness during conversation (such as repeating same content or losing train of thought) (Kimbarow, 2019). Furthermore, patients with CCD may have difficulty appreciating intent, making connections, and using contextual clues during social interactions (Kimbarow, 2019). These deficits can have a significant impact on patients' social participation in regards to interpersonal relationships as well as occupational activities and independent living skills (Hewetson et al., 2018).

Given that CCD may occur more frequently after a right hemisphere stroke (RHS), it is important to elucidate potential disparities in clinical assessments between persons with right and left hemisphere lesions. That is, RHS clinical symptoms may be harder to recognize and more nuanced compared to left hemisphere symptoms (Foerch et al., 2005). This could be further compounded by RHS patients' reduced awareness and/or perception of neurological deficits at the time of stroke presentation (Foerch et al., 2005).

Moreover, symptoms resulting from right hemisphere events can also be perceived as being less severe or may not be recognized as stroke by physicians in certain cases (Foerch et al., 2005). In fact, RHS patients have been found to score lower on the NIHSS in comparison to those with left hemisphere stroke (LHS) despite having comparably similar lesion volume (Fink et al., 2002; Woo et al., 1999). It is worth noting that the NIHSS has also been criticized for placing more emphasis on focal language deficits that are more attributed to left hemisphere damage (Vitti et al., 2022; Woo et al., 1999). Thus, inadequate identification of RHS can potentially impact patient clinical courses, whereby they may be exempt from receiving acute stroke interventions and have reduced opportunity for optimal recovery and survival after stroke (Legge et al., 2005).

Study Objectives and Research Questions

Currently, there is a paucity of literature that examines the clinical considerations of lesion laterality (i.e. right versus left hemisphere) as it pertains to the clinical course and management of stoke patients in the acute care setting. Additionally, knowledge about the individual and neuroanatomical predictors of cognitive-communication impairments in stroke patients is not well understood. Since the underlying cause of CCD is due to cognitive deterioration, the interplay between communicative and cognitive functions may coincide in specific brain regions and extend well beyond the classical regions that are involved in language processes. Therefore, the primary objectives of this study are to: 1) identify individual and neuroanatomical predictors of post-stroke cognitive-communication impairments in acute ischemic stroke patients and to 2) examine the clinical course and management of acute ischemic stroke patients with cognitive and/or communication impairments according to lesion laterality.

Thus, the following research questions were used to guide the study: 1) Which individual and/or neuroanatomical factors predict the presence of post-stroke cognitive-communication impairments in patients with acute ischemic stroke? and 2) How does the clinical course differ for acute ischemic stroke patients with cognitive and/or communication impairments according to lesion laterality (right versus left hemisphere)? Hypothesis 1: We hypothesized that individual factors such as age, sex as well as neuroanatomical lesion site (e.g., frontal, parietal, and temporal lobes) would predict the presence of cognitive-communication impairments in patients with acute ischemic stroke. Hypothesis 2: We also hypothesized that patients with right hemisphere lesions would experience longer delays in hospital arrival and shorter length of stay compared to those with left hemisphere lesions.

Methods

We obtained data from two different samples to help address the proposed research questions. The first stage of our investigation involved a previously acquired sample of first-ever acute ischemic stroke patients with MR imaging (see Flowers et al., 2017). Information from this prior sample provided the basis for a preliminary neuroanatomical inquiry around post-stroke communication impairments. It formed the basis to develop an understanding of lesion localization for communication impairments (specifically aphasia, dysarthria, and AOS) before engaging in similar inquiry about more diverse cognitive and cognitive-communication impairments from a newly derived second sample. At present, the second sample constitutes a first step towards identifying brain regions that may be implicated in cognitive and cognitive-communication deficits after an acute stroke. Furthermore, the sample will also provide a more comprehensive overview of clinical and stroke-based factors that may contribute to the development and expression of CCD.

MRI Dataset

The prior sample included 160 first-ever acute ischemic stroke patients with MRI scans from a previous study by Flowers et al. (2017). The sample was derived from the Ontario Stroke Registry database from a consecutive series of acute stroke patients across multiple hospital sites from which a random selection was taken for 250 acute stroke patients at the Toronto Western Hospital (TWH) (Flowers et al., 2013). The sample was then restricted to patients without prior neurological impacts (e.g., dementia or neuroimaging evidence of tumour, etc.) and who received an MRI scan within 2 weeks of stroke onset resulting in a subsample of 160 patients being accepted in this previous study (Flowers et al., 2017). Multiple scan types were acquired including a B0 scan, followed by a DWI scan, and a computation of its corresponding ADC map

(Flowers et al., 2017). All lesions were manually traced on the DWI scans at the time, but only used for the analysis of lesion volume (Flowers et al., 2017). For the current study, we used the lesion tracings to enable a voxel-based lesion symptom mapping (VLSM) paradigm for communication impairments. Our specific methods are described accordingly.

Eligibility Criteria

For the purpose of our study, only patients from the prior dataset who had unilateral hemispheric lesions were included in the final sample. Given our research interests in lesion laterality and cognitive functions, patients with bilateral and/or infratentorial lesions (i.e. brainstem and/or cerebellum) were excluded. In addition, those with evidence of covert stroke (Flowers et al., 2017) were also excluded.

Image Normalization Procedure

To ensure optimal comparisons of lesion data across patients, all MRI scans were normalized including the previously traced lesions (which had been stored as a volume of interest (VOI) file for each patient) prior to conducting the VLSM analysis. The first step involved obtaining the B0 scan and anatomical DWI by first converting patients' MRI scans, originally in digital imaging and communications in medicine (DICOM) format, into neuroimaging informatics technology initiative (NIfTI) format. Subsequently, the image matrices from the anatomical DWI scans (in NIfTI format) were copied onto the VOI files. This step was completed to ensure that the lesion overlay accurately matched the corresponding anatomical DWI scans based on the original B0 matrix. Next, the image origin of the anatomical DWI image for each subject was manually reset to a new starting estimate (according to the anterior commissure – posterior commissure line) using SPM12 software. This step enables better warping to the standard template space during the normalization process. Subsequently, the

corresponding DWI images and VOI file for each subject were also reoriented to this new starting estimate. Thereafter, the VOIs were coregistered and normalized to the Montreal Neurological Institute (MNI) T1 template using SPM12 clinical toolbox (https://www.nitrc.org/projects/clinicaltbx/) (Rorden et al., 2012). This procedure excludes information from the lesion when performing image registrations and normalizations. Finally, the quality of the image normalization was reviewed by a neuroimaging expert (J.S) and a previously trained researcher (H.F, see Flowers et al., 2017).

Voxel-Based Lesion Symptom Mapping Analyses

Next, voxel-based lesion symptom mapping (VLSM) analyses (Bates et al., 2003) were performed to identify neuroanatomical correlates of aphasia, dysarthria, and AOS in patients in LHS and RHS groups. These analyses were performed using MatLab and the NiiStat add-on software (https://www.nitrc.org/projects/niistat/). For the LHS group, VLSM analysis was conducted using only damaged voxels that were present in at least 3 individuals. Because there were fewer patients in the RHS group, only damaged voxels that were present in at least 2 individuals were included in the analysis. To correct for multiple comparison, a false discovery rate (FDR) permutation threshold at $p < 0.05$ was used to identify significant voxels. These analyses were also performed while accounting for lesion volume as a covariate. In the event that no voxels survived the FDR correction threshold, we also reported anatomical regions containing clusters of at least 20 voxels for each impairment using an uncorrected p threshold of < 0.01 from MRIcroGL software. Significant anatomical regions were identified using the Automated Anatomical Labeling (AAL) atlas (Lancaster et al., 2000; Tzourio-Mazoyer et al., 2002).

Chart Review Dataset

Information from the MRI analysis served as a preliminary inquiry into neuroanatomical substrates of post-stroke communication impairments. This analysis has also formed a pathway to examine more diverse cognitive functions that may impact communication, which was not previously assessed by Flowers et al. (2017). As the MRI dataset did not provide any information regarding cognitive and cognitive-communication impairments, a separate retrospective chart review was conducted to extract data pertaining to these deficits from a similar subset of patients. The sample included a consecutive series of adult patients who were admitted to The Ottawa Hospital (TOH) with first acute ischemic stroke from April 2020 to March 2021. A total of 110 admissions to the stroke unit were identified through simple random sampling as potentially eligible for the chart review.

Eligibility Criteria

Patients were included if they met the following criteria: a) were 18 years of age or older, b) spoke English as their first and primary language, c) were diagnosed with ischemic stroke based on physician clinical determination and/or with confirmed infarction as visualized on CT or MRI. For patients whose primary language information was unknown, their eligibility was determined based on surrogate indicators of English language status when English was listed as their preferred language in the health information system (HIS) and they had other confirmatory characteristics. For instance, individuals were included if their first and last names were of English origin. When the origin was unclear, language status was inferred (again when English was listed as the preferred language) from clinician consultation reports and/or assessment tools. As with the MRI study, the target population included first acute ischemic stroke patients. Our identification of eligible patients was based on similar criteria to those in the MRI dataset. That

is, patients with hemorrhagic stroke or transient ischemic attack were excluded. Additionally, those who were previously diagnosed with stroke, dementia, mild cognitive impairment and/or other neurological compromise (such as brain injury, tumours, contusions, abscess, or previous brain surgery) were also excluded from the study. Finally, patients who presented with bilateral stroke and/or exclusively infratentorial lesions were also excluded.

Outcome Variables

Patients' medical charts were reviewed by one rater (K.H) for data extraction. The data collection process involved gathering information related to patient demographics, stroke presentation, previous medical history, clinical processes, neuroimaging results, and discharge disposition.

Independent Variables. Outcome variables related to patient clinical course and stroke presentation were extracted and sorted according to stroke laterality. These variables included estimated time from stroke onset to hospital admission, length of stay, stroke diagnosis and etiology, past medical history, clinical processes, and discharge location and status. Estimated time of stroke onset was extracted from neurology stroke code consultation report as either "time of stroke onset" or "time of last seen well/normal". When times of stroke onset or last seen well/normal were unclear, 12:00 PM EST was used as the default time on the closest day of symptom onset. Time of hospital admission was extracted from a dataset provided by Data Analytics and Health Records at TOH. This dataset also provided information about other pertinent variables such as total length of stay in hospital and in acute care unit (in days), Alpha FIM score, and thrombolysis treatment. Lesion laterality was determined based on neuroimaging results as derived from radiology reports and/or physician clinical determination as shown in neurology stroke code consultation or discharge summary reports.

Data about patients' stroke severity, disability, and functional status in the acute stage were also collected and extracted from the NIHSS and Alpha FIM scores. In addition, information related to in-hospital interventions was also documented and characterized based on the following categories: thrombolysis, endovascular treatment/embolectomy, and neurosurgery/carotid stenting. Furthermore, information related to in-hospital infections was gathered from discharge summary reports. Information about discharge location and status were also collected and sorted based on the following categories: rehabilitation facility (in-patient or out-patient), repatriation to another acute care hospital, long-term care facility, home, or death in facility. Additionally, information about patient's neurological status at the time of discharge was extracted from NIHSS score indicated on discharge summary report. If this information was not available at discharge, the most recent score recorded on NIHSS flowsheet was documented instead.

Dependent Variables. The presence or absence of cognitive deficits and cognitive-communication impairments was documented for each patient. Reports of cognitive impairments were categorized into the six established domains: language, learning and memory, social cognition, complex attention, executive function, and/or perceptual-motor function (Sachdev et al., 2014). The presence of post-stroke cognitive and cognitive-communication impairments were documented if patients were identified as having the deficits based on informal or formal assessment by one of the following specialists: SLP, OT and/or neurologist.

As descriptions of patient cognitive function and cognitive-communication performance may vary across different healthcare professions, we established a list of key terminology to guide our classification and identification of these deficits in a chart review manual. The manual was developed based on information obtained from a literature review (Blake et al., 2002;

College of Audiologists and Speech-Language Pathologists (CASLPO), 2018; Sachdev et al., 2014) and consultation with research team members with expertise in speech-language pathology and neuropsychology. By default, absence of an impairment was recorded when there was no evidence of a positive assessment finding. To obtain a comprehensive picture of other communication (e.g., dysarthria and AOS) and associated motor functions (e.g., dysphagia), we extracted information from SLP assessments (whether via informal or standardized testing) and other specialist consultation reports where relevant. Examples of standardized tools used during communication assessments by SLP included the Western Aphasia Battery (WAB), Boston Diagnostic Aphasia Examination (BDAE), Australian Aphasia Rehab Pathway, modified Ross Information Processing Assessment (version 2) (RIPA-2), Cognitive Linguistic Quick Test (CLQT), and the Source for Dysarthria 2nd edition. Following the chart review process, the number of patients with language impairments was verified by an SLP (H.F). Furthermore, identification of cognitive and cognitive-communication deficits was verified by an SLP (H.F) for a small number of patients whose impairment status was unclear.

Data Analysis

For the first research question (i.e. which individual and/or neuroanatomical factors predict the presence of post-stroke cognitive-communication impairments in patients with acute ischemic stroke?), logistic regression analyses of the chart review data were performed to evaluate predictors of cognitive and cognitive-communication impairments with a $p < 0.05$ threshold to obtain odds ratios (OR) and their 95% confidence intervals (95% CI). A number of predictor variables were selected for these analyses based on review of existing literature on cognitive-communication impairments (Gauthier et al., 2018; LeBlanc et al., 2021) and clinical judgment from team members with expertise in SLP, OT, and neuropsychology. Choices for

predictors were also limited to variables with consistent documentation (i.e. missing data <10 percent of patients). The logistic regression models were computed with a minimum of three outcome events per predictor variables which were deemed to be acceptable for the purpose of this exploratory study (see Vittinghoff & McCulloch, 2007).

For the second research question (i.e. how does the clinical course differ for acute ischemic stroke patients with cognitive and/or communication impairments according to lesion laterality (right versus left hemisphere)?), we conducted Mann-Whitney U tests to examine the differences in time from stroke onset to hospital admission as well as length of stay between LHS and RHS patients who had cognitive impairments from the chart review sample. These statistical analyses were computed using SAS software (version 9.4).

Ethical Considerations

Previous ethics approval from the Toronto Western Hospital (TWH) was renewed to permit ongoing use of MRI data for secondary analysis via a data sharing agreement with University of Ottawa. For the chart review data, we obtained ethics approval from the Ottawa Health Science Network Research Ethics Board (OHSN-REB) to enable access to the stroke patient dataset from Data Analytics and Health Records at TOH. A secondary institutional approval was also approved by the University of Ottawa Research Ethics Boards (REB) and a data sharing agreement was executed between The Ottawa Hospital Research Institute (OHRI) and University of Ottawa prior to conducting the study.

Results

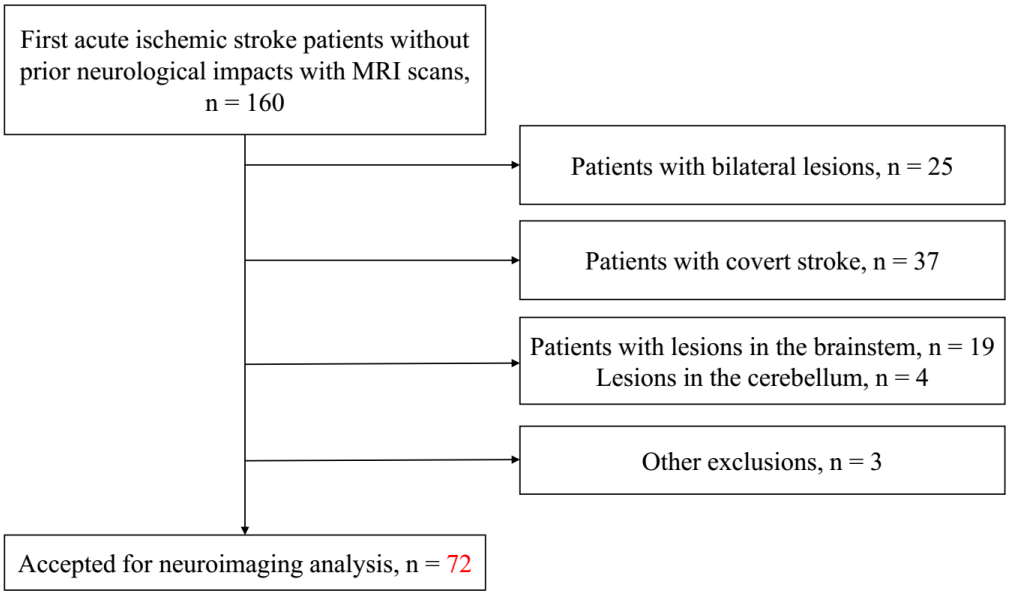
MRI Dataset

Among the 160 patients, there were 72 who met the inclusion criteria for neuroimaging analysis (Figure 1). There were 44 patients with lesions in the left hemisphere and 28 with

lesions in the right hemisphere. In the LHS group, aphasia, dysarthria, and AOS were present in 61%, 43%, and 16% of the patients, respectively (Table 1). As for the RHS group, aphasia and dysarthria were present in 7% and 54% of the patients, respectively, while AOS was not evidenced.

Figure 1

Flowchart Diagram of Eligible Patients for Neuroimaging Analysis



Neuroimaging Results

Findings from the VLSM analyses were reported based on an uncorrected *p* threshold of $p < 0.01$ as none of the voxels have survived the FDR correction for multiple comparison. Voxel clusters associated with aphasia, dysarthria, and AOS were identified for patients in LHS and RHS groups. In the LHS group, VLSM results for aphasia and AOS were represented in Figures 2 and 3, respectively. Voxel clusters associated with aphasia and AOS were shown in Table 2. Voxel clusters associated with aphasia were located in the putamen. Significant anatomical structures associated with aphasia and AOS included the insula, rolandic operculum and superior temporal gyrus for this group. Additionally, significant structures correlated with AOS also

included the Heschl's gyrus and inferior frontal gyrus (opercular part). As for dysarthria, no voxel clusters survived the uncorrected *p* threshold in this group.

In the RHS group, VLSM results for aphasia and dysarthria were represented in Figures 4 and 5, respectively. Voxel clusters correlated with aphasia and dysarthria were shown in Table 3. Significant structures correlated with aphasia included the precentral and postcentral gyri. In contrast, significant structures correlated with dysarthria consisted of the insula and superior temporal gyrus.

Table 1

Post-Stroke Communication Impairments by Stroke Laterality for Patients from MRI Dataset

Communication impairments	**All patients (N=72)**	**Left hemisphere stroke (n=44)**	**Right hemisphere stroke (n=28)**
Aphasia, n (%)	29 (40)	27 (61)	2 (7)
Dysarthria, n (%)	34 (47)	19 (43)	15 (54)
AOS, n (%)	7 (9.7)	7 (16)	-
Co-occurring impairments			
Aphasia and dysarthria, n (%)	15 (20.8)	13 (30)	2 (7)
Aphasia and AOS, n (%)	7 (9.7)	7 (16)	-
Dysarthria and AOS, n (%)	3 (4)	3 (7)	-
Aphasia, dysarthria, and AOS, n (%)	3 (4)	3 (7)	-

Table 2

Anatomical Structures Results for Aphasia and AOS in LHS Group (from Uncorrected Z Map)

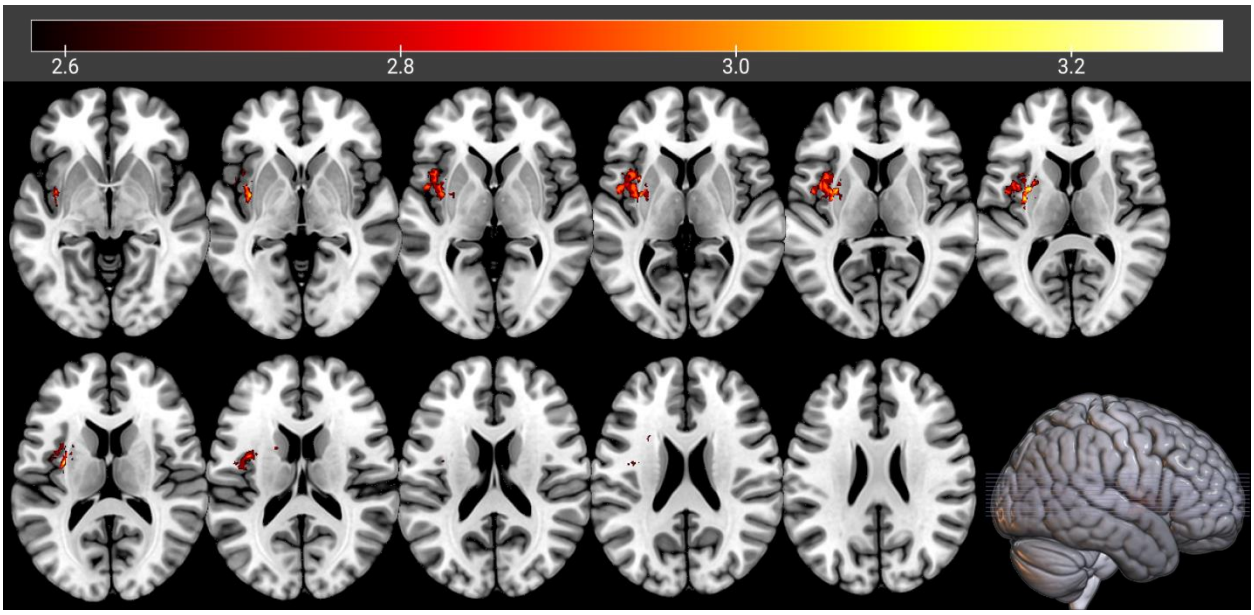
Behavioral Variable	**Structure**	**Z-value**	**X**	**Y**	**Z**	**Volume**
Aphasia	Insula Rolandic Oper Putamen Temporal Sup	2.95	-38.2	1.3	6.4	3248
	Rolandic Oper Insula	2.70	-39.6	-6.0	21.2	35
AOS	Insula	3.25	-40.4	0.6	6.4	4589

	Rolandic Oper			
	Temporal Sup			
	Heschl			
	Frontal Inf Oper			

Abbreviations**:** Rolandic Oper, Rolandic operculum; Temporal Sup, Superior temporal gyrus; Heschl, Heschl's gyrus; Frontal Inf Oper, Inferior frontal gyrus (opercular part).
Note: X, Y, and Z columns represent coordinates on the MNI-152 template.

Figure 2

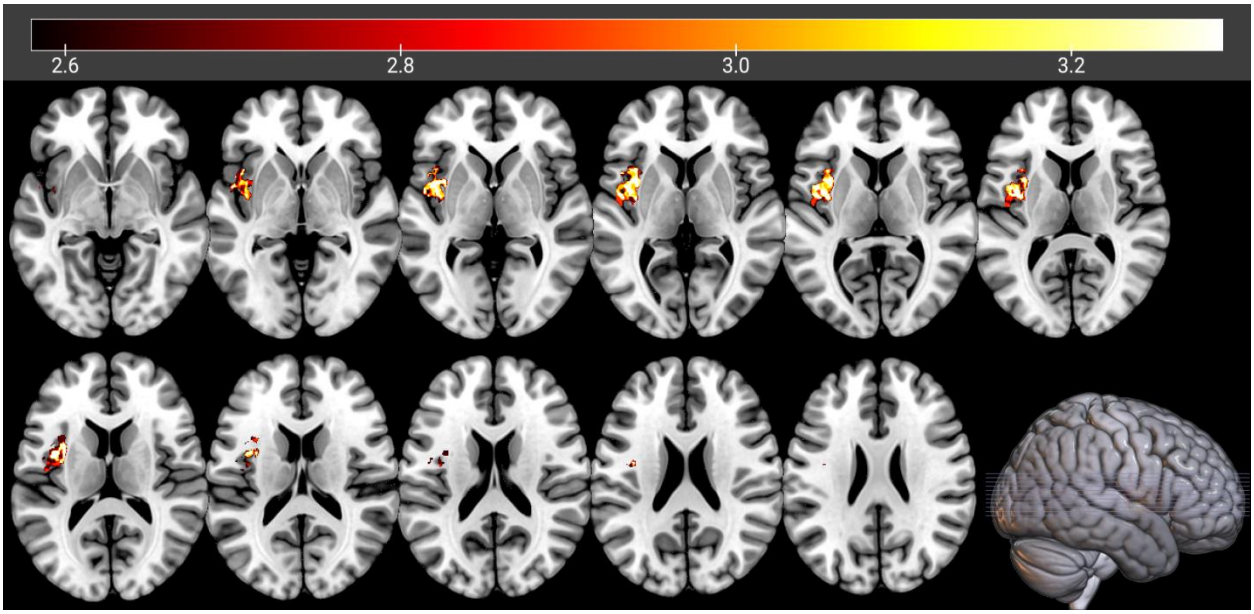
VLSM Results for Aphasia for Patients in LHS Group from Uncorrected Z Map



Note. Results are depicted on an MNI-152 template across multiple slices in the axial plane (Slice numbers: A H -0.1 V -0. -5 -2 1 4 7 10; 13 16 19 22 25S X R 0). Slices ordered from the upper left to the bottom right indicate inferior to superior layers of the MNI-152 template. The colour bar represents the Z scores corresponding to the uncorrected p threshold range of p < 0.01 (Z=2.58) to 0.001 (Z=3.29).

Figure 3

VLSM Results for AOS for Patients in LHS Group from Uncorrected Z Map



Note. Results are depicted on an MNI-152 template across multiple slices in the axial plane (Slice numbers: A H -0.1 V -0. -5 -2 1 4 7 10; 13 16 19 22 25 S X R 0). Slices ordered from the upper left to the bottom right indicate inferior to superior layers of the MNI-152 template. The colour bar represents the Z scores corresponding to the uncorrected p threshold range of p < 0.01 (Z=2.58) to 0.001 (Z=3.29).

Table 3

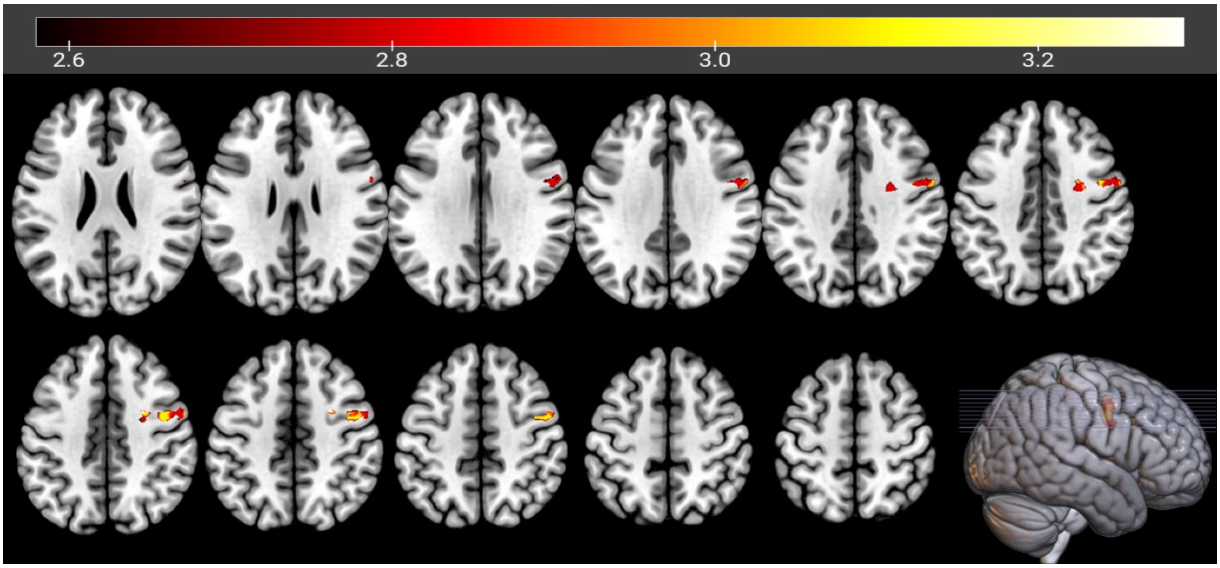
Anatomical Structures Results for Aphasia and Dysarthria in RHS Group (from Uncorrected Z Map)

Behavioral Variable	Structure	Z-value	X	Y	Z	Volume
Aphasia	Precentral Postcentral	2.95	45.2	-1.6	40.3	2311
Dysarthria	Insula Temporal Sup	3.20	40.8	-1.6	-6.1	100
	Insula	2.92	38.5	-14.9	-3.2	29

Abbreviations: Precentral, Precentral gyrus; Postcentral, Postcentral gyrus; Temporal Sup, Superior temporal gyrus.
Note: X, Y, and Z columns represent coordinates on the MNI-152 template.

Figure 4

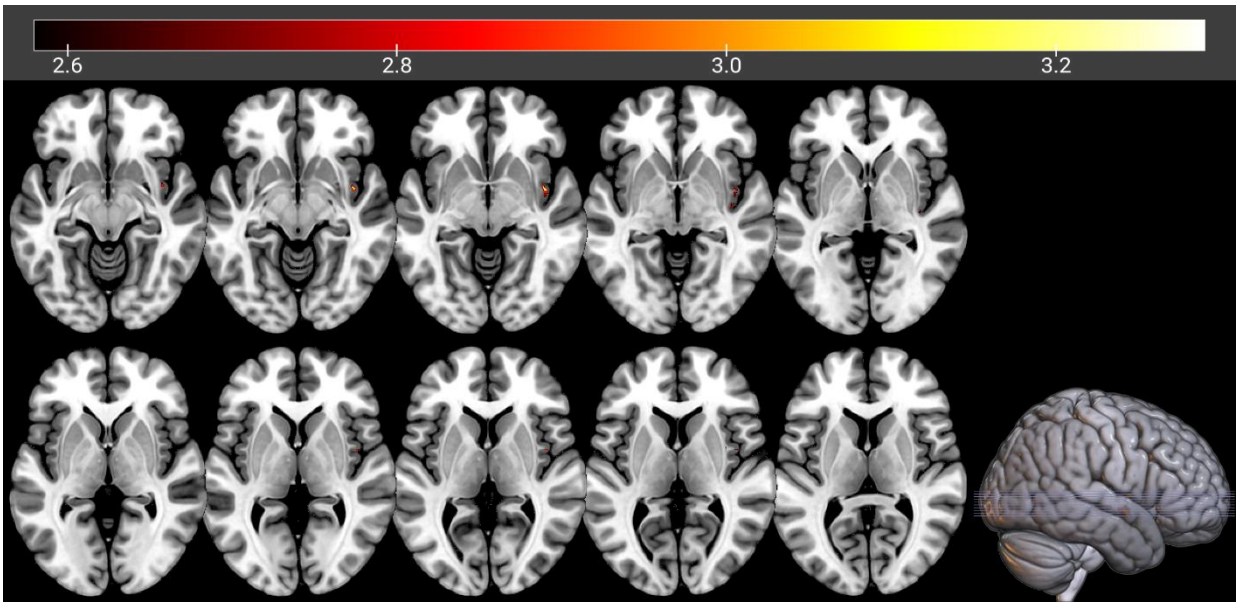
VLSM Results for Aphasia for Patients in RHS Group from Uncorrected Z Map



Note. Results are depicted on an MNI-152 template across multiple slices in the axial plane (Slice numbers: A H -0.1 V -0.1 25 28 31 34 37 40; 43 46 49 52 55S X R 0). Slices ordered from the upper left to the bottom right indicate inferior to superior layers of the MNI-152 template. The colour bar represents the Z scores corresponding to the uncorrected p threshold range of p < 0.01 (Z=2.58) to 0.001 (Z=3.29).

Figure 5

VLSM Results for Dysarthria for Patients in RHS Group from Uncorrected Z Map



Note. Results are depicted on an MNI-152 template across multiple slices in the axial plane (Slice numbers: A H -0.1 V -0. -10 -8 -6 -4 -2; 0 2 4 6 8 S X R 0). Slices ordered from the upper left to the bottom right indicate inferior to superior layers of the MNI-152 template. The colour bar represents the Z scores corresponding to the uncorrected p threshold range of p < 0.01 (Z=2.58) to 0.001 (Z=3.29).

Chart Review Dataset

Sample Characteristics

There were 32 patients who met the inclusion criteria for retrospective chart review (Figure 6). Patients in this sample had a mean age of 70 years (SD=16) and 50% were women. There were 29 patients who had ischemic stroke and 3 who had mixed stroke, characterized as an ischemic stroke with a secondary hemorrhage (Table 4). There were 17 patients with LHS and 15 with RHS. The median estimated time from stroke onset to hospital admission for LHS and RHS groups were 5 hours and 8 hours, respectively. Additionally, the median total length of stay for LHS and RHS patients were 6 and 7 days, respectively. The median length of stay in the acute care unit were 4 days for both groups. Frequency data of patients' neuroanatomical

characteristics as obtained from radiology reports were shown in Table 6. Lesions in the frontal, temporal, parietal, and occipital lobes were identified in 31%, 28%, 25%, and 6% of patients, respectively. Additionally, there were 37.5% of patients with reported infarct in the insula.

Cognitive and cognitive-communication impairments were present in 62.5% and 34% of patients, respectively (Table 5). Cognitive impairments were identified in 76% of patients with LHS and 46.7% of those with RHS. Cognitive-communication impairments were present in 35% of patient with LHS and 33% with RHS. In the LHS group, 76% of patients had aphasia, 47% had dysarthria, and 41% had AOS. In contrast, dysarthria was present in 40% of patients in the RHS group. Aphasia and AOS were not identified in any patients in this group. Furthermore, dysphagia was present in 34% of patients in this sample. The frequency of this impairment among patients in the LHS and RHS groups were 47% and 20%, respectively.

Statistical Analyses

The logistic regression analysis for clinical and demographic predictors of cognitive impairments showed significant effects for lesion laterality (i.e. left hemisphere lesions) (OR 8.106, 95% CI 1.259 – 77.265) and estimated time from stroke onset to hospital admission (in hours) (OR 1.010, 95% CI 1.000 – 1.076) (Table 7). In contrast, no significant predictors were found for cognitive-communication impairments.

Estimated time from stroke onset to hospital admission in hours for patients with cognitive impairments in the LHS group (*Mdn* = 5) were lower than those in the RHS group (*Mdn* = 27). Results from the Mann-Whitney U test indicated that this difference was statistically significant, $U(N_{LHS} = 13, N_{RHS} = 7,) = 99.00$, $z=1.99$, $p = 0.0471$. Additionally, total length of stay in days for patients with cognitive impairments in the LHS group (*Mdn* = 7) were lower than those in the RHS group (*Mdn* = 14). Findings from the Mann-Whitney U test indicated that this

difference was statistically significant, $U(N_{LHS} = 13, N_{RHS} = 7,) = 99.50, z=2.02, p = 0.0429$. Similarly, length of stay in the acute care unit in days for patients with cognitive impairments in the LHS group (*Mdn* = 4) were lower than those in the RHS group (*Mdn* = 7). However, results from the Mann-Whitney U test indicated that this difference was not statistically significant, $U(N_{LHS} = 13, N_{RHS} = 7,) = 89.50, z=1.24, p = 0.2167$.

Figure 6

Flowchart Diagram of Eligible Patients for Chart Review (Admitted from April 2020 to March 2021)

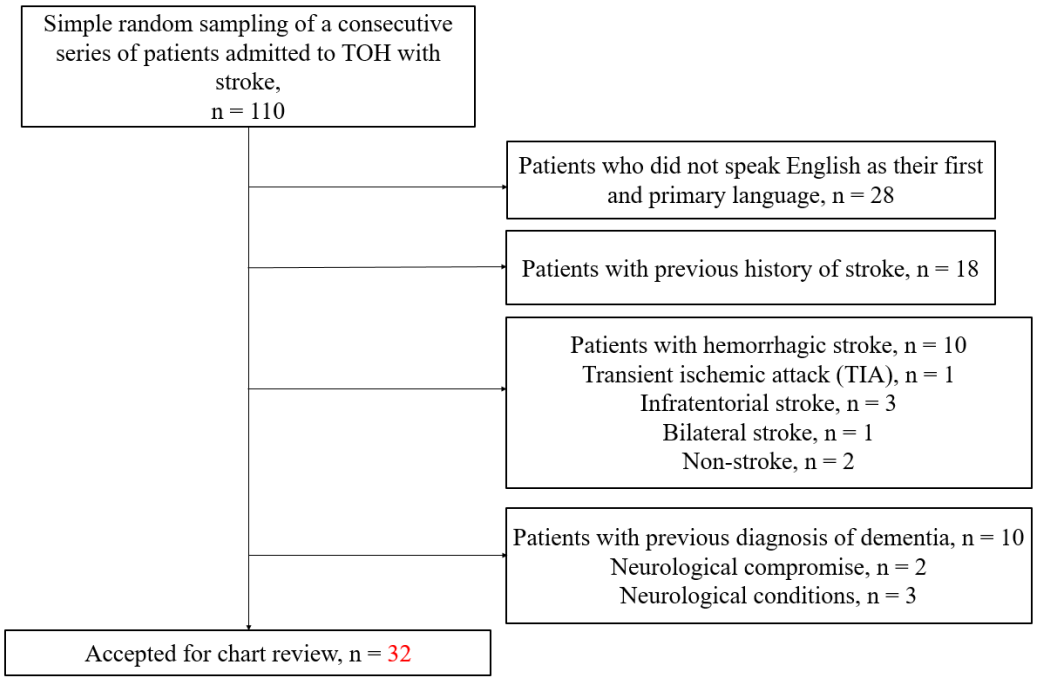


Table 4

Patient Characteristics by Stroke Laterality from Chart Review Dataset

Sample characteristics	All patients (N=32)	Left hemisphere stroke (n=17)	Right hemisphere stroke (n=15)
Age in years, median (IQR)	71.5 (21)	71 (18)	72 (23)
Female, n (%)	16 (50)	7 (41)	9 (60)
Right handedness, n (%)	27 (84)	14 (82)	13 (86.7)

Stroke presentation			
Estimated time from stroke onset to admission in hours, median (IQR)	5.5 (13)[a]	5 (11)	8 (23)
NIHSS on admission, median (IQR)	6 (7.5)	7 (9)	6 (7)
Alpha FIM, median (IQR)	84 (38)	73.5 (44)	92 (35)
Total length of stay in days, median (IQR)	6.5 (8.5)	6 (8)	7 (13)
Length of stay in acute care in days, median (IQR)	4 (5)	4 (6)	4 (4)
Stroke interventions			
Thrombolysis (tPA), n (%)	12 (37.5)	7 (41)	5 (33)
EVT/Embolectomy, n (%)	11 (34)	6 (35)	5 (33)
Neurosurgery/Carotid Stenting, n (%)	3 (9)	2 (11.8)	1 (6.7)
Stroke Subtypes			
Ischemic Stroke, n (%)	29 (90.6)	14 (82)	15 (100)
Mixed stroke, n (%)	3 (9)	3 (17.7)	-
Stroke etiology			
Cardioembolic, n (%)	16 (50)	8 (47)	8 (53)
Large vessel, n (%)	5 (15.6)	2 (11.8)	3 (20)
Small vessel/lacunar, n (%)	2 (6)	1 (5.9)	1 (6.7)
ESUS, n (%)	3 (9)	3 (17.7)	-
Other determined etiology, n (%)	2 (6)	-	2 (13)
Unknown/cryptogenic, n (%)	4 (12.5)	3 (17.7)	1 (6.7)
Previous medical history			
Heart disease, n (%)	12 (37.5)	6 (35)	6 (40)
Diabetes, n (%)	6 (18.8)	2 (11.8)	4 (26.7)
Mental health impairments, n (%)	5 (15.6)	4 (23.5)	1 (6.7)
Hypertension, n (%)	17 (53)	12 (70.6)	5 (33)
Dyslipidemia, n (%)	11 (34)	7 (41)	4 (26.7)
Discharge information			
NIHSS at discharge, median (IQR)	2 (4)[b]	2.5 (3)	1.5 (4)
Discharge location			
Acute care hospital (repatriation), n (%)	4 (12.5)	4 (23.5)	-
Home, n (%)	15 (46.9)	6 (35)	9 (60)
In-patient rehabilitation, n (%)	12 (37.5)	6 (35)	6 (40)
Out-patient rehabilitation, n (%)	1 (3)	1 (5.9)	-

Abbreviations: tPA, tissue plasminogen activator; EVT, endovascular therapy; ESUS, embolic strokes of unknown source

Notes: [a]= 12:00 PM EST was used as the default time of stroke onset for three patients

[b]= Most recent score on NIHSS flowsheet was recorded for three patients; missing scores for two patients

Table 5

Post-Stroke Impairments by Stroke Laterality for Patients from Chart Review Dataset

Clinical characteristics	All patients (N=32)	Left hemisphere stroke (n=17)	Right hemisphere stroke (n=15)
Post-stroke impairments			
Cognitive impairments, n (%)	20 (62.5)[a]	13 (76)	7 (46.7)
Cognitive-communication impairments, n (%)	11 (34)[b]	6 (35)	5 (33)
Cognitive domains impacted			
Executive functions, n (%)	10 (31)	6 (35)	4 (26.7)
Learning and memory, n (%)	12 (37.5)	5 (29)	7 (46.7)
Language, n (%)	13 (40.6)	13 (76)	-
Complex attention, n (%)	6 (18.8)	3 (17.7)	3 (20)
Perceptual motor functions, n (%)	8 (25)	4 (23.5)	4 (26.7)
Social cognition, n (%)	3 (9)	2 (11.8)	1 (6.7)
Other post-stroke impairments			
Aphasia, n (%)	13 (40.6)	13 (76)	-
Dysarthria, n (%)	14 (43.8)	8 (47)	6 (40)
Apraxia of speech, n (%)	7 (21.9)	7 (41)	-
Dysphagia, n (%)	11 (34)	8 (47)	3 (20)

Note: [a]= cognitive impairment status was reviewed and confirmed by SLP for three patients
[b]= cognitive-communication impairment status was reviewed and confirmed by SLP for four patients; cognitive-communication status was undetermined/missing in one patient

Table 6

Neuroanatomical Characteristics for All Patients According to Cognitive and Cognitive-Communication Impairment Statuses

Regions	All Patients (N=32)*	Cognitive Impairment	Cognitive-communication Impairment

		Present (n=20)	Absent (n=12)	Present (n=11)	Absent (n=20)
Insula, n (%)	12 (37.5)	9 (45)	3 (25)	4 (36)	7 (35)
Basal ganglia, n (%)	11 (34)	7 (35)	4 (33)	1 (9)	9 (45)
Internal capsule, n (%)	3 (9)	1 (5)	2 (16.7)	-	3 (15)
Thalamus, n (%)	1 (3)	-	1 (8)	-	1 (5)
Frontal lobe, n (%)	10 (31)	7 (35)	3 (25)	2 (18)	7 (35)
Temporal lobe, n (%)	9 (28)	9 (45)	-	5 (45)	4 (20)
Parietal lobe, n (%)	8 (25)	8 (40)	-	4 (36)	4 (20)
Occipital lobe, n (%)	2 (6)	2 (10)	-	1 (9)	1 (5)

Note: Neuroimaging information obtained from patients with confirmed acute and/or subacute infarcts based on radiology report.
*= cognitive-communication status was undetermined/missing in one patient

Table 7

Clinical and Demographic Predictors of Cognitive and Cognitive-communication Impairments

Predictor Variables	**Cognitive Impairments, OR (95% CI) (n=32)**	**Cognitive-communication Impairments, OR (95% CI) (n=32)**
Age	1.022 (0.956 – 1.094)	1.024 (0.975 – 1.084)
Sex	0.278 (0.027 – 1.994)	-
Laterality (left)	8.106 (1.259 – 77.265)*	0.952 (0.206 – 4.429)
Diabetes	7.963 (0.549 – 283.160)	-
NIHSS on admission	1.209 (0.994 – 1.584)	1.003 (0.826 – 1.212)
Estimated time from stroke onset to admission in hours	1.010 (1.000 – 1.076)*	-

Abbreviations: CI, Confidence Intervals; OR, Odds Ratios

Note: *= significant findings

Discussion

Results from our VLSM analyses of the MRI dataset showed that no voxels have survived the FDR correction threshold for multiple comparisons for aphasia, dysarthria, or AOS. Nevertheless, our voxel cluster analyses of the uncorrected lesion maps have identified some significant brain structures that were associated with these deficits. For patients with left hemisphere damage, significant regions associated with aphasia and AOS included the insula, rolandic operculum, and superior temporal gyrus. The putamen was identified as a region with significant voxel clusters related to aphasia. Additionally, significant voxel clusters related to AOS were also found in regions such as the Heschl's gyrus and inferior frontal gyrus (opercular part). Regions associated with dysarthria were not identified for patients in this group as no voxels have survived the cluster threshold. As for patients with right hemisphere damage, significant voxel clusters related to dysarthria were located in the insula and superior temporal gyrus. With respect to aphasia, significant structures related to this deficit included the precentral and postcentral gyri.

Findings from our chart review dataset revealed that cognitive and cognitive-communication impairments were present in 62.5% and 34% of patients, respectively. The frequency of cognitive impairments reported in LHS and RHS groups were 76% and 46.7%, respectively. Additionally, cognitive-communication impairments were identified in 35% of patient with LHS and 33% of those with RHS. Our logistic regression analysis showed that lesion laterality (i.e. left hemisphere lesions) and estimated time from stroke onset to hospital arrival were significant predictors of cognitive impairments for patients in this sample. However, our logistic regression model did not identify any significant predictors of cognitive-

communication impairments. Lastly, our analyses also showed there was a significant difference in estimated time from stroke onset to hospital arrival and length of stay between LHS and RHS patients who had cognitive impairments. More specifically, our results indicated that RHS patients with cognitive impairments had a longer onset-to-arrival time and extended length of stay in comparison to those with LHS.

Significance

In this study, we have identified a number of neuroanatomical correlates of post-stroke communication impairments, specifically pertaining to aphasia, dysarthria, and AOS. For all three impairments, the insula proved to be a common region where lesioned voxel clusters were identified, suggesting that this brain region may play an integral role in mediating different aspects of speech and language processing. According to existing literature, the functions of the insula have been linked to numerous processes in language and cognition such as: auditory processing of speech sounds, recognition of emotion, as well empathy and social cognition (Uddin et al., 2017). The role of the insula in dysarthria was also supported by another VLSM study by Baier et al. (2011) who indicated that lesions in the posterior insular cortex were associated with dysarthria in acute stroke patients. Likewise, Dronkers (1996) also found that damage to the left precentral gyrus of the insula was linked to deficits in motor planning of speech in patients with AOS. As the occurrence of AOS often coincide with aphasia, it would be interesting for future studies to examine whether there is a specific region of the insula that may be implicated in the co-occurrence of these two motor impairments. Our neuroimaging analysis of the MRI dataset served as a basis for a more comprehensive neuroanatomical inquiry around post-stroke communication impairments, which propelled us to examine more complex cognitive and cognitive-communication deficits in a similar subset of stroke patients.

At this point, results from our chart review dataset have elucidated the frequency of post-stroke cognitive and cognitive-communication impairments in the acute stage. The frequency of reported cognitive impairments was high but in keeping with a previous study by Nys et al. (2005) who reported that 48% of acute stroke patients showed cognitive impairments in the first three weeks after stroke. In contrast, our results were lower in comparison to a study conducted by Blake et al. (2002) who examined the frequency of cognitive and communicative deficits in RHS patients in the context of in-patient rehabilitation setting. Overall, cognitive and communicative deficits were reported in 96% of patients (Blake et al., 2002). This difference in reported frequencies could be attributed to the fact that their classification of cognitive and communication deficits was made based on more broad definitions in comparison to our study. Additionally, their results were obtained from patients who were admitted to in-patient rehabilitation whereas ours came from those in acute care. This is an important distinction as admission to in-patient rehabilitation is generally restricted to individuals with more rehabilitation needs such as those who sustain more severe injury and/or more than one type of impairment (Teasell et al., 2020). For this reason, the data from this setting may be inherently higher than those from acute care due to the difference in patient intake characteristics.

In rehabilitation settings, clinicians also have more opportunity to conduct more comprehensive assessments of patients' cognitive functions as compared to acute care (Teasell et al., 2020). Such information can further increase identification of deficits even those that are more subtle like cognitive-communication deficits.

Additionally, findings from rehabilitation settings could also vary across different facilities due to other considerations such as regional diversity (e.g., rural versus urban settings), admission criteria, service availability and/or hospital capacity. Nevertheless, our reported

frequency still remained relatively high likely because all patients were seen by an SLP at this stroke center. Therefore, this provided a robust opportunity for patients with this type of impairment to be assessed consistently by SLP either through formal or informal assessments.

As for cognitive-communication impairments, our frequency results were lower compared to a previous study by Hewetson et al. (2017) who found that 66% of RHS patients had these deficits. Nevertheless, it would be worth noting that the reported frequency of cognitive-communication impairments for their entire sample was approximately 33% (Hewetson et al., 2017) and thus similar to the results observed in our study. The difference in data observed in RHS patients could be attributed to their larger sample size and the fact that their data derived from two different care settings (i.e. acute care and in-patient rehabilitation), whereas ours were extracted exclusively from the acute care setting. Additionally, their classification of cognitive-communication deficits may differ from ours as the authors did not present an operational definition for CCD in their methods and seemed to rely solely on SLP report to identify these deficits.

Although our analyses did not identify any significant predictors of cognitive-communication impairments, our frequency results were still pertinent as they contributed to the broader literature by expanding our knowledge about the frequency of cognitive and cognitive-communication deficits in acute stroke patients. This was particularly important as the literature on post-stroke cognitive-communication impairments remains quite limited, especially in the context of acute stroke. In this study, cognitive-communication deficits were observed in both LHS and RHS patients which further highlighted the importance for clinicians to conduct routine screening and assessments to identify these deficits in acute stroke patients regardless of lesion side. Although CCD is preferentially associated with right hemisphere damage, our results

indicated that these deficits also occur in LHS patients at a similar rate of frequency. Moreover, our study also helped inform clinical care of stroke patients by emphasizing the need for clinicians to establish clear operational definitions to describe cognitive and cognitive-communication impairments across and between healthcare disciplines. By doing so, this could also help guide researchers to develop more effective and standardized assessment tools to accurately evaluate these deficits in stroke patients.

In this study, our findings also provided some preliminary insight into clinical predictors of cognitive impairments in acute stroke patients, which included lesion laterality (i.e. left hemisphere lesions) and estimated time from stroke onset to hospital arrival. One factor that could account for why left hemisphere lesion was a significant predictor could be due to our sample size. In our chart review sample, there were more patients diagnosed with LHS than RHS. Moreover, there were more LHS patients who were identified to have cognitive impairments, likely due to aphasia, compared to those in the RHS group, who would typically experience potentially more subtle cognitive deficits (such as aprosodia or flat affect) (H. Flowers, personal communication, December 29, 2022).

The implications of increased arrival time from stroke onset to hospital for patients with cognitive deficits may involve more complex speculations given numerous factors potentially involved. For example, delays in hospital arrival could be impeded by issues related to lack of awareness about stroke symptoms and/or living arrangements. To illustrate, stroke symptoms that primarily impact cognitive functions (such as anosognosia and confusion) may be more subtle compared to focal deficits in language or motor skills, which could delay symptom recognition by patients or signs of stroke to those around them.. Even if they are aware of recent campaigns to identify stroke signs, such as BE-FAST (Balance, Eyes, Face, Arm, Speech, Time)

(Aroor et al., 2017), their cognitive symptoms may remain elusive, especially if their communication is not particularly affected.

In addition, living alone could be another contributing factor prolonging delay in hospital arrival time as patients may be more secluded from social support and/or the general public at the time of stroke presentation. As a result, these individuals may be at risk of inappropriate symptom/sign identification preventing them from arriving to hospital in time for reperfusion therapies. This notion was supported by a study by Reeves et al. (2014) who found that living alone was associated with increased delays to hospital arrival and reduced access to thrombolytic treatment in acute stroke patients. Moreover, another study by Redfors et al. (2016) also found that living alone was a predictive factor for long-term mortality in ischemic stroke patients. Thus, the association between stroke onset-to-arrival time and post-stroke cognitive deficits may result from a culmination of different factors that contribute to stroke severity exacerbation and poorer clinical outcomes.

Moreover, our study also demonstrated a significant difference in the total length of stay and estimated time from stroke onset to hospital arrival between LHS and RHS patients with cognitive impairments. Our results indicated that RHS patients with cognitive impairments had experienced longer delay to hospital arrival as well as longer length of stay in hospital in comparison to those in the LHS group. These findings were partly in keeping with our initial hypothesis that RHS patients would experience longer delay in hospital arrival. This could be attributed to the fact that LHS symptoms may be more easily recognizable, particularly when aphasia occurs, and lead to faster arrival time. That is, LHS patients may be more prone to exhibit language/communication deficits at the time of stroke presentation which could be more readily perceived as a symptom of stroke. This disparity in stroke symptom recognition was

demonstrated by previous studies showing a significant difference in symptom recognition between patients with LHS and those with RHS (Foerch et al., 2005; Portegies et al., 2015).

The current study has further highlighted the need for further investigation surrounding the clinical relevance of lesion laterality on symptom recognition and acute stroke management. The use of acute stroke reperfusion interventions rely heavily on rapid hospital arrival. When persons with RHS arrive outside the window of opportunity, their treatment and recovery trajectories may be greatly compromised. In general, healthcare centres should consider implementing more rigorous stroke education programs for the elderly, the general public, and for healthcare workers so that they can collectively recognize RHS symptoms or signs of cognitive impairment. Additionally, researchers should also develop new assessment tools that help address areas of potential disparities in clinical assessment between LHS and RHS patients.

Limitations

In this study, there are a number of limitations that should be taken into consideration as to how they may influence our findings. Firstly, it is important to acknowledge that the results of our neuroimaging analysis of the MRI dataset were obtained from the uncorrected lesion maps as none of the voxels have survived the FDR correction threshold for multiple comparisons. To circumvent this issue, we also conducted a voxel cluster analysis using the uncorrected lesion maps by applying an uncorrected p threshold of <0.01 in conjunction with a voxel cluster threshold of at least 20 voxels. As VLSM analysis typically calculated a test statistics at each brain voxel, the purpose of applying a voxel cluster threshold enabled us to reduce the number of tests being conducted which in turn helped in mitigating the risk of false positives in our results. Although these findings were obtained based on a more lenient criteria of significance, our analyses still enabled us to examine trends in the lesion data that were correlated with the

presence of aphasia, dysarthria, and AOS. From these results, we were able to gain valuable insight regarding brain regions that may be implicated in the occurrence of different post-stroke communication impairments that could further inform our future neuroimaging studies. Another limitation within this dataset was the lack of information regarding the severity of each impairment (i.e. aphasia, dysarthria, and AOS) which could have provided more insight about the clinical profiles of patients in this sample as well as the extent of their deficits at the acute stage.

Another challenge that emerged from the chart review dataset was the lack of consistency in terminology used to describe cognitive and cognitive-communication deficits among different healthcare disciplines. This was a key limiting factor for our chart review process as it was difficult to categorize these deficits within specific cognitive domains due to the lack of clear descriptions between clinicians' reports. At times, it was also difficult to discern whether a patient had an impairment in cognition or cognitive-communication as the clinicians did not make a definitive statement according to our pre-defined terminology in their reports. This issue further highlighted the need for allied health professionals to establish clear operational definitions for these deficits and develop standardized assessment tools that enable effective and efficient identification of these impairments in acute stroke patients.

Our sample was restricted to patients who were speakers of English as a primary language from one stroke center. This selection criterion was established to limit heterogeneity and potential confounds in the sample. However, the external validity of our findings may also be limited accordingly. By extension, as stroke is known to largely affect older adult population (those over the age of 65), it is important to consider the implications of potential age-induced impairments in primary sensory functions on communication assessment results. For example,

older patients may be more likely to have auditory and/or visual impairments that may impede their ability to complete certain cognitive and language assessment tasks.

Another limiting factor of the chart review was that neuroanatomical characteristics were obtained primarily from radiology reports. Although these reports allowed us to gather data about presence of infarcts in certain brain regions, they did not provide any information about lesion volume thus limiting our ability to fully comprehend the extent of the lesions. Moreover, it is important to note that information provided in these reports were subject to radiologists' interpretation. Certain aspects of patient brain health including chronic brain disease may be underreported by radiologists in favour of careful diagnosis of acute stroke impacts. This limitation is consistent with retrospective design, as certain variables of interest may not be available for data collection and/or not consistently documented. For example, we were not able to gather information about certain measures (i.e. MoCA score, education level, and severity of impairment) that could have provided more insight about our sample characteristics and the impairment factors. On a similar note, we did not address the issue of statistical power in this study due to the exploratory nature and sampling method. Thus, our study may be underpowered due to our resulting relatively small sample sizes from an initial consecutive and large dataset.

Another key factor that should be taken into consideration was the fact that the chart review sample was retrieved during the early phases of the COVID-19 pandemic. The implementation of COVID-19 precaution measures could add another layer of complexity to clinical evaluation processes. This could have hindered clinicians' ability to adequately assess patients' cognitive and communicative functions as the interpretation of facial expressions and nonverbal communication may have been impeded by the presence of face masks and other personal protective equipment. Despite this, it is still important to note that our identification of

impairments were made based on clinical evaluations from specialists with expertise in stroke who routinely dealt with patients of different ages and communication profiles in a clinical setting.

Future Directions

Data from the MRI dataset have propelled us to examine more complex post-stroke cognitive and cognitive-communication deficits in acute stroke patients. At this point in time, our study has provided some preliminary insight regarding the frequency of these impairments in the acute setting. This represents a stepping stone for us to conduct subsequent VLSM analyses of post-stroke communication impairments as well as cognitive and cognitive-communication deficits using neuroimaging data from patients in the chart review or new samples. Such inquiry would corroborate and extend our VLSM findings from the MRI dataset and permit us to identify neuroanatomical predictors implicated in the interplay between cognitive and communication functions in acute ischemic stroke patients. Additionally, it would be important to extend subsequent inquiries to other populations with intracerebral hemorrhages and/or those with other language backgrounds. Future prospective studies should examine the potential impact of other individual factors on cognition such as education level, baseline participation status (e.g., activities of daily living), and post-stroke depression and anxiety.

Conclusion

In summary, our study highlighted the potential implications of the insula and surrounding brain regions in the occurrence of aphasia, dysarthria, and AOS in acute ischemic stroke patients. It also provided preliminary insight into the clinical presentation and frequency of post-stroke cognitive and cognitive-communication impairments in the acute stage. Our relatively high frequencies of cognitive and cognitive-communication impairments have

contributed to the literature for the acute care setting. We demonstrated that patients with RHS and cognitive impairments have longer length of stay in the acute stage and more delayed arrival to hospital from symptom onset than those with LHS. Ultimately, our findings could be used to inform future management of acute stroke patients with cognitive and cognitive-communication impairments, particularly with respect to the need for routine screening and ensuing comprehensive assessment of cognitive and cognitive-communication impairments in the acute stage. Such directions into management of stroke patients should be preceded by educational endeavours targeting right hemisphere stroke symptoms and early presenting deficits. Additional inquiry into lesion mapping correlates of post-stroke cognitive and cognitive-communication disorders is warranted to help us understand the neuroanatomical substrates that could point to the development of new therapies and understand recovery trajectories in patients with RHS in particular.

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Appendix A

University Health Network
Research Ethics Board
700 University Ave, 4th Floor
Toronto, Ontario, M5G 1Z5
Phone: (416) 581-7849

NOTIFICATION OF REB RENEWAL APPROVAL

Date: September 13, 2022

To: Rosemary Martino
University of Toronto, Rehabilitation Sciences Building, 500 University Avenue, Toronto, Ontario, Canada, M5G 1V7

Re: 07-0423
Incidence and Neuroanatomical Associations of Dysphagia, Dysarthria and Aphasia in First-Time Acute Stroke (Chart Review)

REB Review Type:	Delegated
REB Initial Approval Date:	September 13, 2007
REB Renewal Approval Effective Date:	September 13, 2022
Lapse In REB Approval:	N/A
REB Expiry Date:	September 13, 2023

The University Health Network Research Ethics Board has reviewed and approved the Renewal (07-0423.19) for the above mentioned study.

Best wishes on the successful completion of your project.

Sincerely,
Kristina Commisso
Ethics Coordinator, University Health Network Research Ethics Board
Approved and Digitally signed by Kristina Commisso on September 13, 2022 at 10:56 AM

For: Morris Sherman
Co-Chair, University Health Network Research Ethics Board

The UHN Research Ethics Board operates in compliance with the Tri-Council Policy Statement; ICH Guideline for Good Clinical Practice E6(R1); Ontario Personal Health Information Protection Act (2004); Part C Division 5 of the Food and Drug Regulations; Part 4 of the Natural Health Products Regulations and the Medical Devices Regulations of Health Canada.

Appendix B

The Ottawa Hospital RESEARCH INSTITUTE | L'Hôpital d'Ottawa INSTITUT DE RECHERCHE

uOttawa

UNIVERSITY OF OTTAWA HEART INSTITUTE
INSTITUT DE CARDIOLOGIE DE L'UNIVERSITÉ D'OTTAWA

Ottawa Health Science Network Research Ethics Board (OHSN-REB) / Conseil d'éthique de la recherche du réseau de science de la santé d'Ottawa (CÉR-RSSO)

Date:	June 16, 2021
Principal Investigator:	Dr. Lisa Walker, TOH/OHRI
Protocol ID:	20210440-01H
Study Title:	Cognitive and Associated Communication Impairments Following Unilateral Acute Ischemic Stroke: Frequency, Predictors, and Clinical Outcomes
Submission Type:	Initial Application
Review Type:	Delegated
Date of Approval:	June 16, 2021
Approval Expiry Date:	June 16, 2022

Dear Dr. Walker,

An **Institutional approval (OHRI and/or UOHI) letter is required prior to the conduct of the study** at this site. The institutional approval letter is an indication that you have satisfied ethics, contracts, departmental notifications, as applicable.

Thank you for submitting the above referenced study. The Ottawa Health Science Network Research Ethics Board (OHSN-REB) has reviewed the application and granted approval for your study. This approval is granted until the expiration date noted above. This research study is to be conducted by the investigator noted above.

The **OHSN-REB ethics approval** is applicable only for The Ottawa Hospital and University of Ottawa Heart Institute.

Documents Approved:

Document Name	**Document Version Date**
Protocol	January 29, 2021

No deviations from, or changes to, the protocol should be initiated without prior written approval of an appropriate amendment from the OHSN-REB, except when necessary to eliminate immediate hazard(s) to study participants.

REB members involved in the research project do not participate in the review, discussion or decision.

If the study is to continue beyond the expiry date noted above, a Continuing Review Form must be received by the OHSN-REB on or prior to the full board submission deadline date of the meeting scheduled to occur a minimum of 30 days prior to the study expiry date. If the study has been completed by the expiry noted above, a Study Closure Report must be received by the OHSN-REB.

The OHSN-REB operates in compliance with, and is constituted in accordance with, the requirements of the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS 2); International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use; Integrated Addendum to ICH E6 (R1): Guideline for Good Clinical Practice E6 (R2); Part C, Division 5 of the Food and Drug Regulations; or with the definition in the Interim Order Respecting Clinical Trials for Medical Devices and Drugs Relating to COVID-19; Part 4 of the Natural Health Products Regulations; Part 3 of the Medical Devices Regulations; and the provisions of the Ontario Personal Health Information Protection Act (PHIPA 2004) and its applicable regulations. OHSN-REB is qualified through the CTO REB Qualification Program and is registered with the U.S. Department of Health and Human Services (DHHS) Office for Human Research Protection (OHRP).

Please do not hesitate to contact us if you have any questions.

Sincerely,

Raphael Saginur, M.D.
Chairperson
Ottawa Health Science Network Research Ethics Board

/gb

Appendix C

The Ottawa Hospital RESEARCH INSTITUTE | L'Hôpital d'Ottawa INSTITUT DE RECHERCHE

uOttawa

UNIVERSITY OF OTTAWA HEART INSTITUTE
INSTITUT DE CARDIOLOGIE DE L'UNIVERSITÉ D'OTTAWA

Ottawa Health Science Network Research Ethics Board (OHSN-REB) / Conseil d'éthique de la recherche du réseau de science de la santé d'Ottawa (CÉR-RSSO)

Date:	June 3, 2022
To:	Dr. Lisa Walker, TOH/OHRI
Protocol ID:	20210440-01H
Post Form ID:	924
Study Title:	Cognitive and Associated Communication Impairments Following Unilateral Acute Ischemic Stroke: Frequency, Predictors, and Clinical Outcomes
Application Type:	Continuing Review
Review Type:	Delegated
Approval Date:	June 3, 2022
Study Approval Expiry Date:	June 3, 2023

Dear Dr. Walker,

Thank you for submitting the Continuing Review Form to the Ottawa Health Science Network Research Ethics Board (OHSN-REB). The OHSN-REB has reviewed the study and granted approval as of the date noted above.

Protocol dated January 29, 2021 is currently approved by the OHSN-REB.

The OHSN-REB ethics approval is applicable only for The Ottawa Hospital.

No deviations from, or changes to, the protocol should be initiated without prior written approval of an appropriate amendment from the OHSN-REB, except when necessary to eliminate immediate hazard(s) to study participants.

REB members involved in the research project do not participate in the review, discussion or decision.

If the study is to continue beyond the expiry date noted above, a Continuing Review Form must be received by the OHSN-REB 40-50 days prior to the study expiry date. If the study has been completed by the expiry noted above, a Study Closure Form must be received by the OHSN-REB.

The OHSN-REB operates in compliance with, and is constituted in accordance with, the requirements of the Tri¬-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS 2); International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use; Integrated Addendum to ICH E6 (R1): Guideline for Good Clinical Practice E6 (R2); Part C, Division 5 of the Food and Drug Regulations; Part 4 of the Natural Health Products Regulations; Part 3 of the Medical Devices Regulations and the provisions of the Ontario Personal Health Information Protection Act (PHIPA 2004) and its applicable regulations. OHSN-REB is qualified through the CTO REB Qualification Program and is registered with the U.S. Department of Health and Human Services (DHHS) Office for Human Research Protection (OHRP).

Please do not hesitate to contact us if you have any questions.

Sincerely,

[redacted]

Raphael Saginur, M.D.
Chairperson
Ottawa Health Science Network Research Ethics Board

/dw

Appendix D

07/07/2021

Université d'Ottawa
Bureau d'éthique et d'intégrité de la recherche

University of Ottawa
Office of Research Ethics and Integrity

Lettre d'approbation administrative | Letter of administrative approval

Numéro de dossier / Ethics File Number	H-06-21-7165
Titre du projet / Project Title	Cognitive and Associated Communication Impairments Following Unilateral Acute Ischemic Stroke: Frequency, Predictors, and Clinical Outcomes
Type de projet / Project Type	Thèse de maîtrise / Master's thesis
CÉR primaire / Primary REB	Réseau de science de la santé d'Ottawa (RSSO) / Ottawa Health Science Network (OHSN)
Statut du projet / Project Status	Approuvé / Approved
Date d'approbation (jj/mm/aaaa) / Approval Date (dd/mm/yyyy)	07/07/2021
Date d'expiration (jj/mm/aaaa) / Expiry Date (dd/mm/yyyy)	16/06/2022

Équipe de recherche / Research Team

Chercheur / Researcher	Affiliation	Role
Povkannika HOUR	École interdisciplinaire des sciences de la santé / Interdisciplinary School of Health Sciences	Chercheur Principal / Principal Investigator
Heather FLOWERS	École des sciences de la réadaptation / School of Rehabilitation Sciences	Superviseur / Supervisor
Jason STEFFENER	École interdisciplinaire des sciences de la santé / Interdisciplinary School of Health Sciences	Co-superviseur / Co-supervisor

Conditions spéciales ou commentaires / Special conditions or comments:

OHSN REB Protocol ID:20210440-01H

550, rue Cumberland, pièce 154 Ottawa (Ontario) K1N 6N5 Canada
550 Cumberland Street, Room 154 Ottawa, Ontario K1N 6N5 Canada

613-562-5387 • 613-562-5338 • ethique@uOttawa.ca / ethics@uOttawa.ca
www.recherche.uottawa.ca/deontologie | www.recherche.uottawa.ca/ethics

07/07/2021

Université d'Ottawa
Bureau d'éthique et d'intégrité de la recherche

University of Ottawa
Office of Research Ethics and Integrity

L'Université d'Ottawa a signé une Entente, conforme aux exigences de la plus récente version de l'EPTC et tout autre règlement ou législation applicable, permettant au CÉR ci-haut nommé d'être désigné comme CÉR primaire pour les projets de recherche où

1) les activités principales de recherche sont menées sous l'autorité ou sous les auspices de l'établissement lié au CÉR primaire et

2) Une partie du projet est également réalisé sous l'autorité ou sous les auspices de l'Université d'Ottawa.

Cette lettre confirme que l'Université d'Ottawa a autorisé que le CÉR primaire soit le CÉR officiel pour l'évaluation et la supervision de ce projet de recherche. Ceci n'est pas une approbation éthique.

Afin de nous aider à garder votre dossier à jour, veuillez soumettre une copie de toutes demandes de modification, renouvellement d'approbation éthique etc. soumis à et approuvé par le CÉR primaire dès qu'elles sont disponibles.

Cette approbation administrative est valide pour la durée indiquée ci-haut et est sujette aux conditions énumérées dans la section intitulée « Conditions spéciales ou commentaires ».

The University of Ottawa has signed an Agreement, compliant with current TCPS guidelines and any other applicable guidelines or legislation regarding multisite review, allowing the REB named above to serve as Board of Record (BoR) for research projects where

1) the main research activities are conducted within the auspices or jurisdiction of the BoR's institution and

2) parts of the project are also conducted under the jurisdiction or auspices of the University of Ottawa.

This letter confirms that the University of Ottawa has authorized the REB named above to serve as Board of Record for the review and oversight of this research project. This is not an REB approval.

In order to help us keep your file up to date, please submit a copy of all amendment requests, project renewals or any other changes submitted to and approved by the BoR, as they become available.

Administrative approval is valid for the period indicated above and is subject to the conditions listed in the section entitled «Special conditions or comments».

Catherine PAQUET
Directeur / Director
Pour/For **Daniel LAGAREC** Président(e) du/ Chair of the **Comité d'éthique de la recherche en sciences de la santé et sciences / Health Sciences and Sciences Research Ethics Board**

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Appendix E

07/06/2022

Université d'Ottawa
Bureau d'éthique et d'intégrité de la recherche

University of Ottawa
Office of Research Ethics and Integrity

Lettre d'approbation administrative | Letter of administrative approval

Numéro de dossier / Ethics File Number	H-06-21-7165
Titre du projet / Project Title	Cognitive and Associated Communication Impairments Following Unilateral Acute Ischemic Stroke: Frequency, Predictors, and Clinical Outcomes
Type de projet / Project Type	Thèse de maîtrise / Master's thesis
CÉR primaire / Primary REB	Réseau de science de la santé d'Ottawa (RSSO) / Ottawa Health Science Network (OHSN)
Statut du projet / Project Status	Renouvellement partiel / Renewed - Partial
Date d'approbation (jj/mm/aaaa) / Approval Date (dd/mm/yyyy)	07/07/2021
Date d'expiration (jj/mm/aaaa) / Expiry Date (dd/mm/yyyy)	03/06/2023

Équipe de recherche / Research Team

Chercheur / Researcher	Affiliation	Role
Povkannika HOUR	École interdisciplinaire des sciences de la santé / Interdisciplinary School of Health Sciences	Chercheur Principal / Principal Investigator
Heather FLOWERS	École des sciences de la réadaptation / School of Rehabilitation Sciences	Superviseur / Supervisor
Jason STEFFENER	École interdisciplinaire des sciences de la santé / Interdisciplinary School of Health Sciences	Co-superviseur / Co-supervisor

Conditions spéciales ou commentaires / Special conditions or comments:

The uOttawa expiry date was set to match the one from the OHSN-REB.

550, rue Cumberland, pièce 154 Ottawa (Ontario) K1N 6N5 Canada
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07/06/2022

Université d'Ottawa
Bureau d'éthique et d'intégrité de la recherche

University of Ottawa
Office of Research Ethics and Integrity

L'Université d'Ottawa a signé une Entente, conforme aux exigences de la plus récente version de l'EPTC et tout autre règlement ou législation applicable, permettant au CÉR ci-haut nommé d'être désigné comme CÉR primaire pour les projets de recherche où

1) les activités principales de recherche sont menées sous l'autorité ou sous les auspices de l'établissement lié au CÉR primaire et

2) Une partie du projet est également réalisé sous l'autorité ou sous les auspices de l'Université d'Ottawa.

Cette lettre confirme que l'Université d'Ottawa a autorisé que le CÉR primaire soit le CÉR officiel pour l'évaluation et la supervision de ce projet de recherche. Ceci n'est pas une approbation éthique.

Afin de nous aider à garder votre dossier à jour, veuillez soumettre une copie de toutes demandes de modification, renouvellement d'approbation éthique etc. soumis à et approuvé par le CÉR primaire dès qu'elles sont disponibles.

Cette approbation administrative est valide pour la durée indiquée ci-haut et est sujette aux conditions énumérées dans la section intitulée « Conditions spéciales ou commentaires ».

The University of Ottawa has signed an Agreement, compliant with current TCPS guidelines and any other applicable guidelines or legislation regarding multisite review, allowing the REB named above to serve as Board of Record (BoR) for research projects where

1) the main research activities are conducted within the auspices or jurisdiction of the BoR's institution and

2) parts of the project are also conducted under the jurisdiction or auspices of the University of Ottawa.

This letter confirms that the University of Ottawa has authorized the REB named above to serve as Board of Record for the review and oversight of this research project. This is not an REB approval.

In order to help us keep your file up to date, please submit a copy of all amendment requests, project renewals or any other changes submitted to and approved by the BoR, as they become available.

Administrative approval is valid for the period indicated above and is subject to the conditions listed in the section entitled «Special conditions or comments».

Safaa LAMHOUJEB
Coordonnateur de l'éthique / Ethics Coordinator
Pour/For **Daniel LAGAREC** Président(e) du/ Chair of the **Comité d'éthique de la recherche en sciences de la santé et sciences / Health Sciences and Sciences Research Ethics Board**

550, rue Cumberland, pièce 154 550 Cumberland Street, Room 154
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Appendix F

Patient ID: _____
Date of Chart Review: _____ (dd/mm/yy) Name of Reviewer: _____

Patient Eligibility Form

Version date: October 06, 2021

Exclude if the patient:
☐Was under 18 years of age
☐Did not speak English as their first and primary language
☐Had a hemorrhagic stroke or a transient ischemic attack (TIA)
☐Had experienced a stroke before (i.e. diagnosis of stroke from past medical history)
☐Had a history of brain injury
☐Had a history of learning disability*
☐Was previously diagnosed with dementia
☐Was previously diagnosed with mild cognitive impairment*
☐Was previously diagnosed with neurological compromise prior to stroke onset (e.g. brain tumours, contusions, or abscess, etc.)
☐Had bilateral lesions
☐Had infratentorial lesions (i.e. lesions in the brainstem and/or cerebellum only)
☐Otherwise, accept

*= Eligibility may be reconsidered depending on the final sample size

Appendix G

Patient ID: _____
Date of Chart Review: _____ (dd/mm/yy) Name of Reviewer: _____

Medical Chart Review Form

Version date: September 23, 2021

SECTION 1 – Patients' Demographics and General Characteristics	
Sex Legal (var: sex)	☐Male (male) ☐Female (female) ☐Unknown
Gender Identity (if disclosed) (var: gender_id)	_____ ☐Not Disclosed
Age (in years) (var: age)	_____ (years) ☐UTD
Handedness (var: hand)	☐Right (right) ☐Left (left) ☐Ambidextrous (ambi) ☐UTD

SECTION 2 – Stroke Features and Presentation	
Estimated Time from Stroke Onset to Hospital Admission (in full hours) (var: time_onset_admit)	_____ (full hours) ☐UTD
Total Length of Stay (between admission and discharge) (in days) (var: los)	Length of Stay: _____ (in days)
Length of Stay in Acute Care (in days) (var: los_acute)	Length of Stay (Acute care): _____(in days)

Stroke Type (var: stroke_type)	☐Ischemic Stroke (IS) (if selected, specify subtype in the next box) ☐Mixed – Ischemic stroke with secondary hemorrhage (mixed) ☐UTD
Ischemic Stroke Subtype (var: isch_stroke_subtype)	☐Large Artery Atherosclerosis (LAA) ☐Lacunar (lac) ☐Small-Vessel Occlusion (SVO) ☐Cardioembolism (cardio) ☐Embolic Strokes of Unknown Source (ESUS) ☐Other Determined Etiology (ODE) (e.g. dissection): _____ ☐Cryptogenic
Stroke Severity on Admission	
NIHSS (var: NIHSS_admit)	NIHSS score: _____ Time from stroke onset to evaluation:_____(in full hours) ☐Not tested ☐UTD
AlphaFIM (var: AFIM)	AFIM score: _____ Time from admission to evaluation:_____(in full hours) ☐Not tested ☐UTD
Motor Rating (from AlphaFIM) (var: motor_rating)	Motor rating score: _____ ☐UTD
Cognitive Rating (from AlphaFIM) (var: cognitive_rating)	Cognitive rating score: _____ ☐UTD

SECTION 3 – Previous Medical History	
Cognitive Risk Factors (Potential Confounds)	
Heart Disease (var: heart_disease)	☐Yes (yes) (if yes, specify type)

	☐No (no) ☐UTD Type: _____ (e.g. coronary artery disease, congestive heart failure, arrhythmia, valvular disease, previous myocardial infarction, etc.)
Microvascular Disease (var: mvd)	☐Yes (yes) ☐No (no) ☐UTD
Diabetes (var: diabetes)	☐Yes (yes) (if yes, specify type) ☐No (no) ☐UTD Type: ☐Type 1 (type1) ☐Type 2 (type2) ☐Other (other)
Mental Health Impairments (var: mental_health)	☐Yes (yes) (if yes, specify type) ☐No (no) ☐UTD Type: _____ (E.g. depression, anxiety, etc.)
COVID-19 Infection (var: covid19)	☐Yes (yes) (if yes, provide details below) ☐No (no) ☐UTD Details: ☐Current Infection ☐Past Infection
Other (if applicable)	_____ ☐N/A

SECTION 4 – Clinical Processes	
In-hospital Interventions	
Thrombolysis (var: thrombolysis)	☐Yes (yes) (if yes, provide details below) ☐No (no) ☐UTD
Endovascular treatment/Embolectomy (var: evt_emb)	☐Yes (yes) (if yes, provide details below) ☐No (no) ☐UTD
Other interventions (e.g. acute antiplatelet therapy, dual antiplatelet therapy, shunt placement, neurosurgery, etc.) (if applicable)	☐Yes (yes) (if yes, provide details below) ☐No (no) ☐UTD Type: _____ Time from admission to treatment: _____(in full hours)

SECTION 5 – In-hospital Complications	
Pneumonia (var: PNA)	☐Yes (yes) ☐No (no) ☐UTD
Urinary Tract Infection (var: UTI)	☐Yes (yes) ☐No (no) ☐UTD
Gastrointestinal Bleeding (var: GI_bleed)	☐Yes (yes) ☐No (no) ☐UTD
Decubitus Ulcer (var: DU)	☐Yes (yes) ☐No (no) ☐UTD

Pulmonary Embolism (var: PE)	☐Yes (yes) ☐No (no) ☐UTD
Delirium (var: delirium)	☐Yes (yes) ☐No (no) ☐UTD
Other Infections (if applicable)	☐Yes (yes) (if yes, provide details below) ☐No (no) ☐UTD Details: _____
Other Complications (if applicable)	☐Yes (yes) (if yes, provide details below) ☐No (no) ☐UTD Details: _____

SECTION 6 – Neuroimaging Information	
First CT (var: ct_1)	Time from stroke onset to imaging: _____ (in full hours) ☐UTD Most confirmatory CT ☐Yes ☐No
Most confirmatory CT (var: ct_confirm)	Time from stroke onset to imaging: _____ (in full hours) ☐UTD Which CT: ☐1st CT ☐2nd CT ☐Other: _____

First MRI (var: mri_1)	Time from stroke onset to imaging: _____ (in full hours) ☐No MRI ☐UTD Most confirmatory MRI (if applicable) ☐Yes ☐No ☐N/A
Most confirmatory MRI (var: mri_confirm)	Time from stroke onset to imaging: _____ (in full hours) ☐No MRI ☐UTD Which MRI: ☐1st MRI ☐2nd MRI ☐Other: _____
No Scans (if applicable)	Reason:_____ ☐N/A
Side of Lesion (var: lesion_side)	☐Left Hemisphere (LH) ☐Right Hemisphere (RH) ☐UTD

SECTION 7 – Post-stroke Impairments from Specialist Assessments **(**Neuro – Neurology, SLP - Speech-Language Pathologist, OT - Occupational Therapist, Neuropsych – Neuropsychologist, and Other)	
Cognitive Status Based on Screening Tools	
MoCA (if available) (var: MoCA)	Assessed: ☐Yes (yes) (if yes, provide details below) ☐No (no) ☐UTD

	MoCA score: _____ Time from admission to assessment:_____ (in days) ☐UTD
Cognitive Assessments by Healthcare Professionals	
OT	Assessed: ☐Yes (yes) ☐No (no) ☐UTD Time from most confirmatory scan to assessment: _____ (in days) Type of tests used: ☐Standardized Assessment (if selected, provide details below) ☐Informal Assessment (if selected, provide details below) ☐UTD Standardized Assessment (if selected): Time from admission to assessment:_____ (in days) Name of Test: _____ Completed as intended: ☐Yes (yes) ☐No (no) ☐UTD Name of Test: _____ Completed as intended: ☐Yes (yes) ☐No (no) ☐UTD Name of Test: _____ Completed as intended:

	☐Yes (yes) ☐No (no) ☐UTD Name of Test: _____ Completed as intended: ☐Yes (yes) ☐No (no) ☐UTD Informal Assessment (if selected): Time from admission to assessment:_____ (in days) Presence of Cognitive Impairment ☐Yes (yes) (if yes, provide details below) ☐No (no) ☐UTD Severity (if available): ☐Mild (mild) ☐Moderate (mod) ☐Severe (sev) ☐UTD Severity determination: ☐Subjective (based on informal assessment) ☐Objective (based on standardized testing) Cognitive Domains Affected (select all that apply): ☐Executive Function ☐Learning and Memory ☐Language ☐Complex Attention ☐Perceptual-motor Function

	☐Social Cognition ☐Other: _____ ☐UTD Presence of Cognitive-communication Impairment ☐Yes (yes) ☐No (no) ☐UTD Other Notes (if applicable): _____
Neurology	Assessed: ☐Yes (yes) ☐No (no) ☐UTD Time from most confirmatory scan to assessment: _____ (in days) Type of tests used: ☐Standardized Assessment (if selected, provide details below) ☐Informal Assessment (if selected, provide details below) ☐UTD Standardized Assessment (if selected): Time from admission to assessment:_____ (in days) Name of Test: _____ Completed as intended: ☐Yes (yes) ☐No (no) ☐UTD Name of Test: _____ Completed as intended:

	☐Yes (yes) ☐No (no) ☐UTD Name of Test: _____ Completed as intended: ☐Yes (yes) ☐No (no) ☐UTD Name of Test: _____ Completed as intended: ☐Yes (yes) ☐No (no) ☐UTD Informal Assessment (if selected): Time from admission to assessment:_____ (in days) Presence of Cognitive Impairment ☐Yes (yes) (if yes, provide details below) ☐No (no) ☐UTD Severity (if available): ☐Mild (mild) ☐Moderate (mod) ☐Severe (sev) ☐UTD Severity determination: ☐Subjective (based on informal assessment) ☐Objective (based on standardized testing) Cognitive Domains Affected (select all that apply):

	☐Executive Function ☐Learning and Memory ☐Language ☐Complex Attention ☐Perceptual-motor Function ☐Social Cognition ☐Other: _____ ☐UTD Other Notes (if applicable): _____
SLP	Assessed: ☐Yes (yes) ☐No (no) ☐UTD Time from most confirmatory scan to assessment: _____ (in days) Type of tests used: ☐Standardized Assessment (if selected, provide details below) ☐Informal Assessment (if selected, provide details below) ☐UTD Standardized Assessment (if selected): Time from admission to assessment:_____ (in days) Name of Test: _____ Completed as intended: ☐Yes (yes) ☐No (no) ☐UTD Name of Test: _____ Completed as intended:

	☐Yes (yes) ☐No (no) ☐UTD Name of Test: _____ Completed as intended: ☐Yes (yes) ☐No (no) ☐UTD Name of Test: _____ Completed as intended: ☐Yes (yes) ☐No (no) ☐UTD Informal Assessment (if selected): Time from admission to assessment:_____ (in days) Presence of Cognitive Impairment ☐Yes (yes) (if yes, provide details below) ☐No (no) ☐UTD Severity (if available): ☐Mild (mild) ☐Moderate (mod) ☐Severe (sev) ☐UTD Severity determination: ☐Subjective (based on informal assessment) ☐Objective (based on standardized testing)

	Cognitive Domains Affected (select all that apply): ☐Executive Function ☐Learning and Memory ☐Language ☐Complex Attention ☐Perceptual-motor Function ☐Social Cognition ☐Other: _____ ☐UTD Presence of Cognitive-communication Impairment ☐Yes (yes) ☐No (no) ☐UTD Other Notes (if applicable): _____
Neuropsych	Assessed: ☐Yes (yes) ☐No (no) ☐UTD Time from most confirmatory scan to assessment: _____ (in days) Type of tests used: ☐Standardized Assessment (if selected, provide details below) ☐Informal Assessment (if selected, provide details below) ☐UTD Standardized Assessment (if selected): Time from admission to assessment:_____ (in days) Name of Test: _____

	Completed as intended: ☐Yes (yes) ☐No (no) ☐UTD Name of Test: _____ Completed as intended: ☐Yes (yes) ☐No (no) ☐UTD Name of Test: _____ Completed as intended: ☐Yes (yes) ☐No (no) ☐UTD Name of Test: _____ Completed as intended: ☐Yes (yes) ☐No (no) ☐UTD Informal Assessment (if selected): Time from admission to assessment:_____ (in days) Presence of Cognitive Impairment ☐Yes (yes) (if yes, provide details below) ☐No (no) ☐UTD Severity (if available): ☐Mild (mild) ☐Moderate (mod) ☐Severe (sev)

	☐UTD Severity determination: ☐Subjective (based on informal assessment) ☐Objective (based on standardized testing) Cognitive Domains Affected (select all that apply): ☐Executive Function ☐Learning and Memory ☐Language ☐Complex Attention ☐Perceptual-motor Function ☐Social Cognition ☐Other: _____ ☐UTD Other Notes (if applicable): _____
Other (if applicable)	Type of Healthcare Professional: _____ Time from most confirmatory scan to assessment: _____ (in days) Type of tests used: ☐Standardized Assessment (if selected, provide details below) ☐Informal Assessment (if selected, provide details below) ☐UTD Standardized Assessment (if selected): Time from admission to assessment:_____ (in full hours)

	Name of Test: _____ Completed as intended: ☐Yes (yes) ☐No (no) ☐UTD Name of Test: _____ Completed as intended: ☐Yes (yes) ☐No (no) ☐UTD Name of Test: _____ Completed as intended: ☐Yes (yes) ☐No (no) ☐UTD Name of Test: _____ Completed as intended: ☐Yes (yes) ☐No (no) ☐UTD Informal Assessment (if selected): Time from admission to assessment:_____ (in days) Presence of Cognitive Impairment ☐Yes (yes) (if yes, provide details below) ☐No (no) ☐UTD Severity (if available): ☐Mild (mild) ☐Moderate (mod)

	☐Severe (sev) ☐UTD Severity determination: ☐Subjective (based on informal assessment) ☐Objective (based on standardized testing) Cognitive Domains Affected (select all that apply): ☐Executive Function ☐Learning and Memory ☐Language ☐Complex Attention ☐Perceptual-motor Function ☐Social Cognition ☐Other: _____ ☐UTD Presence of cognitive-communication Impairment ☐Yes (yes) ☐No (no) ☐UTD Other Notes (if applicable): _____
OTHER IMPAIRMENTS	
Speech	
Dysarthria	Presence of Impairment: ☐Yes (yes) ☐No (no) ☐UTD First confirmed by: _____ Time from admission to assessment:_____ (in days)

	Time from most confirmatory scan to assessment: _____ (in days) Severity (if available): ☐Mild (mild) ☐Moderate (mod) ☐Severe (sev) ☐UTD Severity determination: ☐Subjective (based on informal assessment) ☐Objective (based on standardized testing)
Apraxia of Speech	Presence of Impairment: ☐Yes (yes) ☐No (no) ☐UTD First confirmed by: _____ Time from admission to assessment:_____ (in days) Time from most confirmatory scan to assessment: _____ (in days) Severity (if available): ☐Mild (mild) ☐Moderate (mod) ☐Severe (sev) ☐UTD Severity determination: ☐Subjective (based on informal assessment) ☐Objective (based on standardized testing)
Swallowing	
Oropharyngeal Dysphagia	Presence of Impairment: ☐Yes (yes)

	☐No (no) ☐UTD First confirmed by: _____ Time from admission to assessment:_____ (in hours) Time from most confirmatory scan to assess:_____ (in hours) Severity (if available): ☐Mild (mild) ☐Moderate (mod) ☐Severe (sev) ☐UTD Severity determination: ☐Subjective (based on informal assessment) ☐Objective (based on standardized testing)

SECTION 8 – Discharge Information	
Stroke Severity at Discharge	
NIHSS (var: NIHSS_dis)	NIHSS score: _____ ☐UTD ☐Not completed for discharge
Other Assessment (if applicable)	Type of assessment: _____ Score/Results: _____ Time from admission to evaluation:_____(in days) ☐N/A ☐UTD
Not Evaluated (if applicable)	Reason(s): _____ ☐N/A ☐UTD

Discharge Location and Status (var: dis_loc_status)	☐Rehabilitation Facility (RF) (if selected, specify type below) ☐Acute Care Hospital (ACH) (repatriation) ☐Long-Term Care Facility (LTC) ☐Home (home) ☐Death in facility (death) ☐Other: _____ ☐UTD Type of Rehabilitation Facility: ☐Out-Patient Rehabilitation ☐Long-Term In-Patient Rehabilitation ☐Short-Term In-patient Rehabilitation ☐Unspecified Additional notes (if applicable):_____

N/A: not applicable

UTD: unable to determine

Var: variable

*Note: If any time points were estimated, please indicate that on the form.

Appendix H

Chart Review Manual

Version date: October 06, 2021

Order of Chart Review

1. Determine patient eligibility → Refer to patient eligibility form. If eligible, proceed to collect data for each section listed below.

Note: Information about the patient's primary language can be found in Speech-language Pathology (SLP) consult notes in the chart review section. Consult notes can be found in the "**Other Notes**" section of **"ED to Hospital admission" discharge summary**.

SECTION 1 – Patients' Demographics and General Characteristics

1. Sex
   - Refer to **Sexual Orientation and Gender Identity SmartForm**
   - See the top left side of the chart (under the yellow sticky note).
   - Click on patient's age and date of birth to display Sexual Orientation and Gender Identity SmartForm
2. Gender Identity
   - Refer to **Sexual Orientation and Gender Identity SmartForm**
3. Age
   - See top left side of the chart
4. Handedness
   - This information can be found in SLP and Occupational Therapy (OT) assessment reports (please see consult notes)
   - For SLP, this information may be listed under "**background information**" in the assessment report
   - For OT, this information may be listed under "**physical abilities/components**" in the assessment report

SECTION 2 – Stroke Features and Presentation

5. Estimated Time from Stroke Onset to Hospital Admission (in full hours)
   - Time of stroke onset may be indicated in the **Neurology stroke code consultation** report.
   - If time of stroke onset is not indicated, estimated time may be used. If time of stroke onset is unclear, 12:00PM EST may be used as default time.
   - Estimated time from stroke onset to hospital admission can be determined by calculating the times from "last seen well/normal" to hospital admission.
   - Time of "Last seen well/normal" may be indicated in Neurology stroke code consultation

6. Total Length of Stay (between admission and discharge) (in days)
    - Refer to the master list obtained from Data Analytics and Health Records.
    - Information about admission and discharge dates are also available in discharge summary
7. Length of Stay in Acute Care (in days)
    - Refer to the master list obtained from Data Analytics and Health Records
8. Stroke Type
    - Refer to the master list obtained from Data Analytics and Health Records
    - Alternative: refer to Neurology stroke code consultation and/or discharge summary
    - If stroke type is listed as EVT, this would constitute an ischemic stroke
9. Ischemic Stroke Subtype
    - This information may be available in Neurology stroke code consultation and/or discharge summary
    - Stroke subtype may be listed as "Etiology"
10. NIHSS (at admission)
    - Refer to "**Neurological examination**" section of Neurology stroke code consultation
    - Time from stroke onset to evaluation can be determined by calculating the times from "stroke onset" to "hospital arrival (ED record)".
    - If time of stroke onset is not indicated, estimated time may be used. In this case, estimated time can be calculated by using "last seen well/normal" and "hospital arrival (ED record" times. Please calculate time in <u>full hours.</u> For example, if the time is 2 hours and 25 minutes (or 2 hours and 35 minutes), this will coded as 2 hours.
11. AlphaFIM
    - Refer to the master list obtained from Data Analytics and Health Records
    - Please calculate the time from admission to evaluation in <u>full hours</u>.
    - Please document the total AlphaFIM score as well as motor and cognitive rating scores (all available in the master list from Data Analytics and Health Records)

<u>SECTION 3 – Previous Medical History</u>

12. For information about a patient's previous medical history, please refer to the "**Past Medical History**" section of Neurology stroke code consultation. Alternatively, you can also click on the **Snapshot tab** to display the patient's medical history. Categories of previous medical conditions may include: heart disease, microvascular disease, diabetes, mental health impairments, and/or COVID-19 infection. If the patient had a history of other medical condition(s), please specify the condition(s) in the "**Other**" section.

For information about COVID-19 Infection, please refer to "**COVID screen**" section of Neurology stroke code consultation

SECTION 4 – Clinical Processes

13. Thrombolysis
    - This information may be available in Neurology stroke code consultation as part of the following sections: **major time points, assessment,** and/or **plan**.
14. Endovascular treatment/Embolectomy
    - This information may be available in Neurology stroke code consultation as part of the following sections: major time points, assessment, and/or plan.
15. Other interventions (e.g. acute antiplatelet therapy, dual antiplatelet therapy, shunt placement or neurosurgery) (if applicable)
    - This information may be available in neurology stroke code consultation
    - Refer to **vascular surgery consultation** for information related to other types of interventions (if available)
    - Please calculate the time from admission to treatment in full hours (if applicable)

SECTION 5 – In-hospital Complications

16. Information about in-hospital complications and/or infections may be listed under "**hospital course**" in the discharge summary. This may include: pneumonia, urinary tract infection, gastrointestinal bleeding, decubitus ulcer, pulmonary embolism, and/or delirium. If there were other types of infections or complications listed in the patient's charts, please provide details about this in the chart review form.

SECTION 6 – Neuroimaging Information

17. Refer to "**Imaging Results**" section which is located at the bottom of the discharge summary. Information related to confirmation of stroke may be listed as "**Indication**" as part of the CT and/or MRI scan narratives.
18. Please calculate the time from stroke onset to imaging for CT and MRI scans in full hours. If time of stroke onset is not available, "last seen well/normal" time may be used to calculate the estimated time. For imaging time, please use "collected" time.
19. Information about the side of the lesion can be found in the narrative section of imaging results. This information is also available in the discharge summary and may be listed as "**Discharge Diagnosis**"
20. If no scans are available, please state the reason.

SECTION 7 – Post-stroke Impairments from Specialist Assessments

21. MoCA

- This information may be available in **social services** report or in the "**Media**" section under the **Chart Review tab**
- Calculate the time from admission to assessment in days
- Estimated time can be used if the official time of the assessment is not recorded. If no official time is indicated, please note the assessment time as 12:00PM EST.

22. Cognitive Assessment by healthcare professionals
    - Refer to physicians, OT, and SLP consult notes
    - Calculate the time from admission to assessment for all assessments that were conducted in full days.
    - Estimated time can be used if the official time of the assessment is not recorded in the reports. If no official time is indicated, please note the assessment time as 12:00PM EST.
    - Calculate the time from most confirmatory scans to assessment in full days. If no official time is recorded for the assessment, 12:00PM EST may be used as the estimated assessment time.
    - Record whether standardized and/or informal assessments were used
    - If standardized tests were used, please record the name of the tests
    - If any tests were not completed as intended, please document that on the chart review form

    - Assessments by SLP may include the following tests:
        - Western Aphasia Battery (WAB)
        - Boston Diagnostic Aphasia Examination (BDAE)
        - Australian Aphasia Rehab Pathway (Spreen & Risser, 2003)
        - modified Ross Information Processing Assessment (version 2) (RIPA-2)
        - Cognitive Linguistic Quick Test (CLQT)
        - The Source for Dysarthria 2nd Edition

23. Presence of cognitive impairment
    - Cognitive impairment will be defined as a pattern of deficits in vascular cognitive impairment that affect at least one cognitive domain (Sachdev et al., 2014).
    - Cognitive impairment(s) would be considered present if it was diagnosed by any one of the following disciplines: neurology, SLP, OT, neuropsychology and/or neurosurgery
    - By default, absence of impairment(s) will be recorded if it was reported to be absent or the deficit was not mentioned by any discipline
    - Record the severity of the impairment(s) if it was indicated in the charts
    - Select all the cognitive domains affected such as: executive function, learning and memory, language, complex attention, perceptual-motor function, social cognition, and/or other. Descriptions of different subdomains in each cognitive domain are provided below.

- In OT consult notes, cognitive deficits may be mentioned as part of "**Problems impacting the ability to engage in self-care, productive, and leisure**" section.

24. Impairments in **executive function** may include comments about the following subdomains (Sachdev et al., 2014):

    - Planning
    - Decision-making
    - Working memory
    - Responding to feedback
    - Inhibition
    - Flexibility
    - Disorganization
    - Impulsivity
    - Perseveration
    - Mental shifting
    - Multi-tasking

25. Impairments in **learning and memory** may include comments about the following subdomains (Sachdev et al., 2014):

    - Free recall
    - Cued recall
    - Recognition memory
    - Semantic and autobiographical long-term memory
    - Implicit learning
    - Forgetfulness
    - Disorientation

26. Impairments in **language** may include comments about the following subdomains (Sachdev et al., 2014):

    - Object naming
    - Wording finding
    - Verbal Fluency
    - Grammar and syntax
    - Receptive language

27. Impairments in **complex attention** may include comments about the following subdomains (Sachdev et al., 2014):

    - Sustained attention

- Divided attention
- Selective attention
- Processing speed
- Distractibility

28. Impairments in **perceptual-motor function** may include comments about the following subdomains (Sachdev et al., 2014):

    - Visual perception
    - Visuoconstructional reasoning
    - Perceptual-motor coordination
    - Spatial disorientation

29. Impairments in **social cognition** may include comments about the following subdomains (Sachdev et al., 2014)

    - Recognition of emotions
    - Theory of mind (i.e. mental state to self and others)
    - Insight
    - Self-awareness
    - Emotional dysregulation

30. Cognitive-communication
    - Information about cognitive-communication impairment(s) may be available in OT and/or SLP consult notes
    - Cognitive-communication identification will be established based on the practice standards and guidelines for acquired cognitive communication disorders provided by the American Speech-Language-Hearing Association (ASHA) (College of Audiologists and Speech-Language Pathologists (CASLPO), 2018). The following key terms may be used to describe patient's cognitive-communication deficits as they relate to production (oral or written) and comprehension (oral or written) of language.
        - Impaired attention, memory, organization, reasoning, inflexibility, impulsivity, impaired information processing (rate, amount and complexity, abstract auditory and visual language, etc.) and reduced insight/awareness
    - Other examples of terms that may be used to describe cognitive communication deficits may include:
        - Aprosodia
        - Tangential conversation

- Difficulty with turn-taking (monopolizing conversation OR the opposite: lack of verbosity)
- Difficulty with topic maintenance
- Difficulty making inferences in conversation/reading
- Focus on details in conversation/reading (can't see the big picture)
- Difficulty with figurative language (responds or interprets very literally)
- Difficulty with perspective taking in social interaction (relates to inferences often)
- Forgetfulness in conversation (repeating same content or trailing off and losing train of thought)

31. Dysarthria
    - Information about dysarthria may be available in Neurology and/or SLP consult notes
    - Calculate the time from admission to assessment in days. If no official time of assessment is indicated, estimated time may be used. In this case, 12:00PM EST may be used as the estimated assessment time.
    - Calculate the time from most confirmatory scans to assessment in days. If no official time of assessment is indicated, estimated time may be used. In this case, 12:00PM EST may be used as the estimated assessment time.
    - Indicate severity of dysarthria (if it is indicated in the charts)
    - Indicate severity determination (if applicable)
32. Apraxia of speech
    - Information about apraxia of speech may be available in SLP consult notes
    - Calculate the time from admission to assessment in days. If no official time of assessment is indicated, estimated time may be used. In this case, 12:00PM EST may be used as the estimated assessment time.
    - Calculate the time from most confirmatory scan to assessment in days. If no official time of assessment is indicated, estimated time may be used. In this case, 12:00PM EST may be used as the estimated assessment time.
    - Indicate severity of apraxia of speech (if it is indicated in the charts)
    - Indicate severity determination (if applicable)

33. Oropharyngeal dysphagia
    - Information about oropharyngeal dysphagia can be found in SLP consult notes
    - Nasogastric tube insertion may be used as a surrogate indicator of dysphagia whether or not a formal assessment was conducted
    - Calculate the time from admission to assessment in days. If no official time of assessment is indicated, estimated time may be used. In this case, 12:00PM EST may be used as the estimated assessment time.
    - Calculate the time from most confirmatory scans to assessment in days. If no official time of assessment is indicated, estimated time may be used. In this case, 12:00PM EST may be used as the estimated assessment time.

- Indicate severity of apraxia of speech (if it is indicated in the charts)
- Indicate severity determination (if applicable)

SECTION 8 – Discharge Information

34. NIHSS at discharge
    - This information can be found in the discharge summary. It may be listed in the "**Pertinent physical exam at time of discharge**" section.
35. Other Assessment (if applicable)
    - If other types of neurological and/or cognitive assessments were completed at the time of discharge, please record this on the form.
    - Indicate type of assessments and results
    - Calculate the time from admission to assessment in full days. If no official time of assessment is indicated, estimated time may be used. In this case, 12:00PM EST may be used as the estimated assessment time.
36. Not Evaluated (if applicable)
    - If the patient was not evaluated for any reasons prior to discharge, please document this on the form and state the reason(s).
37. Discharge Location and Status
    - Refer to the master list obtained from Data Analytics and Health Records
    - This information is listed as "**discharge disposition**"
    - If the patient was discharged to a rehabilitation facility, please specify which type. This may include out-patient, long-term in-patient, or short-term in-patient rehabilitation.
    - Otherwise, please indicate select the options listed on the chart review form which includes: acute care hospital (repatriation), long-term care facility, home, or death in facility

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College of Audiologists and Speech-Language Pathologists (CASLPO). (2018). *PRACTICE STANDARDS AND GUIDELINES FOR ACQUIRED COGNITIVE COMMUNICATION DISORDERS*. 37.

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Spreen, O., & Risser, A. H. (2003). *Assessment of aphasia*. Oxford University Press, USA.