Driving Performance and Underlying Brain Activation Patterns in Chronic Stroke Patients

by

Kristin Aileen Vesely

A thesis submitted in conformity with the requirements for the degree of Master of Science
Institute of Medical Science
University of Toronto

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Abstract

Resuming driving is an important priority for many stroke patients, yet persistent deficits may result in impaired driving performance. The present study used driving simulation and functional magnetic resonance imaging to examine whether stroke patients exhibit behavioural impairments and differences in brain activation patterns during driving tasks of varying complexity. Stroke patients committed more hazardous errors and errors at intersections, specifically when making complex left turns at intersections with oncoming traffic. Patients exhibited deviations from expected neural activation patterns during the most complex driving maneuver. The results of the present study suggest that stroke patients exhibit impairment during complex aspects of driving, specifically during intersections, and display altered patterns of neural activation as the perceptual and cognitive demands of the driving task increase. Further research is required to develop and validate existing screening measures and rehabilitation programs that target these specific driving impairments observed in functionally independent, chronic stroke patients.
Acknowledgments

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Contributions

Kristin Vesely (author) solely prepared this thesis. All aspects of the contents of the thesis including the original research plan, execution, analysis and writing were performed in whole or in part by the author. The following contributions by others are formally acknowledged:

Dr. Tom Schweizer (Supervisor and Program Advisory Committee Member): mentorship; provision of laboratory resources, guidance and assistance in the planning, execution, analysis and interpretation of results of all data and preparation of the thesis

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Megan Hird: assistance in execution and analysis of the data collected in Chapters 3 and 4

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<tbody>
<tr>
<td>Acomm</td>
<td>Anterior Communicating Artery</td>
</tr>
<tr>
<td>ANOVA</td>
<td>Analysis of Variance</td>
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<td>ANT</td>
<td>Attention Network Test</td>
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<tr>
<td>aSAH</td>
<td>Aneurysmal Subarachnoid Hemorrhage</td>
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<td>BADS</td>
<td>Behavioural Assessment of Dysexecutive Syndrome</td>
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<td>BOLD</td>
<td>Blood Oxygenation Level Dependent</td>
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<td>CNS</td>
<td>Central Nervous System</td>
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<td>CSF</td>
<td>Cerebrospinal Fluid</td>
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<td>CT</td>
<td>Computed Tomography</td>
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<td>DALYs</td>
<td>Disability Adjusted Life Years</td>
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<td>DHQ</td>
<td>Driving Habits Questionnaire</td>
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<td>EEG</td>
<td>Electroencephalography</td>
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<td>EPI</td>
<td>Echo Planar Imaging</td>
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<tr>
<td>FOV</td>
<td>Field of View</td>
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<tr>
<td>fMRI</td>
<td>Functional Magnetic Resonance Imaging</td>
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<td>GOS</td>
<td>Glasgow Outcome Scale</td>
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<td>HADS</td>
<td>Hospital Anxiety and Depression Scale</td>
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<tr>
<td>HRQoL</td>
<td>Health-Related Quality of Life</td>
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<tr>
<td>IADLs</td>
<td>Instrumental Activities of Daily Living</td>
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<tr>
<td>ICA</td>
<td>Internal Carotid Artery</td>
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<td>ICH</td>
<td>Intracerebral Hemorrhage</td>
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<tr>
<td>IS</td>
<td>Ischemic Stroke</td>
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<td>MCA</td>
<td>Middle Cerebral Artery</td>
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<td>MMSE</td>
<td>Mini-Mental State Examination</td>
</tr>
<tr>
<td>MoCA</td>
<td>Montreal Cognitive Assessment</td>
</tr>
<tr>
<td>MNI</td>
<td>Montreal Neurological Institute</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic Resonance Imaging</td>
</tr>
<tr>
<td>MVC</td>
<td>Motor Vehicle Crash</td>
</tr>
<tr>
<td>NIfTI</td>
<td>Neuroimaging Informatics Technology Initiative</td>
</tr>
<tr>
<td>NIHSS</td>
<td>National Institutes of Health Stroke Scale</td>
</tr>
<tr>
<td>nSDSSA</td>
<td>Nordic Stroke Driver Screening Assessment</td>
</tr>
<tr>
<td>Pcomm</td>
<td>Posterior Communicating Artery</td>
</tr>
<tr>
<td>PET</td>
<td>Positron Emission Tomography</td>
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<tr>
<td>Acronym</td>
<td>Description</td>
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<tr>
<td>RS-fMRI</td>
<td>Resting State Functional Magnetic Resonance Imaging</td>
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<td>SAH</td>
<td>Subarachnoid Hemorrhage</td>
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<tr>
<td>SDSA</td>
<td>Stroke Driver Screening Assessment</td>
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<tr>
<td>TE</td>
<td>Echo Time</td>
</tr>
<tr>
<td>TIA</td>
<td>Transient Ischemic Attack</td>
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<tr>
<td>TMT</td>
<td>Trail Making Test</td>
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<tr>
<td>TMT-A</td>
<td>Trail Making Test Part A</td>
</tr>
<tr>
<td>TMT-B</td>
<td>Trail Making Test Part B</td>
</tr>
<tr>
<td>TR</td>
<td>Repetition Time</td>
</tr>
<tr>
<td>UFOV</td>
<td>Useful Field of View Test</td>
</tr>
<tr>
<td>UFOV-DA</td>
<td>Useful Field of View - Divided Attention Subtest</td>
</tr>
<tr>
<td>UFOV-PS</td>
<td>Useful Field of View - Processing Speed Subtest</td>
</tr>
<tr>
<td>UFOV-SA</td>
<td>Useful Field of View - Selective Attention Subtest</td>
</tr>
<tr>
<td>VCI</td>
<td>Vascular Cognitive Impairment</td>
</tr>
<tr>
<td>VR</td>
<td>Virtual Reality</td>
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<tr>
<td>WFNS</td>
<td>World Federation of Neurological Societies</td>
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Chapter 1 : Introduction

1.1 Background

Stroke is the development of a neurological deficit secondary to an acute and focal vascular injury that results in damage to the central nervous system (CNS) (R. Sacco et al., 2013). After ischemic heart disease, stroke is the most common cause of death, accounting for 9% of deaths worldwide (Murray & Lopez, 1997a). According to the Global Burden of Disease Study, stroke ranks sixth as the cause for the greatest number of disability-adjusted life years (DALYs), which is the sum of life years lost due to the combination of early mortality and years lived with disability (Murray & Lopez, 1997b). With the population expected to age substantially in the coming decades, stroke is projected to rise to the fourth-highest contributor to DALYs by the year 2030 (Lopez, Mathers, Ezzati, Jamison, & Murray, 2006).

In western countries, stroke mortality has seen a consistent decline due to more rapid diagnosis, improved acute medical management, control of stroke risk factors (especially hypertension and cigarette smoking), and improved living conditions (Bonita, 1992; Thrift et al., 2006). It is estimated that approximately 500 people per 100,000 population are currently living with the effects of stroke (Donnan, Fisher, Macleod, & Davis, 2008). Many stroke survivors suffer some degree of persistent cognitive or functional impairment, often relying on caregivers to help accomplish common daily activities, such as self-care and managing personal finances. Post-stroke cognitive impairment has a significant impact on functional dependency after hospital discharge (Tatemichi, Desmond, Stem, & Paik, 1994). As many as 72.5% of stroke patients experience cognitive impairment in one or more cognitive domains persisting greater than one year after stroke, with the domains of attention, language, short-term memory and executive function most commonly affected (Leśniak, Bak, Czepiel, Seniów, & Członkowska, 2008). Furthermore, these deficits often persist for the years after stroke (Patel, Coshall, Rudd, & Wolfe, 2003).
Driving is an important marker of functional status, allowing individuals to fulfill both personal and professional responsibilities. There is a well-documented association between cessation of driving after acquired brain injury, and increased rates of feeling isolated and burdensome to friends and family, leading to increased rates of depression (Griffen, Rapport, Coleman Bryer, & Scott, 2009; Ragland, Satariano, & MacLeod, 2005; Windsor, Anstey, Butterworth, Luszcz, & Andrews, 2007). The relationship between driving status and post-stroke depression is potentially bi-directional, as Rozon & Rochette, (2015) found a significant association between depression immediately following stroke and driving status 6 months after hospital discharge. The termination of driving privileges is also known to reduce out-of-home activity levels and has been shown to precede a more rapid decline in overall health and earlier mortality than that of individuals who maintain their driving privileges (Edwards, Lunsman, Perkins, Rebok, & Roth, 2009; Marottoli et al., 2000). Driving cessation after stroke has been associated with a 42% decline in health-related quality of life (HRQoL) (Poissant, Mayo, Wood-Dauphinee, & Clarke, 2003). Despite the aforementioned consequences of driving cessation on the patient’s overall wellbeing and independence, particular attention must be paid to the impact of post-stroke cognitive and functional impairments on driving ability in the interest of protecting the safety of patients, as well as the general public.

1.2 Stroke Classifications

Stroke is broadly classified as ischemic, resulting from a focal decrease in blood supply to a region of the brain, or hemorrhagic, resulting from a collection of blood in or around the brain. The most recent revision of the *International Classification of Diseases* system sub-classifies cerebrovascular disorders into the categories of cerebral ischemic stroke (IS), transient ischemic attack (TIA), intracerebral hemorrhage (ICH) and subarachnoid hemorrhage (SAH). These categories are discussed in more detail below.
1.2.1 Ischemic Stroke

The definition of IS encompasses clinical neurological symptoms and the presence of an ischemic infarction, whereas a TIA is diagnosed in a patient presenting with symptoms that are transient (less than 24 hours) with no evidence of an ischemic infarction found on diagnostic neuroimaging. Earlier definitions of stroke concentrated on the duration of neurological symptoms to distinguish a TIA from a stroke; however, more recent evidence suggests that irreversible damage to the CNS may occur with a short duration (less than 24 hours) of symptoms; the current consensus defines a stroke as any episode of neurological dysfunction, regardless of duration, that results from a CNS infarction (R. Sacco et al., 2013). Patients with IS commonly present with impairments in movement, perception and vision or language that are dependent on the location of the ischemic event (Di Carlo et al., 1999; Lawrence et al., 2001). Ischemic stroke severity is commonly assessed using the National Institute of Health Stroke Scale (NIHSS), which is a 15-item neurological examination that provides a quantitative measurement of the neurological deficits (Brott et al., 1989). In a population-based study of stroke recovery, scores on the NIHSS in the acute stage have been correlated with long-term HRQoL (Sturm et al., 2004).

A “silent infarct” occurs when a CNS infarction is identified in a patient with no known episode of acute neurological dysfunction that can be attributed to the lesion (R. Sacco et al., 2013). A systematic review examining silent CNS infarctions in the general population using MRI reported a prevalence ranging between 8-28% of the studied cohorts (Vermeer, Longstreth, & Koudstaal, 2007). The inclusion of silent CNS infarctions in the definition of stroke is somewhat controversial as the diagnosis depends on the accurate detection of CNS tissue damage, which is dependent on the criteria for identifying lesions and the neuroimaging modality that is used. A review by Zhu, Dufouil, Tzourio, & Chabriat, (2011) found wide variability in the MRI diagnostic criteria for silent infarction but concluded that the majority of studies used a threshold of ≥ 3mm for diagnosis. Although a silent CNS infarction occurs in the absence of an episode of an acute stroke syndrome, patients may not be asymptomatic, and often have persistent cognitive and functional impairments (Saini et al., 2012; Schmidt et al., 2004; Vermeer et al., 2003).
1.2.2 Hemorrhagic Stroke

The diagnosis of stroke from cerebral hemorrhage results from injury to the CNS and is caused by a spontaneous (non-traumatic) vascular event (R. Sacco et al., 2013). In contrast, hemorrhage caused by a traumatic event is not considered a stroke. Non-traumatic ICH and SAH comprise the subtypes of hemorrhagic stroke.

ICH results from a spontaneous accumulation of blood in the brain parenchyma or ventricles and may be caused by systemic hypertension, cerebrovascular malformation, amyloid angiopathy, congenital or acquired platelet-vessel or coagulation deficits, or otherwise can occur with unknown etiology. Diagnosis of ICH is confirmed reliably by the presence of intraparenchymal or intraventricular blood as detected by magnetic resonance imaging (MRI) or computed tomography (CT) (Kidwell et al., 2004). ICH is considered one of the most disabling stroke subtypes, with almost a 40% fatality rate within 30 days and only 20% of patients able to regain functional independence (Counsell, Dennis, Mcdowell, & Warlow, 2002; Kleindorfer et al., 2015; Palm et al., 2010). Patients who present with ICH often have symptoms that are non-focal in nature, and that are not easily attributed to damage of a specific brain structure. Headache is the primary complaint on presentation in almost one-third of ICH patients, followed by nausea, decreased level of consciousness and increased blood pressure (Kleindorfer et al., 2007). Similar to a silent CNS infarction, silent cerebral hemorrhages are small parenchymal hemorrhages in patients without a history of acute neurological dysfunction that could conceivably relate to the lesion. Present in approximately 6% of elderly adults (Roob et al., 1999), silent cerebral hemorrhages are also associated with cognitive impairment (Qui et al., 2010; Werring, 2004).

SAH results from the collection of blood in the subarachnoid space, confirmed primarily using neuroimaging with non-contrast CT or MRI, or less commonly with a lumbar puncture to detect the presence of blood in the cerebrospinal fluid (CSF) (van Gijn, Kerr, & Rinkel, 2007). Spontaneous SAH is caused by cerebral aneurysm rupture in approximately 85% of cases, but may also be attributed to other causes such as intracranial artery dissections, arteriovenous malformations, substance abuse, moyamoya disease and cerebral amyloid angiopathy (Rinkel,
van Gijn, & Wijdicks, 1993; van Gijn & Rinkel, 2001). A “thunderclap headache”, seizure, vomiting and decreased level of consciousness are all symptoms associated with acute SAH (van Gijn et al., 2007). Aneurysmal SAH (aSAH) is treated acutely with the repair of the ruptured aneurysm using either endovascular coiling or neurosurgical clipping followed by supportive care and hospitalization for several weeks to monitor for development of angiographic vasospasm and delayed cerebral ischemia, a complication that occurs in 67% of SAH patients (Crowley et al., 2011; Dabus & Nogueira, 2013; Macdonald, Diringer, & Citerio, 2014; Macdonald et al., 2008). Reported mortality rates for SAH range from 20-45% and approximately 10% of patients are left with profound disability (Biotti et al., 2010; S. Sacco et al., 2009; Shea et al., 2007). Predictors of poor outcome include worse neurological grade on admission, increased age, high blood pressure, posterior circulation aneurysms, subarachnoid clot volume and pre-existing medical conditions (Rosengart, Schultheiss, Tolentino, & Macdonald, 2007).

1.3 Long-term Stroke Outcomes

Although many stroke patients experience permanent, long-term deficits, recovery of impairments is a dynamic and continuous process that enables the patient to at least partially regain function (Hochstenbach, den Otter, & Mulder, 2003). Most patients show some degree of improvement in neurological functions within the first three months of the stroke, and 40-60% are able to regain functional independence within three to ten years (Hardie, Hankley, Jamrozik, Broadhurst, & Anderson, 2004; Lai & Duncan, 2001; Weimar et al., 2002).

Cognitive impairment is a known predictor of poor functional outcome and risk of long-term dependence after being discharged from the hospital (Saxena, Ng, Koh, Yong, & Fong, 2007; Tatemichi et al., 1994). A number of stroke-related problems such as fatigue and emotional distress also contribute to exaggerated impairment and deficits in cognitive status during the acute phase of stroke recovery (Lezak, Howieson, & Loring, 2004). The most rapid improvements in cognitive function occur in the first-month post-stroke, with subsequent slower gains in recovery (Nys, Van Zandvoort, et al., 2005a). Prognostic indicators of cognitive
recovery include age, lesion location, lesion volume, and comorbid diabetes (Nys, van Zandvoort, et al., 2005b)

Vascular cognitive impairment (VCI) is a syndrome describing cognitive disorders resulting from stroke (Wentzel et al. 2001). Although VCI is often referred to as a unitary condition, the actual cognitive profiles of VCI patients are quite heterogeneous and can relate to specific lesion locations (Barnes, Dobkin, & Bogousslavsky, 2005). Lesniak et al. (2008) highlight the importance of detecting impairments in specific cognitive domains, stating that detection of domain-specific cognitive impairments informs the prediction of functional outcome, and should influence decisions for management and targeted rehabilitation (Cicerone et al., 2011; Toby B Cumming, Marshall, & Lazar, 2013). In particular, deficits in executive function, identified in 18.5% of chronic stroke patients, are a strong predictor of poor functional recovery after stroke.

1.3.1 Cognitive and Functional Outcomes After Ischemic Stroke

Functional outcomes on an individual patient basis can be predicted with some success at baseline by combining age and stroke severity (as determined using clinical rating scales such as the NIHSS), but the prediction of cognitive outcomes is more difficult (Saposnik, Guzik, Reeves, Ovbiagele, & Johnston, 2013; Vogt, Laage, Shuaib, & Schneider, 2012). Based on the results of detailed cognitive assessment in IS patients with good clinical recovery (modified Rankin Scale 0-1), 71% exhibited impairment in at least one cognitive domain at three months post-stroke (Jokinen et al., 2015). Although the NIHSS includes measures of attention, language and orientation, it does not assess some of the higher cognitive functions such as memory and visuospatial functioning (Cumming, Blomstrand, Bernhardt, & Linden, 2010). This is perhaps why NIHSS scores obtained on admission are not strong independent predictors of cognitive dysfunction (Lees et al., 2014). Studies examining the impact of lesion volume on cognitive outcomes are inconsistent with some investigators endorsing the relevance of lesion volume (Hope, Seghier, Leff, & Price, 2013) and others reporting no relationship (Marchina et al., 2011).
Lesion location is generally a better predictor of cognitive dysfunction in IS patients than in hemorrhagic stroke patients because specific regions of focal infarction are associated with specific cognitive deficits such as neglect (Karnath, Rennig, Johannsen, & Rorden, 2011) or aphasia (Bates et al., 2003; Magnusdottir et al., 2013). Lesion mapping studies also support a relationship between certain infarct locations and greater global cognitive dysfunction due to disruption in functioning of distant regions that compromise network integrity. For example, executive dysfunction is associated with focal damage to the prefrontal cortex, but also to the thalamus, basal ganglia and cingulate cortex (Stebbins et al., 2008; Szirmai, Vastagh, Szombathelyi, & Kamondi, 2002).

Ischemic stroke is traditionally perceived as a disease of elderly individuals; however, one-quarter of IS occurs in people under age 65, and the number of people experiencing a stroke between the ages of 20 and 64 increased by 25% between 1990 and 2010 worldwide (Feigin et al., 2014). Thus, the number of working-age individuals living with the consequences of IS is increasing. Approximately half of patients between the ages of 16-65 who are employed prior to suffering a stroke are able to return to work after stroke (Daniel, Wolfe, Busch, & McKevitt, 2009; Wozniak & Kittner, 2002). In addition, patients who are able to return to driving after stroke are also more likely to return to work, and engage in community activities (Doucet, Muller, Verdun-Esquer, Debelleix, & Brochard, 2012). Depressive symptoms, cognitive impairment, fatigue, reduced mobility and lack of social connection are all factors that restrict IS patients from community involvement (Chau, Thompson, Twinn, Chang, & Woo, 2009; Kubina, Dubouloz, Davis, Kessler, & Egan, 2013; Mayo, Bronstein, Scott, Finch, & Miller, 2014).

1.3.2 Cognitive and Functional Outcomes after Subarachnoid Hemorrhage

Most studies investigating post-stroke outcomes refer extensively to IS. This is not surprising given that IS accounts for approximately 80% of all stroke cases (Feigin, Lawes, Bennett, & Anderson, 2003). Although relatively less common, hemorrhagic stroke still presents a substantial threat to public health due to higher rates of mortality and morbidity relative to IS (Feigin et al., 2003). As SAH patients are a population of focus in this thesis, outcomes
pertaining to SAH will be described in further detail here. Since patients with ICH were not included, their outcomes will not be discussed. The interested reader is referred to Rost et al., (2008) for a comprehensive discussion of long-term outcomes of ICH.

As many as 76% of SAH patients suffer from some level of long-term cognitive dysfunction, despite meeting the criteria for “good outcome” according to the Glasgow Outcome Scale (GOS) (Mavaddat, Sahakian, Hutchinson, & Kirkpatrick, 1999). Impairments in a wide range of cognitive functions including attention, executive function, memory, language and, to a lesser degree, visuospatial function have been reported (Al-Khindi, Macdonald, & Schweizer, 2010). The prediction of domain-specific cognitive impairment is difficult in SAH patients, as studies reporting on the relationship between the location of aneurysm rupture and cognitive deficits are inconsistent (Al-Khindi et al., 2010). Furthermore, there is growing evidence of increased risk-taking behaviour, impulsivity and poor judgment in SAH patients (Al-Khindi, Macdonald, & Schweizer, 2014; Mavaddat, Kirkpatrick, Rogers, & Sahakian, 2000; Salmond et al., 2006). Patients with good outcomes tend to have minimal residual physical deficits and can regain their ability to perform most basic activities of daily living such as feeding, dressing and personal hygiene (Hackett, Hons, & Anderson, 2000). The occurrence of impairments in high-level executive functions lead to impairment in the more complex instrumental activities of daily living (IADLs) such as managing finances and housework (Powell, Kitchen, Heslin, & Greenwood, 2004).

In addition to cognitive dysfunction, debilitating levels of fatigue are another common concern during both the acute and chronic phases of recovery, as indicated by the fact that as few as 21% of SAH patients are able to return to full-time employment (Haug et al., 2010). Increased levels of anxiety and depression commonly observed in up to half of SAH survivors are also strongly linked to functional outcomes including return to work and social engagement (Morris, Wilson, & Dunn, 2004). Due to the sudden, unpredictable nature of SAH and its possible recurrence, post-traumatic stress disorder is another common consequence that persists up to three years in one third of patients and has a negative impact on HRQoL (Visser-Meily et al., 2013).
1.4. Driving after Stroke

To many individuals, driving is considered a fundamental civil liberty and has an important role in fulfilling their personal and professional responsibilities. Returning to driving after stroke is an important aspect of community reintegration and allows patients to maintain a sense of independence and autonomy (Finestone et al., 2010). Persistent cognitive, motor and visual deficits in stroke patients compromise safe driving ability. However, up to 30% of all stroke survivors do resume driving, but the proportion is likely greater when considering patients who are able to live independently in their homes (Fisk, Owsley, & Pulley, 1997). Patients who return to driving have reported greater difficulty during certain conditions, such as driving at night or in adverse weather conditions (Fisk, Owsley, & Mennemeier, 2002).

1.4.1 Driving as a Complex Task

Driving a motor vehicle is a complex task, which requires intact motor function, visual perceptual abilities and cognitive functioning across multiple cognitive domains (Anstey, Wood, & Lord, 2005). Although most driving skills can become well-trained over time, these skills must still be performed simultaneously by the driver. Drivers must also be capable of adapting rapidly to changing circumstances, as the environment may change from safe to dangerous very quickly. Models outlining a conceptual framework for driving have been developed to describe how these functions are interrelated to produce safe driving behaviour. The most common model, first developed by Michon (1971), is comprised of a hierarchical structure describing three levels of driving decision-making. Michon posited that there is a distinctly ordered cognitive control structure of human behaviour in the driving environment. From top-to-bottom, these levels are named strategic, tactical and operational. The strategic level, also referred to as the navigational component, is the goal-setting aspect of driving that encompasses the ability to follow a planned route toward a certain destination. The strategic level includes tasks such as choosing the destination, deciding the most appropriate route and approximating an arrival time. The tactical level, also known as the maneuvering component, involves the actions taken to reach the strategic goals, including interacting with other road users. Examples of tactical level of driving include maintaining appropriate distance from other vehicles, and making safe turns at intersections. The lowest level, the operational level, describes the manipulation of the vehicle’s
controls. This includes handling the steering wheel, pedals and any other controls in the vehicle. According to Michon, the three levels are constantly adjusted through internal feedback loops in response to environmental cues.

Simpler aspects of driving, such as driving down a straight road with minimal traffic or other obstacles, demand primarily lower levels of the framework (i.e. the operational and tactical elements) whereas more complex driving maneuvers, such as navigating through urban intersections demand coordination of all three levels. In an adaptation to his earlier model, Michon, (1985) hypothesized that in addition to the “top-down” interactions occurring between the ordered levels previously defined, there was potential for “bottom-up” processes to occur in unexpected driving situations. For example, if the vehicle skids while driving down a slippery road, then immediate compensation is required at the operational level.

In the context of driving after acquired brain injury, an adaptation to the Michon’s 1985 model by Galski, Bruno, & Ehle, (1992) includes sensory processing abilities, driving experience and motor abilities as factors required in a framework for safe driving in patient populations. From the established frameworks of driving behaviour, it is evident that driving requires the integration of multiple factors at different levels, and a deficit in a singular component has the potential to compromise overall safe driving ability.

### 1.4.2 Crash Risk After Stroke

One of the common methods used to assess the presence of driving impairment in brain-injured populations is to measure the occurrence of motor vehicle crashes (MVC) after the event. Studying post-stroke collision risk using driving records is beneficial because it is based on long-term observations in naturalistic driving conditions. Both the on-road assessment and simulator assessment are relatively short evaluations that can potentially result in altered behaviour of the patient because there is an observer present and patients have the overt understanding that their
performance is being evaluated. The on-road and simulated driving methods will be discussed in detail in Sections 1.5.1 and 1.5.2, respectively.

Perrier, Korner-Bitensky, Petzold, & Mayo, (2010) conducted a structured review of studies investigating the risk of motor vehicle collisions and traffic citations in stroke patients compared to individuals without prior history of stroke. Seven studies of post-stroke collision risk were identified. Occurrences of MVCs were confirmed by different methods among the studies, including accessing records from the vehicle licensing agency (Haselkorn, Mueller, & Rivara, 1998; Margolis, Kerani, McGovern, Songer, & JA, 2002; McGwin, Sims, Pulley, & Roseman, 2000; Sims, McGwin, Allman, Ball, & Owsley, 2000), or from data entered in insurance databases (Koepsell et al., 1994; Lundqvist, Alinder, & Rönnberg, 2008; Sagberg, 2006). Five studies indicated an increased risk of crashes post stroke with adjusted odds ratios or risk ratios ranging from 1.1 - 7.7 (Lundqvist et al., 2008; Margolis et al., 2002; McGwin et al., 2000; Sagberg, 2006; Sims et al., 2000). Two studies had negative findings, both reporting an adjusted odds ratio or risk ratio of 0.8 (Haselkorn et al., 1998; Koepsell et al., 1994). Although the studies observing an increased collision risk post-stroke had relatively small sample sizes of stroke patients ranging from 9-50, all five studies controlled for driving frequency by adjusting for variables such as self-reported annual and weekly mileage, and days driven per week. This is in direct contrast to the two studies that did not find an increased collision risk, which did not control for any variable relating to driving exposure. Controlling for driving exposure is an important methodological component because stroke patients may be more likely to limit their driving (Finestone et al., 2010).

Perrier et al., (2010) concluded that the risk of collisions in patients with stroke is twice that of drivers who have not suffered a stroke, but it is worth restating that the sample sizes in these positive studies were quite small. The largest scale study was conducted by Haselkorn et al. (1998), and included 1,910 stroke patients. They found that after controlling for age, gender and the occurrence of crashes prior to hospitalization, there was no increase in MVCs in the stroke patient group compared to a cohort of healthy controls. This study used one-year post-stroke as the observation period for collisions, a time during which many patients may self-impose
reductions in their driving exposure or are required not to drive as a result of legislation prohibiting driving for a certain time period immediately following the stroke. For example, in Canada, Australia and the United Kingdom, physician guidelines state that patients should not drive in the month following stroke and patients often are required to complete a formal assessment before they are able to return to driving (Canadian Medical Association 2012; Austroads Ltd. 2012; Driver Vehicle Licensing Agency 2014). Interestingly, Haselkorn et al. (1998) found a decreased risk (RR = 0.8) of receiving traffic citations in the stroke patients relative to the control cohort. A longer follow-up period in a large sample size is required to reproduce and confirm the findings observed in the smaller studies. Furthermore, none of these studies have analyzed the effects of stroke severity or stroke type on post-stroke driving risk, limiting the clinical utility of the findings. Further analysis of the types of collisions (i.e. single versus multi-vehicle collision, environmental conditions, passengers present or absent in the vehicle) would also be useful in developing guidelines and rehabilitation programs for improvement of driving ability in stroke patients.

The use of MVC data to determine driving risk in patient populations has several limitations. First, collisions are rare events, requiring large sample sizes to draw reliable conclusions. Access to these large datasets is limited and variables such as post-stroke driving exposure are not controlled, encouraging many groups to rely on smaller, more comprehensive datasets with a low absolute collision count, often below 20 collisions in total as was reported by Koepsell et al. (1994), Sims et al. (1998) and Lundqvist et al. (2008). Furthermore, interpretation of accident severity varies based on the data collection method and fundamentally changes the level of risk assessed. For example, Haselkorn et al. (1998) measured MVCs that were reported as a result of hospital admission, potentially missing numerous, less severe MVCs.

1.4.3 On-Road Evaluation of Post-Stroke Drivers

The majority of research studies examining driving behaviour in chronic stroke patients have been conducted using on-road assessment, typically conducted from driving rehabilitation centres with patients who are referred for assessment of their driving ability. These studies can
be grouped according to three primary aims: 1) to explore the utility of cognitive tests in predicting the pass/fail result of the on-road assessment; 2) to study the impact of lesion location on on-road driving ability; 3) to test the ability of various rehabilitation programs to improve the result of the on-road assessment. These studies will be discussed in more detail below. The on-road assessment is often favoured due to its high external validity; however, the on-road assessment can be costly, and lacks standardization and reproducibility. The advantages and disadvantages of the on-road assessment will be discussed in more detail in Section 1.5.1.

Cognitive Screening Batteries to Predict On-Road Assessment Result

The most common aim among on-road assessment studies in the current literature is to identify how cognitive assessments can be used as instruments to screen for potentially unsafe drivers who require follow-up assessment. Multiple groups have studied both classic cognitive tests, such as the Trail Making Test (TMT), as well as tests designed specifically for driving assessment, such as the road sign recognition test. In general, the results of these studies are mixed, with some studies claiming high predictive accuracy of a certain test or battery of tests (Akinwuntan et al., 2002; George & Crotty, 2010; Mazer, Korner-Bitensky, & Sofer, 1998), and others concluding that no relationship exists between driving outcomes and cognitive testing (Akinwuntan et al., 2006; Söderström, Pettersson, & Leppert, 2006). A few tests that have emerged as predictive according to the studies with positive results include the Trail Making Test, Stroke Driver Screening Assessment (SDSA), the Useful Field of View Test (UFOV) and the Rey-Osterrieth complex figure test. However, the studies showing positive results have shown lack of reproducibility by other groups, likely a result of changes to the experimental methodologies and criteria for scoring the driving outcomes.

For the TMT, Mazer, Korner-Bitensky, & Sofer, (1998) identified a positive association between the results of the Trail Making Test Part A (TMT-A) and Part B (TMT-B) and the likelihood of passing the on-road assessment, whereas Söderström, Pettersson, & Leppert, (2006) found no such association for the TMT. Both George & Crotty, (2010) and Akinwuntan et al., (2002) reported that results of the UFOV, especially the Divided Attention and Selective Attention
subtests, were predictive of on-road performance but in a later paper by Akinwuntan et al., (2006), they concluded that the UFOV was not predictive of driving ability after using a similar methodology as their earlier paper. The SDSA, which consists of four subtests including a Dot Cancellation Test, Square Matrices Directions, Square Matrices Compass and a Road Sign Recognition Test, has shown more promising but still conflicting results. The findings of George & Crotty 2010 and Akinwuntan et al., (2005) suggest that the SDSA has high sensitivity in predicting the pass/fail outcome of the on-road assessment. Although these are the only studies evaluating the SDSA, an adapted version of the SDSA for the Scandinavian population called the Nordic SDSA (nSDSA) has been evaluated by Lundberg, Caneman, & Samuelsson, (2003) and Selander, Lee, Johansson, & Falkmer, (2011), both concluding that the nSDSA is inferior to the SDSA in predicting on-road driving ability. In a meta-analysis of 27 studies assessing the determinants of fitness to drive after stroke, Devos et al., (2011) investigated the impact of publication bias in the literature regarding the predictive accuracy of cognitive screening measures using the calculation of the fail-safe number, a theoretical indicator of the number of unpublished studies with a zero effect size that would be required to render a significant effect size insignificant. They concluded that publication bias could not be excluded from the literature for almost all five clinically relevant tools they identified (i.e. Cube Copy, Road Sign Recognition Test, Compass Test, SDSA and TMT-B) with the exception of the Road Sign Recognition Test. Taken together, the current literature highlights a few cognitive tests that may be associated with driving fitness but several inconsistencies across studies with different methodologies remain. Currently, there is no consensus regarding a gold-standard cognitive screening assessment for fitness to drive in stroke patients.

Lesion Location and Driving Ability

Limited research has studied the impact of stroke lesion location on driving ability using the on-road assessment. Data correlating driving performance with lesion location could serve to help clinicians inform patients in the early stages of recovery of the potential consequences of their stroke on returning to drive. Two studies by the same group have conducted studies evaluating the relationships between performance during on-road assessment and stroke laterality or location.
Devos, Tant, & Akinwuntan, (2014) conducted on-road assessments and cognitive testing in 99 patients (49 ischemic, 26 hemorrhagic and 24 undefined) with chronic, first ever stroke. They found no difference in the proportion of patients who achieved good scores on the on-road assessment between patients with left and right hemisphere stroke, but there were differences in the on-road variables affecting the driving score in each of those subgroups. For patients with right hemisphere stroke, the tactical cluster, comprised of maintaining proper speed and distance from lead vehicles as well as performing lane changes, was the only driving skill cluster that predicted the on-road decision. In the left hemispheric stroke group, only the visuo-integrative cluster, which describes the perception of road signs and traffic signals, traffic insight and communicating with other road users, was predictive of the driving decision. Although there is no evidence from this study that stroke laterality affects overall quality of on-road driving performance, the results of Devos, Tant & Akinwuntan (2014) suggest that the impairments of specific aspects of on-road driving may be influenced by laterality, pointing toward a different approach to driving rehabilitation in patients with left versus right hemispheric stroke.

In a later study, Devos, Verheyden, Van Gils, Tant, & Akinwuntan, (2015) investigated the relationship between the on-road assessment results and the lesion location of 77 IS patients. A significant correlation emerged between the presence of lesions to the parietal lobe and poorer performance on the operational and tactical driving clusters. No differences in driving performance were observed between patients with single or multiple cortical lesions, or between different subcortical structures. Furthermore, no differences in performance were found between patients with lesions of different vascular territories, although the majority of patients were classified as having a middle cerebral artery (MCA) occlusion, with relatively small counts (≤8) among the remaining territories. Further study of the neuroanatomical correlates of driving behaviours is needed to better characterize the relationship between lesion location and specific driving impairments in stroke patients.
Intervention Studies for Driving Rehabilitation

Multiple interventions have been developed to help stroke patients regain the ability to drive. These interventions can be broadly classified into two categories: 1) intervention programs that aim to retrain the underlying physical, cognitive and perceptual processes posited to relate to safe driving ability; and 2) context-specific driving interventions that employ on-road or simulator training protocols to improve driving ability.

Programs designed to retrain underlying processes relevant to driving typically consist of paper and pencil-based or computerized tasks or games that make up an organized program to gradually improve performance in the targeted skill over time. The success of the program depends on the ability of the practiced skill to generalize to improved functional performance in driving. Although the relationship between measures of cognitive function and driving ability is still inconclusive, as was previously discussed in Section 1.4.3, cognitive retraining programs are a common intervention recommended by clinicians and driver rehabilitation specialists. These interventions are cost effective and simple to administer because fewer resources are required. Mazer et al., (2003) investigated the effectiveness of two visual attention-retraining programs to improve performance on the on-road assessment by randomizing 97 stroke patients (of both ischemic and hemorrhagic etiologies) to either training with the UFOV test (see Section 3.2.2 for full description) or a control group that completed a traditional, computerized visuo-perception retraining program. In their previous paper, Mazer, Sofer, Korner-Bitensky, & Gelinas, (2001) demonstrated that stroke patients were impaired on aspects of visual attention scored on the UFOV and that patients could improve their scores after 20 training sessions. The subsequent 2003 study found no significant difference between the two training programs on the pass rate of the on-road assessment or on any measures of visuo-perception, but did report almost a two-fold increase in passing the on-road assessment for patients in the UFOV group with right-sided lesions compared to patients in the control group with right-sided lesions. Patients with right-sided lesions often suffer impairments in attention and visuospatial processing, which may help explain why benefits of training were observed in this group (Suchoff, Gianutsos, Ciuffreda, & Groffman, 2000). However, it is difficult to conclude that this was a direct result of the UFOV training because the baseline UFOV scores of patients with left and right-sided lesions were not
reported separately. Crotty & George, (2009) studied the potential of the Dynavision System, a tool that aims to improve visual processing and motor response time to increase the pass rate of the on-road assessment. After randomizing 26 stroke patients to either the Dynavision group or a control group that received no intervention, no significant differences emerged in the outcome of the on-road assessment, or secondary measures, which included processing speed, visual scanning and a measure of self-efficacy. Overall, there is a lack of evidence at present to suggest that gains made in cognitive training programs translate functionally into improved driving performance.

Training using context-specific methods, such as driving simulator training or on-road driving lessons, offer higher face validity but are more resource intensive and costly than the cognitive retraining programs mentioned above. Direct comparisons between the effectiveness of simulator or on-road training and cognitive interventions provide support for or against adopting a costlier approach (Akinwuntan et al., 2005; Hannes Devos et al., 2009, 2010). Akinwuntan et al. (2005) randomized 83 stroke patients, of ischemic or hemorrhagic etiology that were all within three months of stroke, to complete a five-week, 15-hour training program of either driving simulator training or a control intervention of driving-related cognitive tasks. After the intervention period, they observed an improvement in the scores on cognitive tests (components of the SDSA) in both groups but the pass-rate of the on-road assessment was higher in the experimental group (73%) than the control group (42%). Patients with left-sided strokes were reported to have experienced greater gains in performance as a result of the simulator-based training program compared to patients with right-sided lesions. This was suggested to be because patients with right-sided lesions have greater difficulty with training because of greater impairments in cognition and visual processing that underlie safe driving performance (Sundet, Goffeng, & Hofft, 1995). These findings, however, are in contrast with the findings of Mazer et al. (2003) who reported improved outcomes of the on-road assessment in patients with right hemisphere lesions. Mazer et al. (2003) suggested that a more specific training regimen that targeted impairments found more frequently in patients with right hemisphere lesions was more effective than a simulator training protocol aimed to improve multiple aspects of the driving task. At a five-year follow-up to the study published by Akinwuntan et al. (2005), the prior advantage of the simulator training protocol was no longer present, as there was no significant difference between the two groups in
a fitness to drive decision based on clinical, cognitive and on-road assessments (Devos et al. 2010). Although the literature supports an advantage to simulator-based training protocols over purely cognitive intervention programs, the potential for long-term benefits from either approach are currently unclear. Furthermore, limited information is available regarding the clinical and cognitive profiles of patients who benefit from certain interventions. Further research is required to develop more targeted rehabilitation programs, as stroke patients present with heterogeneous deficits that may not benefit from one single rehabilitation program.

1.4.4 Simulated Driving Evaluation of Post-Stroke Drivers

Few studies have used driving simulators to compare the driving performance of chronic stroke patients to that of healthy control participants (Hitosugi, Takehara, Watanabe, Hayashi, & Tokudome, 2011; Lundqvist, Gerdle, & Ronnberg, 2000; McKay, Rapport, Coleman Bryer, & Casey, 2011; Motta, Lee, & Falkmer, 2014). All of these studies, with the exception of Hitosugi et al., (2011) also conduct some form of cognitive assessment to investigate the relationship between post-stroke cognitive outcomes and driving performance. Further details of these studies are described below.

In an early study using driving simulation in stroke patients, Lundqvist (2000) aimed to validate a neuropsychological testing battery for the prediction of driving outcome using both on-road and driving simulator assessments. The patient group (n=30) had variable stroke etiologies and consisted of 26 cerebral infarctions and four ICH. Specific stroke locations were unspecified but lesions were located in the left hemisphere in 10 patients, the right hemisphere in five patients, bilaterally in five patients and unspecified in the remaining 10 patients. The time since stroke ranged from 3-14 months and 97% of the patients had greater than 10 years of driving experience. It appears that the patients were quite high functioning as the exclusion criteria listed hemianopsia, epilepsy, physical disability, aphasia and apraxia. Twenty-three patients completed the driving simulation, and outcome variables included time and distance to collision with other vehicles, complex reaction time to unexpected events, and the score on the Listening Span Test. These variables, primarily related to speed of information processing, were selected as they were
theorized to correlate to accident causation (Alm, 1989). Results indicated that there was no significant difference between patients and controls on any of the driving measures except the performance on the Listening Span Test, where patients could not manage to process and recall words as well as controls while driving. This finding indicates impairment in a secondary task performed during driving, rather than the primary task of driving itself, which has implications for the ability of patients to maintain driving performance during demanding or distracted driving conditions. Lundqvist (2000) also found that the results of the comprehensive neuropsychological test battery did not accurately predict the outcome of the driving simulation.

McKay et al. (2011) looked at the relationship between impaired self-awareness and driving performance in stroke patients and healthy controls, as self-awareness is an important aspect of subjective driving ability (Scott et al., 2009). In this study, 30 chronic stroke patients (subtype not reported; lesions located 30% left hemisphere, 57% right hemisphere and 13% bilateral) and 30 healthy controls completed a series of simulated driving scenarios reported to contain simple and challenging situations and a neuropsychological test battery. All participants completed pre- and post-test evaluations of their self-perceived performance. Although all patients were required to have driven in the three months preceding the stroke, only 63% had driven since the stroke. The time since stroke varied considerably, ranging from 3-280 months. The outcome of the driving simulation was a total score comprised of performance on multiple measures, which included speed, stopping distance, correct lane placement, traffic signal use, avoiding hazards, and obeying traffic signals. They found that stroke patients performed worse on the results of the cognitive testing and the overall score for the driving simulation than control participants. Furthermore, when they compared the pre- and post-test predictions of performance, they found that the stroke patients greatly overestimated their ability on both the driving simulator and cognitive testing.

Hitosugi et al., (2011) used a driving simulator to measure collision avoidance in 24 stroke patients compared to 20 healthy controls. They specified that 13 patients had IS, nine had ICH and one had SAH. Furthermore, they described the specific neurological deficits of the sample as 20 having hemiplegia, two with aphasia, one with ataxia and one with an orientation disorder,
indicating a moderate level of impairment among the patient sample. Due to the high proportion of patients included with hemiplegia, many of the patients also required in-vehicle adaptations such as a steering spinner to operate the simulator. On a braking task requiring the participant to avoid a collision with a truck, they found that patients performed significantly worse than controls, using outcome measures consisting of reaction time and braking time. They also observed that performance on this task improved with subsequent exposures, supporting the potential for driver retraining in stroke patients.

Most recently, Motta et al., (2014) specifically looked at the relationship between measures of executive function and simulated driving outcomes in 19 stroke patients and 22 healthy controls. The driving simulation was stated to include a variety of driving situations, including simple and complex. The TMT-B and Behavioural Assessment of Dysexecutive Syndrome (BADS) were the measures of executive function selected for analysis. The patients performed worse overall than controls on the driving simulation, and, in particular, performed poorly in the areas of collisions, stopping at proper distances, and demonstrating caution. Only the TMT-B correlated to a score of overall driving ability.

The results of the above studies of driving simulator performance in stroke patients suggest that some stroke patients demonstrate driving impairment, but the results are not conclusive or specific. The studies are variable regarding stroke type, severity, as well as the content and evaluation of the driving simulation. Both Lundqvist et al., (2000) and Hitosugi et al., (2011) specify that patients with ischemic and hemorrhagic stroke were included, but no sub-analysis of driving outcomes was completed, likely due to the small sample sizes of hemorrhagic stroke patients tested. Studies by Hitosugi et al., (2011) and Motta et al., (2014) both found significant differences in driving performance between patients and controls, but it should be noted that both studies used control groups that were significantly younger than the patients group, introducing the possibility that age-related cognitive decline may have confounded the analysis or magnified the between-group differences. Furthermore, the patients included by Hitosugi et al., (2011) were described as having significant motor and language deficits, rendering it difficult to combine the results with the other studies, which included patients with more minor deficits. Lastly, studies
by both McKay et al., (2011) and Motta et al., (2014) describe the driving scenarios they used as including both simple and complex tasks, but in their analyses they only refer to overall driving scores, and do not investigate any differences between tasks of different difficulty level.

Overall, the current literature highlights that some stroke patients may exhibit impaired overall performance on a driving simulator, but has not addressed the impact of stroke subtype on driving ability, or how performance may differ during simple and more complex aspects of driving. By grouping patients with different stroke subtypes together, it is unclear how deficits unique to a subtype may influence driving behaviour. Understanding these differences will influence the formulation of more targeted screening assessments for driving ability after stroke. In addition, determining how well patients adjust to more complex aspects of driving may reveal the best approach for re-training driving ability.

1.5 Methods of Assessing Driving Behaviour

1.5.1 On-road Assessment

The on-road assessment is regarded as the most ecologically valid measure of driving ability, and currently is the most common method of assessing driving fitness in neurological populations (Dobbs, Carr, & Morris, 2002). In a study comparing the results of the on-road assessment to self-reported retrospective and prospective crashes in a cohort of 267 elderly adults, participants who had experienced a collision also committed more errors during the on-road assessment Wood et al., (2009). Using the Rasch analysis, Kay, Bundy, Clemson, & Jolly, (2008) demonstrated construct validity and inter-rater reliability of the on-road assessment.

Although currently considered the gold standard, the on-road assessment has several limitations. Firstly, the on-road assessment does not permit testing of drivers whose driving ability may be considered too unsafe, which has resulted in incomplete or terminated testing in some participants who begin the assessment (Wood et al., 2009). The dangers associated with on-road testing also prohibit the assessment of the more challenging and cognitively demanding aspects
of driving, such as navigating through high-traffic areas. This is especially pertinent to the assessment of participants with mild impairments, who may not exhibit a decrement in performance during simpler, more routine aspects of driving. Secondly, there is substantial variability in the administration of the assessment (i.e. duration, location, closed course versus open road), as well as the criteria used to evaluate performance and make pass/fail classifications. Conventionally, a gestalt decision based on the overall results of the driving assessment was used but a more standardized approach making decisions based on concrete scoring procedures is increasingly favoured (Di Stefano & Macdonald, 2003; Odenheimer et al., 1994; Withaar, Brouwer, & van Zomeren, 2000). Thirdly, due to the unpredictable nature of external road conditions, the on-road assessment is not standardized across participants and cannot guarantee that each driver encounters the same level of difficulty. Due to the innate inconsistency, the reliability of the on-road assessment has been questioned in previous studies (Akinwuntan et al., 2005).

1.5.2 Driving Simulator Assessment
Driving simulators are an emerging technology that help overcome many of the limitations associated with the on-road assessment. The use of driving simulation software creates standardized evaluations, ensuring that every participant is exposed to the same driving conditions. Simulator software is also programmable and customizable, allowing the researcher to insert specialized situations that the driver is unlikely to encounter in a typical on-road assessment, such as an unexpected accident avoidance scenario. The use of simulators has become an essential instrument in aviation, allowing pilots to train to handle complex and realistic but safe conditions (Lee & Bussolari, 1989). Driving simulators are ideal for populations with cognitive impairment because they expose the participant to realistic and complex driving conditions without the risks of on-road driving (de Simone, Kaplan, Patronas, Wassermann, & Grafman, 2007). A computer-generated output provides a comprehensive evaluation of different aspects of driving that is standard across all drivers.

The validity and reliability of driving simulator protocols have been repeatedly investigated. Although evidence suggests that driving simulators do not provide an exact substitute for the on-
road assessment, several research studies have concluded that an individual’s behaviour on a driving simulator is correlated to their on-road behaviour (Bedard, Parkkari, Weaver, Riendeau, & Dahlquist, 2010; Bella, 2008; Godley, Triggs, & Fildes, 2002; Yan, Abdel-Aty, Radwan, Wang, & Chilakapati, 2008). The results of simulators have also been shown to distinguish between safe and unsafe drivers (H. C. Lee, Lee, Cameron, & Li-Tsang, 2003; Lew et al., 2005; Patomella, Tham, & Kottorp, 2006). Freund, Gravenstein, Ferris, & Shaheen, (2002) found that the number of hazardous errors (i.e. errors in lane positioning and collisions) committed during driving simulation and a failing result of the on-road test were highly related. Furthermore, H. Lee & Lee, (2005) used simulated driving results to successfully predict which individuals had a greater risk of experiencing a future collision in a three-year longitudinal study. Although driving simulators have been shown to possess high reliability and validity, they are not currently used clinically for the assessment of driving ability. Further investigation into the psychometric properties of driving simulators, as well as how specific impairments observed in driving simulation translate to on-road driving ability, is required before driving simulators can become a widely accepted clinical tool for driving assessment.

Driving simulators address many of the challenges associated with on-road testing, but they are not without inherent limitations. During simulator-based assessments, participants perceive a lower level of risk, which may result in participants making riskier decisions than they would if they were driving on the road (Horrey & Wickens 2006). Alternatively, in the presence of a researcher observing performance, participants may drive more cautiously. Furthermore, a phenomenon known as “simulator sickness” occurs in 12-27% of participants undergoing driving simulation (Park, Allen, Fiorentino, Rosenthal, & Cook, 2006; Rinalducchi, Mouloua, & Smither, 2003). Simulator sickness is a form of motion sickness resulting from a state of sensory conflict between visual and vestibular inputs and includes symptoms of disorientation, oculomotor disturbance and nausea (Kennedy & Fowlkes, 1992). There are some unmodifiable risk factors for experiencing simulator sickness such as increasing age, but with careful attention to experimental design and environmental conditions, the occurrence of simulator sickness can be reduced. Specifically, presenting scenarios on a single monitor, using a simulation software with a high refresh rate of the graphics to decrease “choppiness”, and beginning with scenarios that are less visually stimulating and progressing to more complex road geometries are strategies
that have been shown to reduce the occurrence of simulator sickness (Classen, Bewernitz, & Shechtman, 2011).

When applying simulator methodology to a research setting, it is of high importance that individuals who drop out due to simulator sickness do not have fundamentally different driving skill than the rest of the experimental sample. Mullen, Weaver, Riendeau, Morrison, & Bedard, (2010) investigated whether participants who failed to complete a series of simulated driving scenarios due to simulator sickness (dropouts) exhibited different on-road driving behaviour and cognitive test results than the participants who completed the driving simulation (completers). In a population of healthy, older adults, the dropouts did not differ from completers on the results of cognitive testing, and contrary to their initial hypothesis, they actually performed better than the completers during the on-road assessment. Although the sample size was small, the results of Mullen et al., (2010) suggest that simulator sickness does not prevent the evaluation of driving performance of participants who may be most in need of driving assessment.

1.6 Neuroimaging of Driving

Collecting functional neuroimaging data during real driving or driving simulation is a promising method to better understand the neural networks that underlie various driving behaviours. Understanding how activation patterns in patients with neurological conditions differ from those of healthy control participants may help explain why certain behavioural impairments are occurring. Using neuroimaging to study the neural activation patterns of various populations and behaviour states is a relatively new, but expanding area of research that has increased in popularity in recent years. Multiple modalities have been explored, including electroencephalography (EEG) (Borghini et al., 2012; Huang, Pal, Chuang, & Lin, 2015), positron emission tomography (PET) (Horikawa et al., 2005), and functional near-infrared spectroscopy (fNIRS) (Tomioka et al., 2009; Yoshino, Oka, Yamamoto, Takahashi, & Kato, 2013). Although EEG and fNIRS allow data collection under naturalistic driving conditions, these modalities are limited in spatial resolution and cortical depth penetration. PET and fMRI both offer far greater spatial resolution and ability to image the entire brain simultaneously, but due to the confines of the imaging apparatus, require substantial modifications to experimental
protocols to assess driving behaviour (e.g. designing a simulator that can be used in supine position) and therefore, sacrifice some level of ecological validity. Functional MRI may be preferred over PET for research purposes because it is more readily available, has higher spatial resolution and does not require injection of a radioactive tracer. Despite some limitations, including sensitivity to head motion, high cost and lower temporal resolution, fMRI is currently used extensively for functional imaging of the human brain and will be discussed in further detail below (Cui, Bray, Bryant, Glover, & Reiss, 2011).

1.6.1 Functional Magnetic Resonance Imaging

Functional magnetic resonance imaging (fMRI) is a non-invasive technique capable of measuring brain activation patterns that depends on the competing effects of cerebral blood flow (CBF), cerebral blood volume and cerebral metabolic rate of oxygen consumption. The neurovascular coupling concept posits a relationship between local neural metabolism and changes in CBF. Activation in different regions of the brain elicit an increase in cellular oxygen and glucose uptake, supplied by the vascular system. Thus, brain activation patterns are inferred indirectly by measurements of blood flow, measured at the level of the microvasculature. The most commonly used fMRI contrast is the Blood Oxygenation Level Dependent (BOLD) signal, which is a measurement of venous oxygenation, flow and volume. MRI is able to measure the BOLD response because oxygenated and deoxygenated hemoglobin possess different magnetic properties. This creates perturbations in the magnetic field as a result of changes in neural activation. The disruption in the magnetic field is measured by the T2* relaxation time (Jezzard 

During task-based fMRI experiments, participants are exposed to different stimulus conditions that provoke a measurable change in the BOLD signal. Functional MRI experiments are broadly classified into an event-related design where the task stimulus is relatively short relative to the control condition, and a block design, where the task and control stimuli are typically longer in duration (approximately 15 seconds). Multiple repetitions of the task are required to obtain a
A reliable measure of the task-related change in the BOLD signal, which is weak and contaminated by sources of noise (Aguirre, Zarahn, & D’esposito, 1998; Neumann, Lohmann, Zysset, & Von Cramon, 2003).

1.6.2 Neural Correlates of Driving

A select number of studies have explored the neural correlates of driving maneuvers using functional neuroimaging in combination with a virtual reality (VR) environment. Due to the technical challenges associated with embedding a functional driving simulator equipped with pedals and a steering wheel without ferromagnetic components in an MR system, the majority of studies have utilized simpler, passive tasks such as observing videos with different driving situations (Graydon et al., 2004; Hirth, Davis, Fredriksson, Rorden, & Bonilha, 2007; Hsieh et al., 2009; Mader et al., 2009). Although novel information related to processing different types of driving situations can be gained using this approach, these passive tasks do not provide insight into the active planning and initiation of driving maneuvers. A few studies have overcome this limitation by integrating joystick controllers that allow participants to actively control the vehicle during the simulation (Calhoun et al., 2002; Just, Keller, & Cynkar, 2008; Uchiyama, Ebe, Kozato, Okada, & Sadato, 2003; Walter et al., 2001). However, these systems only allow the participant to control one component of the vehicle control (i.e. steering or speed) and therefore still represent an over-simplification of the driving task with compromised external validity.

Only a few studies have utilized an MR-compatible driving simulator with controls for both steering and speed control (Meda et al., 2009; Schweizer et al., 2013; Spiers & Maguire, 2007) Meda et al., (2009) present the simplest experimental paradigm of these studies by comparing neural activation patterns of individuals actively driving on a straight road versus watching videos of driving. Spiers & Maguire, (2007) were the first to analyze activation patterns during several different aspects of active driving, including behaviour during expected and unexpected situations, but the study was still limited in its ability to replicate real-world driving as participants used two joystick controllers, one for speed and one for steering, to operate the vehicle. Schweizer et al., (2013) used an immersive simulator with a functional steering wheel
and pedals to measure brain activation patterns during intersection turns of increasing complexity (i.e. right turns, to left turns, to left turns with a continuous stream of oncoming traffic) as well as during driving in the presence of audio distraction tasks.

Overall, these studies have revealed a network of regions that become more active during driving relative to at rest, which primarily include parietal and occipital cortices, the cerebellum and areas related to motor control and perception. Few of these studies also report specific relationships between areas of brain activation and driving performance. Correlations have been observed between frontal, parietal, occipital and thalamic regions and average driving speed (Calhoun et al., 2002; Horikawa et al., 2005). Uchiyama, (2003) reported a significant negative association between the ability to maintain a safe driving distance from lead vehicles and activity in the anterior cingulate cortex, a region that has previously been implicated in error detection and conflict monitoring based on neuroimaging and lesion studies (Bush, Luu, & Posner, 2000). Schweizer et al., (2013) observed changes in activation patterns with increasing perceptual and cognitive demand, reporting an increase in the magnitude of activation in the previously reported regions associated with driving (parietal-occipital cortices, motor cortex and the cerebellum).

Although some studies have investigated the relationship between lesion location and driving performance, as previously discussed in Section 1.4.3 (Devos et al., 2011, 2014, 2015; Mazer et al., 2003; Söderström et al., 2006), the underlying brain changes associated with driving in stroke patients have not been previously investigated from a functional neuroimaging perspective.

1.6.3 Functional Magnetic Resonance Imaging in Stroke

Functional MRI studies in stroke usually aim to characterize the spontaneous, and rehabilitation-induced neuropsychological changes in brain circuitry during the various stages of stroke recovery (Auriat, Neva, Peters, Ferris, & Boyd, 2015). It is now understood that distant regions of intact brain tissue can influence one another during the recovery process, and can include many brain regions such as the brainstem, corticospinal tract, and interhemispheric connections (Grefkes &
Ward, 2014). For example, studies using fMRI in patients with unilateral hand paresis have found widespread bilateral activation in the motor system during movement of the paretic hand in the acute phase of recovery (Ward, 2011). Task-based BOLD fMRI can characterize differences in the underlying brain activation patterns that relate to certain outcomes in stroke patients. For example, multiple studies have provided evidence that greater increases in activation in the contralesional hemisphere during task performance are correlated with poor outcomes because it represents a less efficient cortical reorganization process, or may be reflective of greater effort required to complete the task (Cramer, Moore, Finklestein, & Rosen, 2000; Marshall et al., 2000). The majority of task-based fMRI studies in stroke patients focus on recovery of motor and language function, in part because these functions can be feasibly assessed in the MR environment, and in part because impairments in these functions are common among stroke patients. The assessment of high-level executive functioning in relation to neuroimaging is most commonly conducted by correlating markers of structural imaging (i.e. gray matter volume, white matter integrity) with out-of-scanner performance on neuropsychological tests (Camilleri et al., 2015; Zi, Duan, & Zheng, 2014).

More recently, resting-state fMRI (rs-fMRI) has emerged as a technique to measure functional connectivity by observing temporal correlations in the BOLD signal (Fox & Raichle 2007; Smith et al. 2013). rs-fMRI is used to evaluate the connectivity in brain regions while participants are not engaged in a particular task (i.e. at rest). From the measurement of low-frequency fluctuations in the BOLD signal over time, inferences about the functional organization of the brain can be made based on the synchronous activation of spatially distant regions (M. H. Lee, Smyser, & Shimony, 2013). RS-fMRI studies in stroke patients have demonstrated that focal brain lesions can induce alterations in functional connectivity in brain regions that are structurally intact and distant from the site of the lesion (Grefkes & Fink, 2011). These changes have been observed in attentional and motor networks, and have been shown to correlate with behavioural improvements during stroke recovery (Carter et al. 2010; He et al. 2007; Wang et al. 2010; Park et al. 2011; Golestani, Tymchuk, Demchuk & Goodyear 2013). One of the advantages of RS-fMRI is that it permits the analysis of multiple networks simultaneously. In contrast, understanding that two separate functional conditions induce different patterns of activation from a traditional, task-based fMRI study does not provide information about how a
certain brain region interacts with other regions to modulate behaviour. As the efficiency of a particular network can be compromised after stroke, several investigators are working to quantify these network disruptions and relate them to clinical outcomes in stroke patients (Honey & Sporns, 2008; Wang et al., 2010).

Functional MRI in stroke patients has provided insight into the relationship between lesion sites and behaviour, as well as the dynamic network changes that occur during the recovery process. As the field of fMRI in stroke is still developing, little has been done to explore the underlying network changes in response to complex, multi-domain real-world tasks. By studying these more complex tasks, greater insight can be gained into recovery of activities that enable stroke patients to stay active in their communities.
Chapter 2: Research Questions, Aims and Hypotheses

2.1 Summary and Rationale

After a stroke, patients often experience a range of deficits in visual, motor and cognitive functioning that may impact driving ability. Driving is an important activity of daily living for many individuals, as it allows them to maintain social connections with the community, and is often a requirement for fulfilling both personal and professional obligations. The loss of driving privileges following stroke may lead to decreased out of home activities as well as decreased access to health care services. Furthermore, the relationship between loss of a driver’s license and increased feelings of isolation, depression and higher rates of medical comorbidities and mortality is well-documented.

Research on the risk of collision in post-stroke drivers suggests that there may be an increased risk of experiencing an MVC after having a stroke relative to healthy individuals, although this evidence is based on relatively small datasets. The environmental circumstances and contributors (e.g. intersection-related errors, driver inattention or distraction) to these MVCs are currently unknown. The current literature studying driving behaviour in stroke patients largely consists of on-road driving studies aiming to understand the cognitive predictors of performance during the on-road assessment. Results have remained inconsistent, with some studies claiming predictive accuracy of a particular test and other studies stating that the same test was not related to on-road driving ability. Furthermore, both cognitive and driving simulator intervention programs to retrain driving skills have yielded inconsistent results, with little empirical evidence that an effective program with sustained benefits exists.

Driving simulators are growing in popularity as a tool to assess driving performance in a controlled, standardized and safe environment. Although currently considered the gold standard tool, the on-road assessment does not provide the opportunity to observe driving behaviour
during unpredictable but inevitable complex situations, as this may place the driver, the assessor and other road users at risk. Driving simulators are an emerging technology offering a unique advantage to study the point at which the cognitive demands of a complex driving situation surpass an individual’s cognitive capacity, resulting in deteriorating driving performance. A handful of studies have reported on the driving behaviour of stroke patients in a simulated environment, but none has analyzed performance on tasks of varying complexity, or on the performance of different stroke subtypes. This lack of understanding of the behavioural impairments may explain why there is limited evidence that rehabilitation programs are effective in improving on-road driving performance. Patients with good outcomes and more minor visual/motor impairments may have more subtle impairments that impact driving ability. These impairments may only emerge in more complex driving situations such as making left-hand-turns at intersections with oncoming traffic.

Functional neuroimaging in stroke has traditionally focused on purely motor or language functions, and further research is needed to describe how the brain responds to varying levels of cognitive demand in complex, real-world situations. RS-fMRI studies in chronic stroke patients have revealed compromises in the integrity of functional networks, and task-related fMRI studies are needed to further explore the consequences of altered functional connectivity.

Due to the importance of maintaining driving privileges for many aspects of overall well-being, it is essential that a balance is found between protecting the safety of the patient and other drivers, while simultaneously maximizing the potential for patients to safely resume driving following a stroke where possible. To achieve this goal, further development of screening assessment tools to identify potentially unsafe drivers, as well as rehabilitation programs to regain safe driving abilities is required. Although significant effort has been invested in developing such tools and programs, there is currently no gold standard cognitive screening assessment tool used in current practice, or a rehabilitation program with long-term benefits and replicated results. As such, more research is required to better understand more specifically which aspects of driving are impaired following a stroke so that the assessment and rehabilitation of driving ability following stroke may take on a more targeted approach.
This thesis aims to gain an improved understanding about driving behaviour in stroke patients, specifically regarding simple versus complex driving situations. Furthermore, the present study will be the first simulated driving study to compare performance of patients with different stroke subtypes, an important step towards developing more accurate screening and assessment tools for patients who wish to resume driving after stroke. Lastly, the study will also be the first to look at the underlying brain activation patterns of driving performance in drivers with stroke using fMRI to compare task-related activation of different driving maneuvers of increasing complexity in stroke patients and healthy controls.
2.2 Research Aims and Hypotheses

The present study aims to provide an objective analysis of simulated driving behaviour and underlying brain activation patterns in good outcome, functionally independent, chronic stroke patients, including contrasts between routine versus complex aspects of driving, and contrasts between different stroke subtypes (i.e. IS versus SAH).

**Aim 1:** To determine if chronic stroke patients exhibit overall impaired performance (i.e. more driving errors) than healthy control participants on a simulator-based assessment.

**Hypothesis 1:** Due to cognitive and functional deficits that persist into the chronic phase of stroke recovery, patients will commit significantly more driving errors than healthy control participants on overall measures of driving performance.

**Aim 2:** To determine if driving behaviour differs in chronic stroke patients during simple versus complex aspects of driving.

**Hypothesis 2:** Patients will exhibit impaired performance (i.e. more driving errors) during intersection turns, especially during the most complex maneuvers involving left turns with oncoming traffic.

**Aim 3:** To determine how behavioural driving performance differs between IS and SAH stroke subtypes relative to healthy control participants.

**Hypothesis 3:** SAH patients will commit a similar number of errors overall as ischemic patients but will exhibit greater impairment (i.e. more driving errors) when navigating intersection turns due to higher prevalence of executive dysfunction.
Aim 4: To determine if there are underlying changes in brain activation patterns in chronic IS patients when performing driving tasks of increasing complexity.

Hypothesis 4: Patients will exhibit similar activation patterns as control participants during simpler, less complex aspects of driving (i.e. completing simple right and left turns) but will exhibit deviations from healthy controls as the driving task becomes more complex (i.e. completing complex left turns with oncoming traffic).

2.3 Outline of the Thesis

The following chapters will contain the details of two experiments that will address the stated aims. Aims 1-3 all pertain specifically to driving behavioural outcomes in chronic IS and SAH patients, and the related hypotheses will all be tested in Chapter 3. Aim 4 will be addressed as a separate experiment described in Chapter 4, and will detail the results of a combined driving simulation and fMRI study in chronic IS patients. Each of Chapters 3 and 4 will contain a separate description of the methodology, experimental results and discussion.

The thesis will conclude in Chapter 5 with a unifying discussion of the findings in relation to the current literature, the limitations of the study, as well as the impact and future directions for this line of research.
3.1 Introduction

The present study uses driving simulator technology to collect objective measures of driving performance in chronic stroke patients, and age-matched control participants. In addition, differences in simulated driving behavior will be explored between two stroke subtypes: IS and SAH. This study was completed with approval from the St. Michael’s Hospital Research Ethics Board. All volunteers enrolled in the study provided written informed consent prior to participation.

3.2 Methods

3.2.1 Participants

Fifteen (15) SAH patients, 13 IS patients and 12 control participants were recruited for this study. All stroke patients were recruited from St. Michael’s Hospital. The inclusion criteria for stroke patients were as follows: 1) diagnosis of either aSAH or IS, confirmed through either CT or MRI scans; 2) age 18-85; 3) in the chronic phase of recovery (at least 3-months post-stroke); 4) fluency in English; 5) either currently holding, or held valid driver’s license immediately prior to stroke with at least 5 years of driving experience. Exclusion criteria included: 1) diagnosis of another neurological or psychiatric disease (e.g. Parkinson’s Disease, Epilepsy, Multiple Sclerosis, Bipolar Disorder); 2) history of traumatic brain injury; 3) untreated or uncontrolled mood disorder; 4) history of substance abuse; 5) visual deficits that do not meet Ontario Ministry of Transportation standards for driving; 6) motor deficits that would impair ability to manipulate the steering wheel and pedals; 7) language deficits that would interfere with the ability to communicate or understand instructions during the driving assessment or neuropsychological testing. Patients in the IS group, must not have had a previous hemorrhagic stroke and patients in the aSAH group must not have experienced a previous IS. Medical records were used to partially screen patients for study eligibility, to confirm the presence of stroke based on the neuroimaging
results and to screen for neurological co-morbidities that would exclude the patient. Although all patients were required to have at least five years of driving experience, 26 out of 28 patients (93%) had greater than 10 years of driving experience. Ischemic stroke patient characteristics are listed in Table 3.1 and aSAH patient characteristics are listed in Table 3.2. All IS patients had NIHSS scores in the mild to moderate range (Brott et al., 1989). Although four patients had an NIHSS of zero, indicating an absence of stroke symptoms according to the NIHSS, scores of zero have been associated with positive findings on MRI (Martin-Schild et al., 2012) and definitive diagnosis of stroke was made on the basis of MRI findings for inclusion in this study. All SAH patients scored between 1-3 on the WFNS Classification and were therefore considered to have “good grade” SAH (Leira et al., 2007). The cause of SAH was aneurysmal in all patients. The average time between stroke onset and time of testing was 34.9 months for IS patients and 22.5 months for SAH patients.

Twelve healthy control participants were recruited from the community through networking and local advertising. Control participants underwent an eligibility-screening questionnaire before entering the study and were screened under the same inclusion and exclusion criteria, with the exception that they did not have any diagnosis of previous stroke, and must have currently held a valid Ontario G-class driver’s license. Control participants were matched to the patient groups on demographic variables including age and years of driving experience. Demographic information is listed for all participants in Table 3.3.

### 3.2.1 Clinical Data

Available information pertaining to the clinical characteristics of each stroke patient was gathered to characterize the stroke severity and features of the patient sample. Clinical data were extracted for each patient enrolled in the study from Soarian Clinicals [Version 3.03, Siemens Healthcare, Germany], the electronic patient information system used at St. Michael’s Hospital. The clinical data collected for analysis included the date of stroke, clinical deficits on presentation, clinical scores (i.e. WFNS, NIHSS) and the location of stroke or aneurysm rupture.
The MRI results were accessed to obtain information of the location of brain ischemia (for IS patients) or the location of hemorrhage (for SAH patients).

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (Years)</th>
<th>Sex</th>
<th>Lesion Location</th>
<th>Time Since Stroke (Months)</th>
<th>NIHSS</th>
</tr>
</thead>
<tbody>
<tr>
<td>IS-001</td>
<td>68</td>
<td>F</td>
<td>L posterior parietal and L posterior temporal</td>
<td>50.6</td>
<td>0</td>
</tr>
<tr>
<td>IS-002</td>
<td>75</td>
<td>M</td>
<td>R frontal (M3 branch)</td>
<td>12.4</td>
<td>3</td>
</tr>
<tr>
<td>IS-003</td>
<td>72</td>
<td>M</td>
<td>R parietal lobe</td>
<td>50.5</td>
<td>2</td>
</tr>
<tr>
<td>IS-004</td>
<td>57</td>
<td>M</td>
<td>R hippocampus</td>
<td>45.7</td>
<td>1</td>
</tr>
<tr>
<td>IS-005</td>
<td>59</td>
<td>M</td>
<td>L periinsular region</td>
<td>88.6</td>
<td>8</td>
</tr>
<tr>
<td>IS-006</td>
<td>44</td>
<td>M</td>
<td>L basal ganglia</td>
<td>40.9</td>
<td>4</td>
</tr>
<tr>
<td>IS-007</td>
<td>50</td>
<td>M</td>
<td>R thalamus</td>
<td>20.6</td>
<td>0</td>
</tr>
<tr>
<td>IS-008</td>
<td>71</td>
<td>M</td>
<td>R thalamus</td>
<td>24.4</td>
<td>10</td>
</tr>
<tr>
<td>IS-009</td>
<td>63</td>
<td>M</td>
<td>R MCA territory</td>
<td>50.5</td>
<td>7</td>
</tr>
<tr>
<td>IS-010</td>
<td>48</td>
<td>F</td>
<td>L posterior temporal</td>
<td>26.4</td>
<td>0</td>
</tr>
<tr>
<td>IS-011</td>
<td>79</td>
<td>M</td>
<td>R subcortical white matter</td>
<td>Unknown*</td>
<td>Unknown*</td>
</tr>
<tr>
<td>IS-012</td>
<td>43</td>
<td>M</td>
<td>Anterior corpus callosum</td>
<td>5.1</td>
<td>0</td>
</tr>
<tr>
<td>IS-013</td>
<td>68</td>
<td>M</td>
<td>R striatum, lentiform nuclei, corona radiata, centrum semiovale, fronto-opercular region and insula</td>
<td>3.2</td>
<td>4</td>
</tr>
</tbody>
</table>

Table 3.1 Characteristics of IS patients who completed the driving simulation study. Lesion locations are based on the most specific localization documented in the radiologist’s clinical notes. *Patient was diagnosed with silent stroke, therefore time since stroke and NIHSS scores are unavailable.
Table 3.2 Characteristics of SAH patients who completed the driving simulation study. Pcomm, posterior communicating artery; Acomm, anterior communicating artery; ICA, internal carotid artery; MCA, middle cerebral artery.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (Years)</th>
<th>Sex</th>
<th>Aneurysm Rupture Location</th>
<th>Time Since Aneurysm Rupture (Months)</th>
<th>WFNS Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAH-001</td>
<td>65</td>
<td>M</td>
<td>Basilar</td>
<td>60.1</td>
<td>1</td>
</tr>
<tr>
<td>SAH-002</td>
<td>60</td>
<td>F</td>
<td>L Pcomm</td>
<td>9.7</td>
<td>2</td>
</tr>
<tr>
<td>SAH-003</td>
<td>76</td>
<td>F</td>
<td>R Pcomm</td>
<td>18.2</td>
<td>2</td>
</tr>
<tr>
<td>SAH-004</td>
<td>68</td>
<td>F</td>
<td>Acomm</td>
<td>8.8</td>
<td>2</td>
</tr>
<tr>
<td>SAH-005</td>
<td>41</td>
<td>F</td>
<td>L paraclinoid ICA</td>
<td>27.2</td>
<td>1</td>
</tr>
<tr>
<td>SAH-006</td>
<td>66</td>
<td>F</td>
<td>Acomm</td>
<td>5.8</td>
<td>1</td>
</tr>
<tr>
<td>SAH-007</td>
<td>64</td>
<td>M</td>
<td>R MCA</td>
<td>20.9</td>
<td>3</td>
</tr>
<tr>
<td>SAH-008</td>
<td>41</td>
<td>F</td>
<td>R MCA</td>
<td>22.3</td>
<td>1</td>
</tr>
<tr>
<td>SAH-009</td>
<td>44</td>
<td>F</td>
<td>L MCA</td>
<td>10.9</td>
<td>1</td>
</tr>
<tr>
<td>SAH-010</td>
<td>50</td>
<td>M</td>
<td>Acomm</td>
<td>29.2</td>
<td>3</td>
</tr>
<tr>
<td>SAH-011</td>
<td>52</td>
<td>M</td>
<td>Acomm</td>
<td>15.5</td>
<td>3</td>
</tr>
<tr>
<td>SAH-012</td>
<td>58</td>
<td>F</td>
<td>L MCA</td>
<td>23.9</td>
<td>1</td>
</tr>
<tr>
<td>SAH-013</td>
<td>68</td>
<td>F</td>
<td>Acomm</td>
<td>35.8</td>
<td>1</td>
</tr>
<tr>
<td>SAH-014</td>
<td>53</td>
<td>M</td>
<td>Acomm</td>
<td>32.6</td>
<td>1</td>
</tr>
<tr>
<td>SAH-015</td>
<td>65</td>
<td>M</td>
<td>R MCA</td>
<td>17.0</td>
<td>1</td>
</tr>
</tbody>
</table>
### Table 3.3 Demographic and driving habits data for all participant groups. No between group differences exist in age, years of education, employment status, or any measures on the Driving Habits Questionnaire or Hospital Anxiety and Depression Scale. A significant relationship between sex and group type was observed [$X^2(2, N=40) = 6.847, p = 0.033$].

<table>
<thead>
<tr>
<th></th>
<th>IS</th>
<th>SAH</th>
<th>CTL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age Mean (SD)</strong></td>
<td>61.3 (12.1)</td>
<td>58.1 (10.8)</td>
<td>63.0 (11.6)</td>
</tr>
<tr>
<td><strong>Sex N(%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>11 (84.6)</td>
<td>6 (40.0)</td>
<td>9 (75.0)</td>
</tr>
<tr>
<td>Female</td>
<td>2 (15.4)</td>
<td>9 (60.0)</td>
<td>3 (25.0)</td>
</tr>
<tr>
<td><strong>Education Level N(%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High School</td>
<td>0 (0.0)</td>
<td>7 (46.7)</td>
<td>2 (16.7)</td>
</tr>
<tr>
<td>College</td>
<td>2 (15.4)</td>
<td>3 (20.0)</td>
<td>5 (41.7)</td>
</tr>
<tr>
<td>Bachelor's</td>
<td>10 (76.9)</td>
<td>4 (26.7)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Master's</td>
<td>0 (0.0)</td>
<td>1 (6.7)</td>
<td>5 (41.7)</td>
</tr>
<tr>
<td>PhD or Professional Degree (e.g. LLB)</td>
<td>1 (7.7)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td><strong>Employment Status</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Currently Employed N(%)</td>
<td>6 (46.2)</td>
<td>6 (40.0)</td>
<td>4 (33.3)</td>
</tr>
<tr>
<td>Not Currently Employed N(%)</td>
<td>7 (53.8)</td>
<td>9 (60.0)</td>
<td>8 (66.7)</td>
</tr>
<tr>
<td><strong>Hospital Anxiety and Depression Scale Mean(SD)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxiety</td>
<td>6.2 (4.0)</td>
<td>7.7 (5.2)</td>
<td>4.1 (2.6)</td>
</tr>
<tr>
<td>Depression</td>
<td>3.9 (2.4)</td>
<td>3.9 (2.4)</td>
<td>3.7 (2.3)</td>
</tr>
<tr>
<td><strong>Driving Habits Questionnaire Mean(SD)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Years of driving experience</td>
<td>41.2 (15.4)</td>
<td>33.6 (16.1)</td>
<td>42.4 (15.9)</td>
</tr>
<tr>
<td>Number of hours driven per week</td>
<td>8.2 (8.5)</td>
<td>6.4 (13.2)</td>
<td>8.5 (6.9)</td>
</tr>
<tr>
<td>Self-rated quality of driving (out of 5)</td>
<td>4.2 (0.6)</td>
<td>3.8 (0.6)</td>
<td>4.2 (0.6)</td>
</tr>
<tr>
<td>Number of previous MVCs</td>
<td>0.92 (0.9)</td>
<td>1.1 (1.27)</td>
<td>1.6 (2.9)</td>
</tr>
</tbody>
</table>
3.2.2 Data Acquisition

The experimental protocol took between two and three hours for each participant to complete. The entire session took place in a designated testing room with minimal noise distraction and consistent lighting conditions. To begin, each participant was given a detailed consent form outlining the study components and participant responsibilities. Upon completion of the consent process, participants completed a demographic questionnaire and driving habits questionnaire. Participants then underwent training on the driving simulator to become familiar with the apparatus. Following training, participants completed four different driving scenarios. After the driving scenarios were completed, participants underwent a battery of both paper-based and computerized neuropsychological tests. The details of each study component are described in the following sections.

3.2.2.1 Cognitive Testing and Questionnaires

Participants completed a series of questionnaires including a demographic questionnaire, the Driving Habits Questionnaire (DHQ) and the Hospital Anxiety and Depression Scale (HADS). A short cognitive testing battery that consisted of tests that have been investigated in the literature for their relation to driving ability was then administered. This consisted of the Trail Making Test (Part A and Part B), the Montreal Cognitive Assessment (MoCA), the Attention Network Test (ANT) and the Useful Field of View Test (UFOV). The cognitive data were collected for descriptive purposes and do not directly address the stated aims.

Driving Habits Questionnaire

The DHQ was administered to collect information regarding the driving history and self-reported awareness of current driving ability. Data about the years of driving experience, current driving exposure, history of traffic accidents, avoidance of difficult driving situations and preferred methods of transportation are included as items on the questionnaire. The DHQ was originally validated in older individuals by Owsley, Stalvey, Wells, & Sloane, (1999) and has since been applied to stroke populations as a tool to measure driving habits after stroke (Fisk et al., 2002;
McNamara, Walker, Ratcliffe, & George, 2015). An assessment of driving history and exposure was made between patient and control groups to ensure that baseline levels of driving were comparable.

Hospital Anxiety and Depression Scale

The HADS is a 14-item self-report questionnaire developed as a screening measure for mood disorders in non-psychiatric hospital outpatients (Zigmond & Snaith, 1983). Participants are asked to rate each item on a Likert scale ranging from 0-3, producing a total score ranging from 0 to 42, or two separate sub-scales for depression and anxiety with scores from 0 to 21. Scores on each subscale from 0 to 7 represent a normal range, 8 to 10 a borderline abnormal score and 11-21 an abnormal score in the respective category. The HADS is a well-validated and reliable screening measure of depression and anxiety in stroke patients (Aben, Verhey, Lousberg, Lodder, & Honig, 2002; Johnson et al., 1995; O’Rourke, MacHale, Signorini, & Dennis, 1998).

The Trail Making Test A & B

The TMT is a two-part pencil-and-paper test of processing speed, visuospatial attention, visuomotor tracking, and executive function that specifically probes the components of working memory and set-shifting (Arbuthnott & Frank, 2000); Part A consists of a sheet of paper with numbers 1-25 encircled and distributed on the page. The participant is instructed to draw a line connecting all of the numbers in ascending order as quickly as possible. In Part B, encircled numbers 1-12 and letters A-L are distributed across the page, and the participant is asked to connect the numbers and letters in ascending order, alternating between a number and a letter (i.e. 1 to A, A to 2, 2 to B, B to 3 and so on). The primary measure of performance is the time taken to complete each part of the test. The TMT-A time is often subtracted from the TMT-B time to determine the TMT difference, which is a pure measure of executive function and eliminates the processing speed and visuoperceptual components measured in TMT-A (Sanchez-Cubilla et al., 2009). The TMT ratio, calculated as (B-A)/A or B/A is another measure occasionally used as a measure of executive function (Stuss et al., 2001).
The ability of the TMT to identify executive dysfunction has previously been established by accurate discrimination between individuals with frontal brain damage and individuals with injuries to other brain regions (Stuss et al., 2001). Participants with damage to frontal brain regions take more time to complete the test and also commit more errors (Davidson, Gao, Mason, Winocur, & Anderson, 2008; Gouveia, Brucki, Malheiros, & Bueno, 2007; Yochim, Baldo, Nelson, & Delis, 2007). The relationship between lesion laterality and performance on the two components of the TMT has been studied, with mixed results. Reitan & Tarshes, (1959) found that patients with left-sided lesions tended to perform poorly on Part B, which was hypothesized to result from an inability to process the symbolic information; patients with right-sided lesions performed more poorly on Part A, resulting from an impaired ability to process the spatial arrangement of the numbers on the page. In contrast, Heilbronner, Henry, Buck, Adams, & Fogle, (1991), found that the TMT could not discriminate between patients with left and right sided lesions, but did report that patients with diffuse lesions performed worse than the patients with lesions confined to only one cerebral hemisphere. Functional MRI studies of healthy individuals completing the TMT-B have identified activation in parietal and frontal regions, specifically the dorsolateral, and medial prefrontal cortices (including the supplementary motor area and dorsal anterior cingulate gyrus) (Allen, Owens, Fong, & Richards, 2011; Moll, De Oliveira-Souza, Moll, Bramati, & Andreiuolo, 2002; Zakzanis, Mraz, & Graham, 2005). All three groups observed activation in frontal regions favouring the left hemisphere.

As previously discussed in Section 1.4.3, the TMT is one of the most promising cognitive tests posited to predict driving ability, largely as a result of previous correlations with measures of driving performance. Despite the fact that these correlations are relatively weak and inconsistent, and no distinct agreement on defined cutoff scores has been made, the TMT is commonly used by primary care physicians who are often given the responsibility to make judgments about potentially unfit drivers (Redelmeier, Yarnell, Thiruchelvam, & Tibshirani, 2012). In a recent study evaluating the TMT as a screening instrument for elderly drivers, both Part A and Part B were shown to have relatively low sensitivity and specificity, and a negative predictive value of 96.9%. Thus, the authors concluded that the TMT is not a suitable stand-alone screening measure for driving fitness (Vaucher et al., 2014). With regards to stroke, Devos et al., (2011) identified the TMT as a clinically relevant screening tool for fitness-to-drive after stroke, but this was only
based on the combined results of two studies with moderately high statistical heterogeneity conducted by the same group of authors (Mazer et al., 1998; Mazer et al., 2003). Few comparisons between the TMT and specific aspects of driving have been made. Most commonly, the correlations are drawn between the TMT time to completion and the overall score or pass/fail result of the on-road assessment, and seldom correlate to aspects of driving that may probe the specific components tested by the TMT such as situations requiring rapid decision-making, or instances where the driver’s attention may be divided, such as during a distraction. The TMT was used to assess the reproducibility of the previous data showing a significant correlation between both sub-tests of the TMT and simulated driving performance previously observed by Motta et al., (2014), as well as to investigate if the TMT score correlates to performance on specific aspects of driving (i.e. errors committed during intersection turns, hazardous driving errors).

*The Montreal Cognitive Assessment*

The Montreal Cognitive Assessment (MoCA) is a one-page, brief cognitive assessment that measures global cognitive functioning. The MoCA was originally developed as a screening tool for Mild Cognitive Impairment (MCI), with a validation study citing high specificity and sensitivity for the detection of MCI (Nasreddine et al., 2005). The MoCA is now widely used as a measure of cognitive functioning in many neurological populations. The assessment includes six subtests: visuospatial/executive functions, naming, attention, abstraction, recall and orientation. The participant receives a composite score out of 30, with a one-point addition for fewer than or equal to 12 years of education, and scores below 26 suggestive of mild cognitive impairment.

Despite including measures of executive function and attention postulated to relate to driving ability, scores on the MoCA have generally not been shown to correlate to either simulated or on-road driving performance measures in neurological and elderly populations (Bowers et al., 2013; Motta et al., 2014; Rapoport et al., 2013). A recent study evaluating the screening potential of the MoCA for populations with cognitive impairment (traumatic brain injury, dementia, stroke, Parkinson’s Disease and multiple sclerosis) found that scores less than 12 were 100%
accurate in identifying patients with a “fail” decision for safe driving ability based on an off-road assessment and scores greater than 27 were 100% accurate in identifying a “pass” result of the off-road assessment (Esser et al., 2015). Scores between 12 and 27 resulted in a 50% chance of passing the off-road assessment, indicating that additional assessment is required for individuals who do not score at the two extremes of the scoring scale, as is the case in the majority of stroke patients, who on average score 21.1 with a standard deviation of 7.5 (Cumming, Bernhardt, & Linden, 2011). The MoCA was administered to measure the level of global cognitive function in the aSAH and IS patient groups and to screen healthy control participants for presence of cognitive impairment.

The Useful Field of View

The Useful Field of View test (UFOV), developed by Ball, Beard, Roenker, Miller, & Griggs, (1998) is a computer-based program that presents rapidly disappearing stimuli on a computer screen and requires participants to identify the objects presented on the screen. The UFOV is designed to measure the useful field of view, which is defined as the boundary in which an individual can reliably detect visual information without moving the head or eyes. The UFOV is different from traditional perimetry tests as it relies on cognitive abilities in addition to intact visual functioning. The test is completed with the participant sitting at a fixed distance from the computer screen in a dimly lit room. The UFOV can be administered in two forms: the standard version administered with a touch screen and Visual Attention Analyzer, or the brief version administered with a personal desktop computer using a mouse option. The present study used the brief version of the UFOV, which can be completed within 15 minutes.

The UFOV is comprised of three subtests: Processing Speed (UFOV-PS), Divided Attention (UFOV-DA) and Selective Attention (UFOV-SA). In the UFOV-PS, the participant is required to recognize one central target that may either be a car or a truck. The participant selects a response by choosing between the car and truck image on the computer screen after each presentation of a target. The length of time that the target is shown on the screen decreases with subsequent trials and the software measures the point at which the participant can no longer
accurately identify the target presented on the screen. During the second subtest, the UFOV-DA task, the participant is required to identify a central target that may be either a car or a truck, in addition to identifying the location of a peripheral target that may be placed at any one of eight locations surrounding the central target. Similar to the UFOV-PS subtest, the duration of the target presentation decreases with subsequent trials. Subtest 3, the UFOV-SA task, is similar to subtest 2 in that it requires the identification of a central target, as well as the location of a peripheral target, but there are also white triangles scattered on the screen meant to provide a distraction to the task. A score is automatically generated for each subtest, with lower scores representing shorter reaction times and superior performance relative to higher scores.

![Screenshot of UFOV subtests](image)

**Figure 3.1** Screenshots depicting the stimulus presentation for each of the UFOV subtests.

The UFOV is a widely used cognitive measure in driving research, especially in elderly populations. The UFOV has been shown to predict the outcome of on-road assessments (Myers, Ball, Kalina, Roth, & Goode, 2000), as well as 5-year crash risk in a population of 294 elderly drivers with 89% sensitivity and 87% specificity (Ball, Owsley, Sloane, Roenker, & Bruni, 1993). The UFOV has also demonstrated high test-retest reliability (Edwards et al., 2005). Deficits in performance on the UFOV have been observed in stroke patients (Fisk & Mennemeier, 2006; Fisk et al., 2002; Mazer et al., 2001). In relation to driving in stroke patients, the UFOV has shown inconsistent findings. In a retrospective study, Akinwuntan et al., (2002) found a relationship between an overall score on the UFOV and on-road driving ability. However, a later prospective study by the same group did not find any significant relationship between the results of the on-road assessment and the UFOV overall score (Akinwuntan et al.,
Regarding the UFOV subtests, George & Crotty, (2010) found that the Divided Attention task (Subtest 2) had the highest sensitivity (85.7) and the Selective Attention task (Subtest 3) had the highest specificity (88.9) in relation to the outcome of an on-road assessment. The Divided Attention task (Subtest 2) had the highest prediction accuracy and was able to correctly categorize 77.5% of stroke patients into the pass-fail classification of the on-road assessment. No study has investigated the relationship between the UFOV and driving simulator performance.

The Attention Network Test

The Attention Network Test (ANT) is a test that generates measures of the three distinct aspects of the human attention network model developed by Posner & Petersen, (1990), alerting, orienting and executive attention (also referred to as conflict efficiency). Alerting attention is the ability to maintain alertness to respond to incoming signals. Orienting attention is defined as the ability to change attention from one stimulus to another to incorporate only certain information from sensory processing. Lastly, executive attention encompasses the ability to resolve conflicts and exhibit inhibitory control. Evidence that each of these attentional systems is subserved by a distinct neural network has been established through neuroimaging studies using fMRI (Corbetta, Kincade, Ollinger, McAvoy, & Shulman, 2000; Fan, McCandliss, Fossella, Flombaum, & Posner, 2005). The task itself is a combination of Posner’s cuing task and Erikson’s Flanker task (Eriksen & Eriksen, 1974). During each stimulus presentation, the participant must indicate the direction of a central target arrow (left or right) using one of two directional keyboard keys. For the alerting task, one stimulus presentation provides a visual cue for when a target will appear, with the other condition providing no warning. In the orienting task, one stimulus presentation provides a visual cue of where the target will be presented, the other stimulus providing no location cue. In the executive or “conflict” task, one stimulus presentation has flanker objects in the same direction as the target arrow, the other condition showing flanker objects in the opposite direction of the target arrow. The scores are reported as the average difference in reaction time between the two conditions. The present study used a shorter, 10-minute version of the ANT developed by the Centre for Research on Safe Driving that has shown strong correlations in the reaction times obtained during the original, 20-minute version of the test (Weaver, Bédard, & McAuliffe, 2013).
A study of performance on the ANT in 110 stroke patients was conducted by Rinne et al., (2013) to determine if different stroke locations were related to impairments in specific attentional components. The alerting, orienting and the conflict components were significantly associated with lesions to the thalamus and upper brainstem, right pulvinar and right temporoparietal cortex, and bilateral prefrontal and premotor regions. This work demonstrates impairment across different aspects of attention in stroke patients and supports the assertion that each component has its own unique anatomical correlate.

Despite being a well validated and easy to administer test of the human attentional networks, the ANT has not often been conducted in driving research studies. Weaver, Bédard, McAuliffe, & Parkkari, (2009) found a strong correlation between a summative score of UFOV performance and the overall reaction time and percentage of errors committed on the ANT in a population of healthy individuals (age 18-83), concluding that the measures had high concurrent validity. In their study, they also found that the ANT and UFOV were similarly able to predict the score of a simulated driving assessment, but neither was strongly associated with the result of an on-road assessment. The ANT has also been explored in driving research studies of individuals with sleep deprivation by Jongen, Perrier, Vuurman, Ramaekers, & Vermeeren, (2015) and cardiovascular disease by Gaudet et al., (2013), but has not been investigated in any driving study involving stroke patients.
3.2.2.2 Driving Simulation

Driving Simulator Apparatus

Driving scenarios were completed using a high-fidelity driving simulator. Scenarios were displayed on a 30-inch (diagonal) viewing monitor (NEC MultiSync LCD3090WQXi) at a constant distance of 26-inches between the monitor and steering wheel. The scenarios were run in STISIM Drive™ (Systems Technology Inc., Hawthorne, CA, USA). STISIM Drive™ is commonly used in research as it allows the researcher to construct a customized set of scenarios that are standardized across each participant. STISIM Drive™ software has previously been used in several driving simulator studies of various populations including stroke (Motta et al., 2014), cardiovascular disease (Gaudet et al., 2013) and elderly drivers (Freund, Colgrove, Burke, & McLeod, 2005; Stinchcombe, Gagnon, Zhang, Montembeault, & Bedard, 2011). The simulator components include a steering wheel with turn indicator levers affixed to a table and a brake and gas pedal unit on the floor at the participant’s feet. Please see Figure 3.2 for a diagram of the experimental setup.

A realistic roadway was presented on the monitor with a view of the car hood, speedometer and rearview mirror. Data points were auto-acquired at 30Hz using a Dell XPS1730 gaming laptop computer (17-inch display, 2.4 GHz Intel Core Duo T7700 Processor, 4.0 GB RAM, 512MB NVIDIA GeForce 8700M GT graphics card).

Driving Scenarios

For each scenario, participants were given a standard set of instructions by the researcher to ensure consistency in testing administration. Participants were reminded that they should follow the rules of the road and drive safely, just as they would while operating a real vehicle. Participants were also asked not to talk or engage in conversation with the researcher during any of the scenarios. Computer screenshots of the scenarios are displayed in Figure 3.3 and Figure 3.4.
i) **Training Scenario**

The training scenario is 6130m in virtual length and takes approximately 12 minutes to complete. The scenario begins with straight driving for 1700m with variable speed limits, allowing participants to practice maintaining proper speed. Subsequently, the scenario requires participants to make both right and left turns at stop signs and traffic light-controlled intersections to become familiar with maneuvering through more complex driving situations.

ii) **Full Scenarios**

Full Scenario 1 and Full Scenario 2 were designed to represent a portion of the official Ontario licensing exam for the G2-test, an assessment required for obtaining a driver’s license in Ontario, Canada. Due to limitations of the driving simulator equipment, reversing and parking are aspects of the typical assessment that are excluded from the evaluation. The scenario involves straight driving, simple right and left turns at intersections without oncoming traffic, as well as complex left turns at intersections with oncoming traffic. Speed limits change throughout the scenario but are specified on road signs as either 50 or 60 kilometers per hour. The scenarios are 5700m in virtual length and each take approximately 10 minutes to complete. The scenario presents varying degrees of driving complexity. In more perceptually and cognitively demanding situations, such as making left turns at intersections with oncoming traffic, participants are required to make decisions about when it is safe while avoiding collisions with other vehicles and pedestrians. This decision-making procedure is associated with the processes of selective attention, error-monitoring and visuospatial and visuomotor control.

iii) **Bus Following Task**

This scenario requires participants to follow a bus on a rural highway. The goal of the task is to maintain a safe and constant distance from the bus. Participants are instructed not to pass the bus. Throughout the scenario, the bus constantly changes speed, requiring the participant to respond accordingly. The posted speed limit during the
scenario is 90 kilometers per hour. The scenario is 5000m long and takes approximately five minutes to complete. The bus following scenario is primarily a task of sustained attention, with elements of visuomotor control (Uchiyama et al., 2003).

iv) **Construction Zone Task**
This scenario requires participants to drive through two construction sites where participants are required to maneuver around pylons, pedestrians, construction debris and other obstacles. The posted speed limit in construction sites is 30 kilometers per hour. The scenario is 3300m long and takes approximately eight minutes to complete. The construction sites contain novel and ambiguous situations that require attention monitoring, response selection and response inhibition.
**Figure 3.2** Experimental set-up for the driving simulator displaying the viewing monitor, stimulus computer and the steering wheel and pedal system.
Figure 3.3 Screenshots of the STISIM Drive simulation full scenarios depicting: a) rural driving scenery; b) urban driving scenery; c) a stop-sign controlled intersection and d) a traffic-light controlled intersection with the turn signal (green triangle) indicating a left-hand turn.

Figure 3.4 Screenshots of the STISIM Drive simulation scenarios depicting the bus following task (left) and the construction zone task (right).
3.2.3 Data Analysis

Statistical analyses were conducted using SPSS software (version 22.0; SPSS, Chicago, USA). The Kolmogorov-Smirnov test for normality was used to evaluate the distribution of the data. Data were then analyzed using parametric and non-parametric tests where applicable, depending on whether the data met the normality assumption. Comparisons of two groups (i.e. stroke patients versus healthy controls) were conducted parametrically using an independent samples t-test and non-parametrically using the Mann-Whitney U test. Analyses of greater than two groups (i.e. SAH versus IS versus healthy controls) were conducted parametrically using a one-way ANOVA with post hoc comparisons using the Games-Howell test due to its ability to account for unequal group variances, as is expected when comparing healthy controls to patient groups where intra-group variability may be high (Kromrey & La Rocca 1995). Non-parametric omnibus tests of more than two groups were conducted using the Kruskall-Wallis test with post hoc analyses performed using the Mann-Whitney U test. Significant differences were concluded at the p < 0.05 level using a two-tailed interpretation. Statistical analyses were not corrected for multiple comparisons due to low sample size and thus, a higher probability of encountering a Type II error (Feise, 2002).

The paper-based tests and questionnaires (i.e. TMT, MoCA and HADS) were scored manually and scores of the computer-based tests (ie. ANT and UFOV) were automatically generated by the respective software programs. Variables of interest for each of the cognitive measures are described in Table 3.4.
<table>
<thead>
<tr>
<th>Test</th>
<th>Variable of Interest</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>TMT</td>
<td>TMT A time</td>
<td>Time to complete (Seconds)</td>
</tr>
<tr>
<td></td>
<td>TMT A errors</td>
<td>Number of errors committed (Count)</td>
</tr>
<tr>
<td></td>
<td>TMT B time</td>
<td>Time to complete (Seconds)</td>
</tr>
<tr>
<td></td>
<td>TMT B errors</td>
<td>Number of errors committed (Count)</td>
</tr>
<tr>
<td></td>
<td>TMT Difference (B-A)</td>
<td>Difference between TMT A and TMT B time (Seconds)</td>
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<td></td>
<td>TMT Ratio ((B-A)/A)</td>
<td>Ratio of TMT Difference to TMT A time</td>
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<td>MoCA</td>
<td>Total Score</td>
<td>Score out of 30</td>
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<td></td>
<td>Visuospatial/Executive Score</td>
<td>Score out of 5</td>
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<td>Naming Score</td>
<td>Score out of 3</td>
</tr>
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<td></td>
<td>Attention Score</td>
<td>Score out of 6</td>
</tr>
<tr>
<td></td>
<td>Language Score</td>
<td>Score out of 3</td>
</tr>
<tr>
<td></td>
<td>Abstraction Score</td>
<td>Score out of 2</td>
</tr>
<tr>
<td></td>
<td>Delayed Recall Score</td>
<td>Score out of 5</td>
</tr>
<tr>
<td></td>
<td>Orientation Score</td>
<td>Score out of 6</td>
</tr>
<tr>
<td>ANT</td>
<td>Alert Score</td>
<td>Difference between reaction time with a cue and without a cue.</td>
</tr>
<tr>
<td></td>
<td>Orient Score</td>
<td>Difference between reaction time with a centre cue and with a spatial cue.</td>
</tr>
<tr>
<td></td>
<td>Conflict Score</td>
<td>Difference between reaction time with incongruent flankers and with congruent flankers.</td>
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<td></td>
<td>Mean Reaction Time</td>
<td>Average reaction time for all trials.</td>
</tr>
<tr>
<td></td>
<td>Percentage correct</td>
<td>Percentage of all trials with correct responses.</td>
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<tr>
<td>UFOV</td>
<td>Processing Speed</td>
<td>Stimulus presentation time at which participant reliably answers 75% of trials correctly for each respective subtest.</td>
</tr>
<tr>
<td></td>
<td>Divided Attention</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Selective Attention</td>
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</tbody>
</table>

**Table 3.4** Variables of interest and scoring descriptions for each of the cognitive tests administered.
Driving Data Preparation and Analysis

Measures describing the simulated driving performance were automatically recorded during the simulation run by the STISIM Drive™ software. The data output contained a summary of the driving errors committed during the run and a section of raw data detailing parameters of the vehicle’s speed and positioning from which additional variables could be calculated. Purely quantitative measures of performance either directly obtained from the software or calculated from the raw data were used in the data analysis. Various methods of assessing simulated driving have been used in the previous literature, including using simulator-recorded errors, or by using an assessment checklist similar to those used for the on-road assessment. Bedard et al., (2010) found that STISIM simulator-recorded errors were correlated with scores on an assessment checklist used on the same driving simulation run. In absence of a professional driving rehabilitation specialist to complete an assessment checklist, the simulator-recorded errors were used as a measure of performance to maintain objectivity and consistency in the analysis.

For the two full scenarios, additional variables were calculated according to the type of error committed and the timing of the errors. Errors were divided into “hazardous errors” and “traffic/rule violations”. Hazardous errors included errors in lane positioning (i.e. centerline crossings, road edge excursions) and collisions with cars, pedestrians or road elements whereas traffic/rule violations included speed exceedances, missed stop signs and incorrect turns. For clarification, missed stop signs indicate an instance where the driver did not come to a complete stop of zero kilometres per hour at the stop sign. A complete failure to slow down at a stop sign and continue through the intersection by the participants would be rare. A similar distinction was previously used in a driving simulator study by Freund et al., (2005) based on the idea that fitness-to-drive decisions are traditionally determined by the severity of the errors committed. It is common in real-world driving for drivers to have imperfect driving habits, and not all driving errors are a definitive indication of driver incompetence (Dobbs, Heller, & Schopflocher, 1998). It is therefore expected that both healthy controls and stroke patients will experience errors in some behaviours such as proper adherence to speed limits or not coming to a complete stop at a stop sign. Although it could be argued that any error places the driver and other road users in danger, dividing errors into hazardous and traffic/rule violations provides further insight into the
frequency of particularly dangerous driving behaviours that are collisions themselves or may lead to a collision.

Driving errors were next divided into “turning errors” and “non-turning errors”. Errors related to intersection turns were of interest because these are locations where drivers must make rapid decisions, and integrate multiple dynamic stimuli in the environment, creating a more visually and cognitively demanding situation. Accident data demonstrates that a majority of real-world collisions are intersection-related (Choi, 2010). Furthermore, the data by Schweizer et al. (2013) suggest that different turning maneuvers recruit a different magnitude of brain resources. As discussed previously in Section 1.6.2 they noted that activation in a core network of posterior brain regions increases as the complexity of the driving situation increases from right turns, to left turns and then to left turns with traffic. This relationship is of particular interest to the stroke population who, as a result of the brain injury, may have disruptions to these networks that can lead to impaired performance on those tasks. For the purposes of this analysis, “turning errors” were defined as errors that could occur both during an intersection and during regular driving. These errors included collisions, lane positioning errors (i.e. centerline crossings and road excursions) and speed exceedances. The turn was defined from the moment the vehicle turned into the intersection (quantified as a car hood angle of greater than 15 degrees relative to the vehicle’s starting position, which is parallel to the centerline) until three seconds after the vehicle returned to a straight position on the roadway after the turn (quantified as a car hood angle of less than 15 degrees). A three second period was added to the end of the turn to account for errors in the recovery of the turn, which most commonly manifest as incorrect lane positioning during the turn (i.e. turning into the on-coming traffic lane) due to over steering. Once the timing of each turn was isolated, the errors were matched to either turning or non-turning events based on the time that the error occurred. The turning errors were then further stratified into right turning errors, left turning errors, and left turning errors with oncoming traffic present in the opposing lane.

For the bus following scenario, data analysis consisted of extracting the simulator recorded errors, as well as measures of adherence to the task. As participants were asked to match the
speed of the bus while maintaining a safe distance from the vehicle, the average distance from the bus as well as the variation in that distance were of interest. The variables used to describe task adherence included the mean range, standard deviation of the range (SD Range) and the standard deviation of the lateral lane position (SDLP). These three variables were all calculated manually from the raw data produced by the simulation software. The mean range was calculated as an average of the instantaneous range values (the distance in metres from the bus) during the task. The SD range was calculated as the standard deviation of those values, to indicate the variability in the distance between the driver and the bus. The SDLP was calculated as the standard deviation of the instantaneous lane position values (the distance between the vehicle and the centerline, in meters). These instantaneous measures were automatically recorded by the simulation software at 30Hz.

The analysis for the construction zone consisted of the simulator-generated error summary as well as the time taken to complete the scenario. The construction zone scenario required the participant to drive off road in multiple occurrences to maneuver around obstacles. The resulting lane positioning errors (i.e. centerline crossings and road-edge excursions) were removed manually from the error summary.
3.3 Results

3.3.1 Summary of Cognitive Data

The results of the analysis of the cognitive scores for the SAH, IS and control groups revealed a significant between-group difference in the following measures: TMT-A time (chi square = 7.625, p = 0.022), TMT-B time (F(2,37) = 3.419, p = 0.043), TMT A errors (chi square = 8.809, p = 0.012), the MoCA overall score (F(2,37) = 4.123, p = 0.023) and the UFOV-DA score (F(2,37) = 3.911, p = 0.03). The results of the entire cognitive assessment, including the statistical results of the post hoc analyses are displayed in Figures 3.5-3.8.

On the overall MoCA score, SAH patients (mean = 24.5) scored significantly lower than the control group (mean = 27.5), with mean difference = 3.039, p = 0.038. Although the overall MoCA scores were not significantly different between the control and IS groups, five (39%) of the patients scored in the “impaired” range, with overall scores below the recommended cutoff of 26, where scores of 26 and above indicate normal cognition. Seven (47%) of the SAH patients scored below 26 on the MoCA. On the TMT time measures, the SAH group performed worse (i.e. took longer to complete the tasks) than the control group for the TMT-A (U = 58.0, p = 0.014) and the TMT-B (mean difference = 42.258, p = 0.028). The SAH group did not have significantly more errors on either subtest. The IS group took longer than controls only on the TMT-A (U = 53.500, p = 0.025) and also had significantly more errors on the TMT-A (U = 47.0, p = 0.012).

Notably, the only significant difference between the groups on any of the scores of the computer-based assessments was the UFOV-DA task, where IS patients scored worse than control participants (mean difference = 130.135, p = 0.033) Summary measures of the ANT and UFOV are shown in Figures 3.7-3.8. Overall, the results of the cognitive assessment suggest that the SAH group was more impaired cognitively across more cognitive measures than IS patients. On average, the IS patients did not perform worse on the cognitive assessment than control participants, although several patients scored in the impaired range on the MoCA.
A) TMT Time

B) TMT Errors

C) TMT Ratio

**Figure 3.5** Displays mean results for each study group for A) TMT-A time, TMT-B time and TMT Difference, B) TMT-A errors and TMT-B errors, C) TMT Ratio score. * indicates significance at the level of p < 0.05. Error bars represent +/- one SEM.
**Figure 3.6** Mean overall MoCA scores for each study group. * indicates statistical significance at the level of \( p < 0.05 \). Error bars represent +/- one SEM.

**Table 3.5** Scores on each MoCA sub-score for each study group. Error bars represent +/- one SEM. All individual comparisons are non-significant.

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>IS</th>
<th>SAH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visuospatial/Executive</td>
<td>4.55 (0.93)</td>
<td>4.6 (0.77)</td>
<td>4.1 (0.96)</td>
</tr>
<tr>
<td>Naming</td>
<td>2.91 (0.30)</td>
<td>2.6 (0.51)</td>
<td>2.5 (0.74)</td>
</tr>
<tr>
<td>Attention</td>
<td>5.82 (0.40)</td>
<td>5.6 (0.51)</td>
<td>5.3 (0.80)</td>
</tr>
<tr>
<td>Language</td>
<td>2.55 (0.52)</td>
<td>1.8 (1.09)</td>
<td>1.8 (1.26)</td>
</tr>
<tr>
<td>Abstraction</td>
<td>1.73 (0.47)</td>
<td>1.7 (0.63)</td>
<td>1.7 (0.49)</td>
</tr>
<tr>
<td>Delayed Recall</td>
<td>4.09 (1.04)</td>
<td>3.8 (1.28)</td>
<td>3.0 (1.77)</td>
</tr>
<tr>
<td>Orientation</td>
<td>5.82 (0.60)</td>
<td>6.0 (0.00)</td>
<td>5.9 (0.26)</td>
</tr>
</tbody>
</table>

**Figure 3.7** Mean overall scores on the UFOV subtests for each study group. * indicates statistical significance at the level of \( p < 0.05 \). Error bars represent +/- one SEM.
A) Component Sub-Scores

B) Percentage of Correct Responses

C) Average Reaction Time

Figure 3.8 Mean results on the ANT for each study group for A) the component subscores, B) the percentage of responses entered correctly, C) the average reaction time for all responses. Error bars represent +/- one SEM.
3.3.2 Overall Measures of Driving performance

All participants included in the analysis were able to complete both full scenarios and the bus following task; however, two participants (one IS patient and one SAH patient) did not complete the construction zone task due to experiencing fatigue as this scenario was always performed last. Two IS patients and three control participants could not complete the scenarios due to experiencing simulator sickness and were excluded from the analysis. In total, 11% of participants ended the study prematurely due to simulator sickness, which is similar to previous studies of virtual reality driving simulator environments that reported ranges from 12-27% of individuals from a similar age cohort (Park et al., 2006; Rinalducchi et al., 2003).

First, the average total number of errors committed on each driving scenario was compared between the stroke and control group. This summative measure of performance is analogous to computing an overall “score” as is typically used to make pass/fail decisions on driving evaluations. The average number of errors committed during the scenarios was only significantly different between stroke patients and controls for the bus following task (see Figure 3.9). Although it appears from Figure 3.9A that, on average, stroke patients committed a higher number of errors overall during the full scenarios, the mean is skewed by two especially poor performers (one IS patient and one SAH patient) who committed greater than 60 errors over the duration of both scenarios. The median values are more similar at 13 and 16 errors for controls and stroke patients respectively, which may help explain the lack of significance in the finding of the pairwise comparison, which was analyzed non-parametrically. The types of errors committed by the stroke patient and control groups are displayed in Table 3.6. Only errors for the full scenarios are subdivided because these scenarios are the most challenging, requiring the participants to navigate through simple and complex driving situations. Error rates for the bus following and construction zone task are comparably much lower overall due to the shorter length and relative simplicity of those tasks. Differences in the types of errors committed during the full scenarios were not statistically different for each individual type of error (see Table 3.6); however, when errors were grouped into hazardous errors and rule/traffic violations, stroke patients committed significantly more hazardous errors than healthy control participants, but not more rule/traffic violations (see Figure 3.10).
Although patients made more errors on the bus following task than controls, the overall error rate average was still relatively low at 2.8 errors for controls and 4.25 errors for patients. On measures of task adherence, there was no difference in performance in stroke patients versus controls, indicating that patients were able to perform the task with a similar quality as controls, but still committed more errors (see Figure 3.11).

On the construction zone, no difference emerged between the number of errors committed, or the time taken to complete the scenario.
Figure 3.9 Mean number of errors committed during the A) full scenarios, B) bus following scenario, C) construction zone scenario for the stroke patient and control groups. * indicates statistical significance at the level of p < 0.05. Error bars represent +/- one SEM.
<table>
<thead>
<tr>
<th></th>
<th>Controls</th>
<th>Stroke</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collisions</td>
<td>0.25 (0.5)</td>
<td>1.36 (2.5)</td>
<td>0.146</td>
</tr>
<tr>
<td>Speed Exceedances</td>
<td>8.7 (6.6)</td>
<td>10.8 (6.7)</td>
<td>0.342</td>
</tr>
<tr>
<td>Stop Signs Missed</td>
<td>3.0 (2.5)</td>
<td>2.0 (2.3)</td>
<td>0.476</td>
</tr>
<tr>
<td>Center Line Crossings</td>
<td>3.08 (4.0)</td>
<td>5.6 (7.0)</td>
<td>0.154</td>
</tr>
<tr>
<td>Road Edge Excursions</td>
<td>0.67 (1.0)</td>
<td>2.1 (2.8)</td>
<td>0.146</td>
</tr>
</tbody>
</table>

**Table 3.6.** Summary of the types of errors committed by patient and control groups in the Full Scenarios. Values are displayed as the mean(SD) of the number of errors committed by the participants in each group.

**Figure 3.10** Mean number of hazardous errors (i.e. centerline crossings, road edge excursions and collisions) and routine traffic or rule violations (i.e. speed exceedances or missed stop signs) committed on average by the stroke patient and control groups. * indicates difference is significant at the level of p < 0.05.
Summary of performance measures for the bus following task for the stroke patient and control group including A) the mean range (distance) from the bus, B) the standard deviation of the range, C) the SDLP. Error bars represent +/- one SEM.
As is displayed in Figure 3.12, stroke patients incurred significantly more errors during intersection turns than control participants ($U = 100.00$, $p = 0.045$), but no significant difference was found between the groups for non-turning errors ($U = 130.5$, $p = 0.273$). When stratified by the type of turn, stroke patients committed significantly more errors only during the left turn with traffic condition ($U = 158.5$, $p = 0.008$), but not during the simple right turn ($U = 143.0$, $p = 0.475$) or simple left turn ($U = 136.0$, $p = 0.358$) conditions. (See Figure 3.13)

![Bar Chart A) Turning Errors](image)

A) Turning Errors

![Bar Chart B) Non-Turning Errors](image)

B) Non-Turning Errors

**Figure 3.12** Mean number of errors associated with intersection turns (i.e. centerline crossings, road edge excursions, collisions and speed exceedances) displaying A) turning errors and B) non-turning errors. * indicates significance at the level of $p < 0.05$. Error bars represent +/- one SEM.

![Bar Chart](image)

**Figure 3.13** Mean number of errors committed during each turn type. * indicates that difference is statistically significant at the level of $p < 0.05$. Error bars represent +/- one SEM. Note difference in absolute values is due to relative increase in the number of right turning events.
3.3.3 Stroke Subtype Analysis

Next, a subgroup analysis was undertaken to evaluate differences in the driving outcome variables for IS and SAH stroke subtypes. When comparing the overall driving performance of IS patients, SAH patients and control participants, there were still no significant differences between groups for the overall performance during the full scenarios or the construction zone task. (See Figures 3.14 and 3.15) On the bus following task, the SAH patients had significantly more errors than the control group, but the IS group did not, indicating that the difference between the stroke and control group reported earlier is primarily driven by greater impairment in the SAH patient group. For error types, no significant results were obtained for the Kruskall-Wallis test between the three groups except for road-edge excursions, where SAH patients committed significantly more road edge excursions than control participants. Average error counts for each error type are displayed in Table 3.7. When stratified into hazardous and traffic/rule violations, only the SAH group had significantly more hazardous errors than the control group (See Figure 3.15). None of the groups were different on the average number of traffic/rule violations. For turning errors, it was again only the SAH group that exhibited significantly more errors than the controls, and none of the groups were significantly different in the average number of non-turning errors (see Figure 3.16). When analyzed by the type of turn, the only significant finding was a greater number of errors at the left turn with traffic turning condition in SAH patients relative to control participants (see Figure 3.17). Overall, the subgroup analysis suggested that the significant differences in driving performance observed between the stroke patients and control participants were driven more by the SAH patient group than the IS patient group.
A) Total Driving Errors

B) Bus Following Errors

C) Construction Zone Errors

Figure 3.14 Mean number of errors committed during the A) full scenarios, B) bus following scenario, C) construction zone scenario for each study group. Error bars represent +/- one SEM. * indicates difference is significant at the level of p < 0.05.
Table 3.7 Types of errors committed by each subgroup during the full scenarios. Values are displayed as mean(SD). P-values indicate results of the Kruskall-Wallis test. SAH patients committed significantly more road edge excursions than control participants (U = 38.00, p = 0.010).

<table>
<thead>
<tr>
<th></th>
<th>Controls</th>
<th>Ischemic</th>
<th>SAH</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crashes</td>
<td>0.25 (0.5)</td>
<td>0.85 (1.7)</td>
<td>1.8 (3.1)</td>
<td>0.082</td>
</tr>
<tr>
<td>Speed Exceedances</td>
<td>8.7 (6.6)</td>
<td>10.9 (5.8)</td>
<td>10.7 (7.7)</td>
<td>0.569</td>
</tr>
<tr>
<td>Stop Signs Missed</td>
<td>3.0 (2.5)</td>
<td>2.6 (2.6)</td>
<td>1.5 (1.9)</td>
<td>0.193</td>
</tr>
<tr>
<td>Center Line Crossings</td>
<td>3.08 (4.0)</td>
<td>6.0 (9.0)</td>
<td>5.3 (4.8)</td>
<td>0.232</td>
</tr>
<tr>
<td>Road Edge Excursions</td>
<td>0.67 (1.0)</td>
<td>1.6 (2.9)</td>
<td>2.5 (2.7)</td>
<td>0.010*</td>
</tr>
</tbody>
</table>

Figure 3.15 Mean number of hazardous errors (i.e. centerline crossings, road edge excursions and collisions) and routine traffic or rule violations (i.e. speed exceedances or missed stop signs) committed on average by each study group. * indicates difference is significant at the level of p < 0.05.
Figure 3.16 Mean number of errors associated with intersection turns displaying A) turning errors and B) non-turning errors for each study group. * indicates significance at the level of $p < 0.05$. Error bars represent +/- one SEM.

Figure 3.17. Mean number of errors committed during each turn type. * indicates that difference is statistically significant at the level of $p < 0.05$. Error bars represent +/- one SEM. Note that the difference in absolute values is due to the larger relative increase in the number of right turning events.
Correlations between Demographics, Cognitive Data and Driving Outcomes

To assess the relationship between the cognitive measures and driving performance, a Spearman rank correlation was conducted between each cognitive measure and three driving measures collected from the Full Scenarios: Total Errors, Turning Errors and Hazardous Errors. The only significant correlations occurred between the score of the UFOV-DA subtest and both turning errors ($\rho = 0.415$, $p = 0.049$) and hazardous errors ($\rho = 0.582$, $p = 0.004$). Furthermore, an exploratory analysis was performed to investigate a commonly accepted cutoff for the TMT B time (90 seconds) used to determine fitness to drive. Patients scoring greater than 90 (n=8) seconds did not have significantly different results on any of the driving measures explored in the correlation than patients scoring below 90 seconds (n = 20) on the TMT B. None of the driving measures were correlated with time since stroke. The only measure found to be correlated with age was hazardous driving errors ($\rho = 0.541$, $p = 0.016$).
3.4 Discussion

Very few studies have investigated simulated driving performance of patients, and several questions remain regarding the specific aspects of driving that may be impaired, as well as the relationship between driving outcomes and stroke subtypes. The present study has aimed to address these gaps in the literature by analyzing objective measures of driving performance during maneuvers of varying complexity, as well as exploring differences in stroke subtypes.

To restate, the three hypotheses in Chapter 2 pertaining to behavioural driving performance were as follows:

**Hypothesis 1:** Due to cognitive and functional deficits that persist into the chronic phase of stroke recovery, patients will commit significantly more driving errors than healthy control participants on overall measures of driving performance.

**Hypothesis 2:** Patients will exhibit impaired performance (i.e. more errors) during intersection turns, especially during the most complex maneuvers involving left turns with oncoming traffic.

**Hypothesis 3:** SAH patients will commit a similar number of errors overall as IS patients but will exhibit greater impairment (i.e. more driving errors) when navigating intersection turns due to higher prevalence of executive dysfunction.

3.4.1 Hypothesis 1: Overall Measures of Driving Performance

Several findings have emerged from this investigation. Firstly, patients did not incur significantly more errors than controls during the full scenarios or construction zone task but did commit more errors during the bus following task. This partially refutes hypothesis 1 predicting that patients would exhibit overall poorer performance across single summative measures of driving performance. These findings are in contrast to the results of Motta et al., (2014) who also used the STISIM driving software to evaluate driving performance in 19 stroke patients. They found a highly significant difference ($p = 0.005$) in overall scores between patients and controls using a driving scenario that was described to include complex intersections in city and suburban driving.
scenes, similar to the full scenarios used in the present study. A plausible explanation for this discrepancy may lie in the demographic and cognitive characteristics of stroke patients of the respective studies. Motta et al. (2014) recruited an older sample of patients with an average age of 70±9 years, compared to 60±11 years in the present study. Furthermore, they performed worse on the TMT-B and MoCA than the patients tested in this study, suggesting that the sample may have had poorer outcomes and higher levels of cognitive impairment. The impact of this is explained by the well-defined relationship between advanced age and poorer cognitive and functional outcomes (Go et al., 2014; Nakayama, Jørgensen, Raaschou, & Olsen, 1994).

McKay et al., (2011) and Hitosugi et al. (2011) also found that the stroke patient group performed worse on an overall summative measure of simulated driving performance than control participants. It is difficult to directly compare the results obtained by Hitosugi et al. (2011) to the data reported here because they included patients who required assistive adaptations (e.g. steering knobs), suggesting that the patients’ overall functional outcome was poorer and that driving performance would have been worse. Patients with hemiparesis were excluded from the present study, and all enrolled participants were able to manipulate the steering wheel and pedals. McKay et al. (2011) did not provide any details regarding the inclusion criteria for the stroke patients enrolled in the study, so it is unclear how the functional status of the patients would have compared to the patients tested here.

The results of hypothesis 1 are similar to those reported by Lundqvist et al., (2000) who found that stroke patients did not perform significantly worse on most measures of simulated driving performance. Interestingly, Lundqvist et al. (2000) also conducted an on-road assessment measuring several abilities including speed maintenance, maneuvering, lane positioning and traffic behaviour and found that patients did have a significant reduction in driving performance as compared to healthy controls. These results are of interest because they seem to suggest that the driving simulation was not sensitive to all driving impairments detected on-road. The variables collected from the simulated data mainly consisted of the time and distance to collision with other vehicles when responding to predictable and unpredictable changes in the speed of the
vehicle driving in front of them. This design is relatively simplistic and did not allow investigation into the more complex aspects of driving requiring planning and decision-making.

In the context of the current literature, the results highlight the importance of considering the patient sample characteristics, especially given the high heterogeneity in possible deficits that stroke patients may experience. Although previous studies have shown that overall scores on a driving assessment are different in stroke patients compared to healthy control participants, a result that was not replicated entirely here as the patients did not commit significantly more driving errors on the full scenarios or the construction zone task, indicating some level of preserved performance. Upon further inspection, it is likely that differences in patient characteristics and driving outcome measures led to these contradictory outcomes. As such, it is important that the characteristics of the sample are well-defined to allow researchers and clinicians to better understand how the results apply to patients with different characteristics.

The source of recruitment for patients is also an important factor in the interpretation of the results. The majority of driving research studies collect research data from patients who have already been referred to a driving rehabilitation center for assessment, indicating some level of concern about that patient’s driving ability. This study recruited stroke patients living independently in the community, many of whom were driving frequently and thus, an obvious impairment on all aspects of driving would be unlikely. However, evidence of an increased risk of on-road collisions in stroke patients discussed previously in Section 1.4.2 supports further study of driving behaviour in individuals who are able to return to driving.

The results also indicate that computing overall measures of driving performance may not be the ideal approach to understanding post-stroke driving impairments, especially in functionally independent patients with more subtle deficits. By combining all aspects of driving into one summative measure of performance, conclusions about specific situations where impairments arise cannot be drawn. Given that improvement in driving ability post-stroke requires targeted
intervention, summative measures may not be adequate to inform new screening measures and rehabilitation programs.

3.4.2 Hypothesis 2: Intersection Turns

Driving through intersections presents a complex challenge to drivers as it requires the involvement of all three hierarchical levels of the driving task (i.e. strategic, tactical and operational) (Schaap, 2012). At intersections the driver becomes faced with a variety of road users and lane types which require alertness, anticipation and sound decision-making on behalf of the driver. Although stroke patients did not commit significantly more errors than controls during the full scenarios, they did commit more errors when making intersection turns during these scenarios. In particular, patients committed significantly more errors than controls when making left turns with traffic, affirming hypothesis 2. The observation that patients only experienced significantly more driving errors than controls during left turns with traffic indicates a decrement in performance as the driving maneuver becomes more perceptually and cognitively demanding. Cantin, Lavallière, Simoneau, & Teasdale, (2009) reported increased mental workload for individuals approaching intersections relative to driving straight, especially for older drivers. As errors in performance are a consequence of increased mental workload, an increase in errors for patients compared to controls on left turns with traffic suggests that patients experienced the greatest difficulty during this most complex task. These results are further supported by previous neuroimaging evidence showing greater increases in brain activation in response to intersection turns, especially left turns with traffic, reported by Schweizer et al. (2013). Studies of MVC characteristics in the elderly have concluded that elderly drivers have disproportionately high rates of collisions when turning at intersections, and particularly when making left turns as a result of inadequate surveillance, failing to yield the right-of-way, or misjudging the speed or distance of another vehicle (Mayhew, Simpson, & Ferguson, 2006). Increased collisions in elderly individuals have shown correlation with cognitive outcomes (Reger et al., 2004). Although no formal research has investigated the factors surrounding MVCs in stroke patients, impairments in perception and cognition threaten safe driving ability during these complex aspects of driving.
3.4.3 Hypothesis 3: Subgroup Analysis

The subgroup analysis is especially novel as to our knowledge, no previous studies have not reported simulated driving performance in SAH patients. Hypothesis 3 predicted that SAH patients would exhibit greater deficits in performance during intersection turns due to the fact that SAH patients frequently experience impairments in executive functioning (Manning, Pierot, & Dufour, 2005; Martinaud et al., 2009). In the context of driving, impairments in planning and decision-making may manifest as difficulty navigating through intersections. The results support hypothesis 3 as only the SAH group had significantly more turning errors relative to the control group. The IS group was not significantly different than the control group, suggesting that the IS group lies somewhere in between the controls and SAH patients with regards to performance during intersections.

Patients in both the SAH and IS group were classified as good outcome patients according to clinical rating scales who were recruited with no preference for specific stroke locations. IS patients most frequently experience focal deficits matched to the area of infarction, and given that the lesion locations of the IS sample were quite heterogeneous, the deficits of that group were quite variable. Although the location of the ruptured aneurysm differed among patients in the SAH group, a growing body of evidence hypothesizing a “diffuse damage” effect has reported no relationship between aneurysm rupture location and specific cognitive profiles (Haug et al., 2007; Hillis, Anderson, Sampath, & Rigamonti, 2000; Orbo et al., 2008; Samra et al., 2007; Vilkki et al., 2004). Thus, although only a proportion of patients had anterior circulation aneurysms, frontal lobe functioning may have been affected in the majority of patients, which is supported by the results showing impaired performance in the TMT-B time measure.

As mentioned above, the IS patient lesion locations were quite variable, and it is possible that this resulted in larger variability in driving performance, which may have contributed to non-significant results. A larger sample size would allow further subanalyses to better understand how specific lesion locations relate to specific aspects of driving.
Overall, it appears that the SAH patients were more impaired than the IS on the driving assessment as the IS group did not show significant differences in performance relative to the healthy controls. It should be emphasized that the IS patient sample was relatively young in comparison to the IS stroke patient population, and therefore were more likely to experience a good outcome. As the average patient who is afflicted with SAH is between 40-60 years or age, the SAH patient sample more closely resembles the SAH population. The fact that IS and SAH patient groups were matched on age eliminates the confound of age-related cognitive decline that would be present had the IS group more accurately represented the population. Based on the characteristics of the sample, it can be concluded that SAH patients experienced greater difficulty during intersection turns than a population of young, high functioning IS patients of the same age.

Correlation with cognitive outcomes

The finding that the UFOV-DA subtest appears as a possible correlate of driving performance in stroke patients is consistent with the findings of the on-road study conducted by George and Crotty (2010), and the present work is the first driving simulator study in stroke patients to examine the utility of the UFOV. The finding is particularly interesting because it demonstrates a cognitive correlate to more specific aspects of driving, such committing more hazardous errors, which was found to be impaired in the stroke group. The findings do, however, disagree with multiple studies suggesting that the TMT-A and TMT-B results correlate with driving ability (Mazer et al., 1998, Mazer et al. 2003) It is possible that very few correlations were found because of a ceiling effect exhibited by the stroke patients on the cognitive assessments. The majority of patients scored in the unimpaired range on the MoCA, and patients with diagnosed cognitive impairment were not preferentially recruited for this study. It may be that the TMT lacks sensitivity in screening for more minor driving impairments. The current literature describing cognitive screening tools for driving is fraught with inconsistencies and methodological limitations, and substantial research is still required to determine how best to assess driving ability with a brief screening tool (Hird, Vetivelu, Saposnik, & Schweizer, 2014).
3.4.4 Limitations

Limitations include the relatively small sample size. Thus, some differences in driving behaviour and cognitive outcomes may not have been detected due to low statistical power. Despite this limitation, significant findings were still obtained. The sample of the current study is comparable to those published by previous groups who conducted a driving simulation study in stroke patients. The small sample size does restrict the possible analyses that can be conducted, and future studies should aim to overcome this limitation to draw stronger conclusions about the relationship between clinical characteristics (e.g., lesion location) and cognitive findings on simulated driving performance. Another potential limitation is the differences in sex among the subgroups. The IS group was comprised mostly of males and the SAH included more females. Although previous driving studies have reported no difference in performance between sexes (Rumschlag et al., 2015), a more balanced gender ratio would have eliminated this potential confound. In addition, the generalizability of the results is limited by the characteristics of the sample. As all patients were considered to have achieved good outcomes by clinical standards, the results are not generalizable to stroke patients with more severe deficits. Aside from the size and composition of the study sample, there are some inherent limitations to the methodology used. To maintain objectivity, the analysis of the driving behaviour was confined to quantitative data automatically generated from the simulation software, or additional variables calculated from that data but this restricts the nature of the information that can be used for analysis. Typical driving assessments are evaluated using standardized checklists that are manually completed by a trained evaluator. These checklists, although more subjective in nature, allow the assessment of subtle driving behaviours not captured by a simulator such as checking blind spots, which could not be assessed in the present study.
3.5 Conclusion

After stroke, patients experience visual, motor and cognitive deficits that may impair the ability to drive. There is widespread uncertainty regarding the optimum screening assessment and rehabilitation programs for patients who wish to resume driving after stroke. It is therefore not surprising that data supports an increased risk of collisions for post-stroke drivers. The present study has assessed driving behaviour of functionally independent, community-dwelling chronic stroke patients using a high-fidelity driving simulator with the aim to understand if stroke patients exhibit more driving errors during more complex aspects of driving, such as making left turns at intersections, where most real-world collisions occur. We observed that during a complex driving scenario including situations of varying complexity, stroke patients did not make more driving errors overall, but did make more hazardous errors and errors during intersection turns. In particular, they committed significantly more errors than controls when making left turns at intersections with oncoming traffic, a situation where drivers are required to integrate many environmental stimuli and use proper judgment to turn safely.

The heterogeneous presentation of stroke should receive greater attention in the driving literature, as many studies include patients with different stroke subtypes, without regard for the fact that ischemic and hemorrhagic stroke patients often have different profiles of cognitive and functional impairment. For the first time, the data has shown that when comparing age-matched groups of IS and SAH patients, it is SAH patients that on average committed more driving errors during complex aspects of driving. This may be explained by the fact that high levels of executive dysfunction are observed in SAH patients, including the patients in this sample who performed significantly worse on the TMT B (time), a measure of executive dysfunction. Conversely, IS patients may suffer from a widely heterogeneous list of deficits that may manifest as greater variability in driving performance. Further investigation is required to study the variability in driving performance in both groups, prioritizing a way to differentiate safe from unsafe drivers.
Chapter 4: Functional MRI Investigation of Driving Maneuvers of Increasing Complexity in Ischemic Stroke Patients

4.1 Introduction

A large focus of previous neuroimaging studies of stroke patients is the mechanism of recovery with respect to motor function, and the brain’s response to rehabilitation interventions. No previous fMRI studies have used an immersive VR driving simulator to measure neural activation patterns of stroke patients during driving simulation. By studying the patient’s response to driving maneuvers of increasing complexity, we are able to draw conclusions about why certain behavioural driving impairments are occurring.

In Chapter 3, it was established that stroke patients commit more driving errors than healthy controls, particularly when making left turns with oncoming traffic. These errors primarily consisted of hazardous-type errors including collisions with other vehicles or errors in lane positioning such as crossing over into the opposing lane when finishing a turn or driving beyond the confines of the outer lane boundary. In real-world driving, errors at intersections are especially dangerous because drivers are encountering vehicles travelling in many directions, increasing the probability of collision. Chapter 4 will investigate the underlying brain activation networks when the stroke patient encounters intersections, including situations of varying complexity (i.e. simple right and left turns versus left turns with oncoming traffic relative to straight driving).

As previously discussed in Section 1.6.2 only a handful of studies have conducted fMRI studies of driving behaviour, the majority of which have used passive tasks such as viewing videos of different driving situations, or simple tasks using a joystick or button box to control either the speed or the steering. The driving simulator hardware and software used for the present experiment was used in a prior study of the neural correlates of driving in young, healthy individuals (Schweizer et al. 2013). This novel simulator includes both a steering wheel and
pedal system, requiring the participant to control both steering and speed components simultaneously. Using this ecologically-valid, immersive, fMRI-compatible driving simulator, the experiment aimed to evaluate the hypothesis that stroke patients demonstrate altered brain activation patterns in response to performing driving tasks with increasing cognitive demand in comparison to healthy control participants. Specifically, it was hypothesized that patients will exhibit similar activation patterns as control participants during simpler, less complex aspects of driving (i.e. completing simple right and left turns) but will exhibit deviations from healthy controls as the driving task becomes more demanding (i.e. completing complex left turns with oncoming traffic).
4.2 Methods

4.2.1 Participants

Ten IS patients (9 males, age = 57.8 +/- 12.2 years) and 10 healthy controls (6 males, age = 59.8 +/- 12.6 years) participated in the experiment. The patients who participated in the fMRI study also completed the behavioural driving study in Chapter 3, with the exception of one patient (Patient 1) who was lost to attrition. Please refer to Table 4.1 for the characteristics of the IS patient sample and to Figure 4.1 for representative MRI slices of the ischemic lesion locations. SAH patients were not included in the fMRI study due to time constraints in recruitment. Participants were screened using the same criteria outlined in Section 3.2, and also met MRI-screening guidelines (no metallic implants and no claustrophobia). All participants had normal vision or corrected-to-normal vision using a set of MR-compatible glasses with interchangeable lenses. All participants also held a valid driver’s license and were active drivers. Participants gave written, informed consent for participation in the study under a protocol approved by the St. Michael’s Hospital Research Ethics Board.
<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (Years)</th>
<th>Sex</th>
<th>Handedness</th>
<th>Lesion Location</th>
<th>Time Since Stroke (Months)</th>
<th>NIHSS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>56</td>
<td>M</td>
<td>L</td>
<td>L Internal capsule</td>
<td>5.2</td>
<td>9</td>
</tr>
<tr>
<td>2</td>
<td>71</td>
<td>M</td>
<td>R</td>
<td>L posterior temporal lobe, L occipital lobe</td>
<td>62.3</td>
<td>10</td>
</tr>
<tr>
<td>3</td>
<td>44</td>
<td>M</td>
<td>R</td>
<td>L Basal ganglia</td>
<td>36.8</td>
<td>4</td>
</tr>
<tr>
<td>4</td>
<td>63</td>
<td>M</td>
<td>R</td>
<td>R MCA territory</td>
<td>47.0</td>
<td>7</td>
</tr>
<tr>
<td>5</td>
<td>57</td>
<td>M</td>
<td>R</td>
<td>R hippocampus</td>
<td>44.3</td>
<td>1</td>
</tr>
<tr>
<td>6</td>
<td>72</td>
<td>M</td>
<td>L</td>
<td>R parietal lobe, R corona radiata</td>
<td>49.2</td>
<td>2</td>
</tr>
<tr>
<td>7</td>
<td>59</td>
<td>M</td>
<td>R</td>
<td>L periinsular region</td>
<td>88.1</td>
<td>8</td>
</tr>
<tr>
<td>8</td>
<td>43</td>
<td>M</td>
<td>R</td>
<td>Anterior corpus callosum, L cingulate cortex</td>
<td>5.9</td>
<td>0</td>
</tr>
<tr>
<td>9</td>
<td>48</td>
<td>F</td>
<td>L</td>
<td>L posterior temporal lobe, L anterior occipital lobe</td>
<td>26.5</td>
<td>0</td>
</tr>
<tr>
<td>10</td>
<td>79</td>
<td>M</td>
<td>R</td>
<td>R subcortical white matter</td>
<td>*Unknown</td>
<td>*Unknown</td>
</tr>
</tbody>
</table>

Table 4.1 Characteristics of patients included in the sample. * Patient was diagnosed with silent stroke and therefore, time since stroke and NIHSS are unknown.
Figure 4.1 Representative MRI slices of ischemic lesion locations. All images were acquired using a T2-Fluid-Attenuated Inversion Recovery (FLAIR) sequence. Images were taken in the acute-subacute phase in all patients with the exception of Patient 10 who had a silent stroke.
4.2.2 Data Acquisition

A driving hardware system developed specifically to create an immersive VR environment in a 3.0 Tesla MRI scanner was used to conduct the study. The same software that was employed in the behavioural driving assessment (STISIM Drive) in Chapter 3 was used to display driving scenarios on a projector that was viewed on a mirror affixed to the head coil. The driving hardware consists of a plastic steering wheel that is stabilized on a support frame around the participant’s waist and a pedal system positioned at the participant’s feet. Participants wore noise-suppressing earplugs that also allowed the participants to hear audio instructions (Conformal Headset™ for MRI Audio, Avotec, Inc., Stuart, Fl). A detailed description of the methodology including analysis of head motion and fMRI compatibility of this novel simulator is described by Kan, Schweizer, Tam, & Graham (2013).

Prior to entering the MRI suite, participants were given a short presentation to become familiar with how the driving set-up works, what they would be viewing and how they should respond during the experiment. An MRI technologist scanned all participants on a research-dedicated 3-Tesla Siemens Magnetom Skyra scanner with a 20-channel head coil at the St. Michael’s Hospital Medical Imaging Department. The imaging session had three components: set-up of the driving simulator equipment (10 minutes), two brief training sessions (15 minutes) and two experimental sessions for functional data acquisition (25-30 minutes). The entire scanning session was approximately one hour in duration.

During the training session, the participants practiced the driving tasks to become familiar with the driving simulator controls and to practice performing the driving while keeping their head still. All participants were able to reach an acceptable level of performance on the task (i.e. were able to control speed and steering while driving straight, and could successfully stop and turn at intersections) by the time that the training sessions were completed. Before collecting functional data, a high-resolution T1-weighted anatomical scan (MPRAGE; echo time (TE) = 2.54ms, flip angle = 9 degrees, 176 slices, slice thickness = 1mm, gap = 0mm, field of view (FOV) = 256mm, voxel size = 1mm isotropic) was acquired. Next, the participants completed the two experimental
scenarios while functional imaging data was collected. The fMRI data was acquired using T2*-weighted echo planar imaging (EPI; repetition time (TR) = 2000ms, TE = 30mm, flip angle = 70 degrees, 32 slices, slice thickness = 4mm, gap = 0.5mm, FOV = 200mm, voxel size = 3.1 x 3.1 x 4.0mm).

Driving Tasks:

The experimental driving scenarios were triggered with the onset of fMRI data acquisition to sync the EPI image collection with the timing of the simulated driving tasks. The two experimental sessions were each approximately 12 minutes in length and consisted of straight driving interleaved with turning events. The events were randomly placed throughout the scenario to reduce anticipation but were presented in a fixed order for each participant. The scenarios were designed such that there were at least seven of each turning event. Pre-recorded audio prompts were embedded in the driving scenarios to indicate to the participant which direction to turn at the upcoming intersection. The onset of the audio instruction occurred 100 metres before the intersection. Participants were either instructed to turn right at “simple” intersections, where there was no traffic present, or to turn left at “complex” intersections where the driving encountered a continuous flow on oncoming traffic. Although the same simulation software was used for both the behavioural and fMRI driving simulation studies, the scenarios for the fMRI study were modified to allow for adequate repetition of trials for fMRI analysis. The turning events for the fMRI study were also spaced farther apart, allowing at least 300 metres (or approximately 20 seconds) in between events to ensure that a stable baseline signal could be reestablished.
4.2.3 Data Analysis

Behavioural driving measures:

The raw data file produced by the STISIM software was used to determine the timing of the intersection turns, using the same method as previously described in Section 3.2.3. To provide an indication of the driving performance in the scanner, the simulator-recorded errors were collected, and the errors during the intersection tasks were manually extracted. Instances where the driver did not complete the turn correctly, or crashed during the turn were eliminated from the analysis, and thus the driver’s response to collisions or mistakes during the driving scenarios was not included, as there were not enough collision events on an individual subject level to analyze them separately. Two stimulus timing files, one specifying the event onset and the other listing the duration of each event, were created for each of the turning conditions (right turns, left turns and left turns with traffic) to be used in the imaging analysis.

Image processing and analysis

The DICOM images collected were first converted to the Neuroimaging Informatics Technology Initiative (NIfTI) format using MRIconvert. The data were processed using Analysis of Functional Neuroimages 2011 (AFNI) software package (Cox, 1996). The first two volumes of the time series data for each run were removed to discard non-equilibrium scans. The rest of the volumes in the time series data were corrected for axis alignment, head motion, physiological artifacts, slice timing, spatial smoothing and spatial normalization onto a standard Montreal Neurological Institute (MNI) template. Data were spatially smoothed using a 6mm full width at half maximum (FWHM) Gaussian kernel and then normalized by the run-wise mean of each voxel. Data from both experimental runs were concatenated together to form a single dataset. Statistical brain activation maps were generated using a General Linear Model (GLM) by convolving the stimulus timing files assuming a fixed-shape HRF. The resulting GLM parameter estimates were transformed to standard Talairach brain atlas space. Each of the turning tasks was compared to a baseline condition of straight driving. Group-level contrasts for each of the turning tasks relative to straight driving were generated using a one-sample t-test. The resulting group brain activation maps were superimposed on the MNI template for visualization.
4.3 Results

4.3.1 Activation Maps

Statistical brain activation maps are shown below in Figure 4.2. All conditions are reported as comparisons to the baseline condition of straight driving. The statistical activation maps were cluster-corrected with a minimum cluster of 20 voxels.

**Figure 4.2** Statistical activation maps \((t = 3.336; p = 0.01)\) showing % BOLD change on a normalized intensity scale for GLM analysis of task stimuli compared to baseline of straight driving for the healthy control and IS groups. Activation maps are displayed in neurological convention.

Visual inspection of the statistical brain maps reveals that during all turning conditions, healthy control drivers show extensive activation of posterior brain networks, including parietal, motor and visual cortices as well as the cerebellum. Greater changes in activation of this core network were observed as the complexity of the task increases from simple right turns, to simple left turns, to complex left turns with oncoming traffic. Patients also demonstrate reliable activation of this core network including the parietal, motor and visual cortices. However, less activation is observed during all tasks in the IS patients relative to the control group. In IS patients, activation increases from right turns to left turns, but is decreased for the most complex, left turn with traffic condition.
4.3.2 Behavioural Results

A two-way repeated measures ANOVA was conducted to compare the time taken to complete each task condition and to determine if there was an interaction between the patient and control groups. The mean and SD values for the time to completion for each turning condition are listed in Table 4.2. The results of the ANOVA indicated a significant main effect for time to completion (Wilks’ Lambda = 0.353, F(1,15) = 13.758, p < 0.001, $\eta^2_p = 0.647$), but the interaction between time to completion and group was not significant (Wilks’ Lambda = 0.800, F(1,15) = 1.871, p = 0.188, $\eta^2_p = 0.2$). Follow-up comparisons using the Least Significant Difference post hoc test indicated that right turns took significantly longer than left turns (Mean Difference = 0.275, p = 0.015) and left turns with traffic (Mean Difference = 0.823, p < 0.001). Left turns were also shown to take significantly longer than left turns with traffic (Mean Difference = 0.548, p = 0.001). Overall the results suggest that when going from right turns, left turns and left turns with traffic the time taken to complete the turn decreases and thus, the participant is driving faster. In addition, there was no between-group interaction indicating that patients did not differ in the time to completion on the turning tasks than control participants.

<table>
<thead>
<tr>
<th>Turn Condition</th>
<th>IS Patients</th>
<th>Healthy Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right Turn Time (seconds)</td>
<td>5.41 (1.00)</td>
<td>5.21 (1.31)</td>
</tr>
<tr>
<td>Left Turn Time (seconds)</td>
<td>4.99 (0.97)</td>
<td>5.08 (1.20)</td>
</tr>
<tr>
<td>Left Turns + Traffic Time (seconds)</td>
<td>4.69 (0.91)</td>
<td>4.28 (0.66)</td>
</tr>
</tbody>
</table>

Table 4.2 Summary of the time in seconds to completion during each turning condition for stroke patients and control participants. Data are presented as mean (SD).
Table 4.3 displays the summary of the types of driving errors committed in the MR scanner for the patient and control groups. Table 4.4 displays the turning errors committed for each of the patient and control groups. Behavioural measures are combined from both experimental sessions. Patient and control groups did not differ on the types of errors committed, or the total number of errors. Groups also did not differ on the number of turning errors, including errors for each turn type (i.e. right turns, left turns and left turns with traffic).

<table>
<thead>
<tr>
<th></th>
<th>IS Patients</th>
<th>Healthy Controls</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collisions</td>
<td>0.89 (1.05)</td>
<td>0.44 (0.73)</td>
<td>0.28</td>
</tr>
<tr>
<td>Centre line crossings</td>
<td>5.00 (6.76)</td>
<td>4.56 (6.98)</td>
<td>0.89</td>
</tr>
<tr>
<td>Road Edge Excursions</td>
<td>1.22 (1.79)</td>
<td>0.44 (1.01)</td>
<td>0.25</td>
</tr>
<tr>
<td>Stop Signs Missed</td>
<td>3.33 (2.78)</td>
<td>2.89 (2.72)</td>
<td>0.72</td>
</tr>
<tr>
<td>Total Errors</td>
<td>10.56 (10.84)</td>
<td>8.33 (10.93)</td>
<td>0.65</td>
</tr>
</tbody>
</table>

**Table 4.3** Summary of the types of driving errors committed by each group, presented as mean (SD)

<table>
<thead>
<tr>
<th></th>
<th>IS Patients</th>
<th>Healthy Controls</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right Turn</td>
<td>1.78 (2.1)</td>
<td>1.33 (1.65)</td>
<td>0.67</td>
</tr>
<tr>
<td>Left Turn</td>
<td>1.00 (2.29)</td>
<td>0.33 (0.50)</td>
<td>0.93</td>
</tr>
<tr>
<td>Left Turn + Traffic</td>
<td>1.11 (1.76)</td>
<td>0.78 (1.71)</td>
<td>0.73</td>
</tr>
<tr>
<td>Total Turning Errors</td>
<td>3.89 (5.13)</td>
<td>2.44 (1.08)</td>
<td>0.39</td>
</tr>
</tbody>
</table>

**Table 4.4** Summary of errors committed by patient and control groups during each turning condition, presented as mean (SD).
4.4 Discussion

4.4.1 fMRI Findings

The aim of this investigation was to determine if there are changes in the brain activation patterns of IS patients completing simulated driving tasks of varying complexity relative to healthy controls. It was hypothesized that patients will exhibit similar activation patterns as control participants during simpler, less complex aspects of driving (i.e. completing simple right and left turns) but will exhibit deviations from healthy controls as the driving task becomes more complex (i.e. completing left turns with oncoming traffic). Overall, consistent activation in the same “core” driving network of occipital, parietal and superior frontal regions was observed in both the patient and control group during all turning tasks although the patient group to a lesser extent. An increase in the magnitude and volume of activation was observed for the control group when comparing right turns, to left turns, to left turns with traffic, but this increase was not observed in the patient group where the group-level activation pattern became less extensive during the most complex task, the left turn with oncoming traffic. Thus, the findings are consistent with the stated hypothesis.

The task-dependent increase in BOLD signal intensity in the control group as the task-demand increased from left turns, to left turns with oncoming traffic is in agreement with the findings of the previous fMRI study in healthy individuals by Schweizer et al. (2013). The findings are also complemented by previous, non-driving related studies that have observed BOLD signal intensity changes as a result of increasing mental workload in tasks of working memory (Gould, Brown, Owen, Ffytche, & Howard, 2003) and delayed item recognition (Stern et al., 2012). The control sample observed here did demonstrate BOLD signal increases in the middle cingulate, putamen and insula that were not observed in the Schweizer et al. (2013) study. This is likely attributable to the fact that the sample here was older than the participants tested in the previous study who were, on average, 25.8 years of age. Previous studies looking at task-related neural activation in older versus younger participants have found that younger individuals recruit a less extensive network of brain regions for a given task, supporting the idea that network efficiency is lower in older individuals (Mattay et al., 2002; Zarahn, Rakitin, Abela, Flynn, & Stern, 2007).
Patients enrolled in the study were recruited without preference for a particular lesion location, so conclusions about the influence of a particular lesion site on activation patterns cannot be drawn from the present study. However, integrating the location of the lesions informs the interpretation. Firstly, the core driving network recruited during the tasks is composed of activation in cortical regions including the occipital, parietal and superior frontal areas for motor planning and execution. Lesions to these cortical areas were not common among the patient sample. Four of the patients had focal lesions to the dorsal grey matter (two occipital, one parietal and one cingulate), with the remaining patients having lesions located in subcortical structures. Neural activation maps are generated on the basis of statistically significant changes in BOLD signal, representing areas that are consistently activated across the subject pool. Therefore, lack of BOLD signal change in a particular area on the statistical map does not necessarily suggest a complete lack of BOLD signal across all patients, but may be attributed to variability in the BOLD response across the group.

The finding that a less extensive area of the core visual-motor network for the driving tasks was observed in the stroke patient group suggests that the ischemic lesions have a common effect on the functional integrity of the network recruited during the driving task. Clinical recovery following stroke has been attributed to neuroplastic reorganization and the recruitment of novel brain regions not previously engaged during a particular task to substitute for areas that are lesioned or disconnected (Cramer, 2008). These widespread changes in connectivity of functional networks have been observed as a consequence of focal ischemic lesions in previous fMRI studies (Carter et al., 2010; He et al., 2007).

Although changes in connectivity are spontaneous and adaptive mechanisms of recovery that correlate with improved functional capacity, these changes do not necessarily restore baseline function. Evidence for this exists in studies aimed to understand the difference in brain activation between patients with good and poor functional recovery. The severity of motor deficit has consistently shown correlation with a reduction in connectivity between the primary motor cortex and supplementary motor cortex in the ipsilateral hemisphere (Grefkes et al., 2008, 2010; Rehme, Fink, Von Cramon, & Grefkes, 2011). The study of the impact of lesions on distant
connections has primarily been undertaken in studies of the motor network, but studies understanding the relationship between cognition and functional connectivity are emerging. In patients with right hemisphere stroke, poor cognitive recovery has shown association with increased resting state functional activity in the contralateral hemisphere (Dacosta-Aguayo et al., 2014).

4.4.2 Behavioural Findings

The time to complete each of the driving tasks was significantly different in both groups, indicating that each task evoked a change in behaviour. When examining the number of driving errors committed by both groups, the quality of the driving performance was not reduced in the IS patients when tested in the MRI machine. This can be explained by the way that the scenarios were designed so that the conditions remain optimal for neuroimaging analysis. To create reliable activation maps, multiple repetitions of the same task must be undertaken, with sufficient time in between them to allow the brain to return to a steady-state baseline condition (i.e. straight driving). Although the tasks were presented in random order to reduce anticipation, they were somewhat simplified because the scenario alternates between the straight driving and the turning tasks, without any intervening events that make the scenario seem more realistic such as requiring that the driver change lanes or respond to sudden unexpected changes as would have been required of the drivers in the experiment presented in Chapter 3.

4.4.3 Strengths

The present study used a novel, MR-compatible driving simulator to obtain the first functional neuroimaging data of IS patients during simulated driving. fMRI provides high spatial resolution and whole-brain coverage, which cannot be attained using more portable imaging modalities such as EEG or fNIRS. In addition, the driving hardware required the participant to control both the steering and speed aspects of the driving task, as opposed to many previous fMRI driving studies that either use a simpler joystick or button box, or ask the participants to passively view videos of driving. Overall, this method maximizes external validity within the confines of MRI. Another relative strength of the present study involved measuring tasks of varying complexity.
As observed in healthy individuals, both the volume and magnitude of activation increase as participants completed tasks of increasing complexity (i.e. from simple right and left turns, to complex left turns with oncoming traffic).

4.4.4 Limitations

Although valuable information can be obtained with task-based, BOLD contrast fMRI, the method is not without limitations, especially when used in populations with diminished vascular health. Neurovascular dysfunction in stroke patients may result from a combination of large and small vessel disease, and is associated with a reduction in the physiological increases in cerebral blood flow that would be predicted as a result of neuronal activity (Veldsman, Cumming, & Brodtmann, 2014). It is regularly assumed that the BOLD signal is a direct measure of neural activity. However, BOLD-signal changes are subject to multiple assumptions and may be confounded by many sources of noise. The hemodynamic response is influenced by cerebral blood flow (CBF), cerebrovascular reactivity, blood volume and blood oxygenation, all of which may be altered in stroke patients (Bangen et al., 2009; Carusone, Srinivasan, Gitelman, Mesulam, & Parrish, 2002; Rossini et al., 2004). Changes in these parameters in patients with cerebrovascular disease can lead to reduced BOLD-signals being misinterpreted as a lack of neuronal activity. A multi-modal approach would have helped circumvent this uncertainty.

Although the use of BOLD-fMRI in stroke patients is not without controversy, the observation of task-dependent changes in activation within the patient group on tasks requiring increasing mental workload helps to overcome this limitation. Comparable activation patterns were obtained for the simple right and left turns for patients and control participants, indicating the presence of a consistent BOLD-response to these tasks. The departure from control activation patterns observed during the complex left turn with traffic condition supports the notion that the changes observed are a result of changes in neural activity rather than due to the inconsistencies between the BOLD-response and neural recruitment. Furthermore, physiological changes such as perfusion deficits and impaired neurovascular coupling are more pronounced in the acute phases of stroke recovery, and would have had a smaller influence on the BOLD-signal in the chronic IS patients enrolled in the present study (Beaulieu et al., 1999; Chalela et al., 2000).
Despite the alterations required to embed the simulator in the MRI, the current set-up maximizes the validity of the study by integrating a realistic steering wheel and pedal apparatus, an advantage over previous fMRI and driving studies that used joysticks or buttons to control the vehicle (Calhoun et al., 2002; Just et al., 2008; Uchiyama et al., 2003; Walter et al., 2001). However, the findings of this experiment are also limited by the extent to which the MR-compatible driving simulator can represent real-world driving. Due to the space constraints of the MR environment, and the requirement that participants lie in a supine position and hold their head very still, the simulator is positioned so that the participant can exert control of the vehicle using minimal movement.

4.5 Conclusion

To date, no studies have collected fMRI data of stroke patients performing simulated driving tasks. Characterizing the underlying changes in brain activation patterns during driving simple and complex driving tasks in stroke patients is important to better understand how the injured brain “copes” during demanding driving situations and to determine relationships between these patterns of activation and driving behaviour. The findings presented in this chapter support the hypothesis that on average, IS patients exhibit similar activation patterns as control participants during simpler, less complex aspects of driving (i.e. completing right and left turns) but exhibit deviations from healthy controls as the driving task becomes more complex (i.e. completing left turns with oncoming traffic). The behavioural significance of this observation needs further investigation in both simulated and on-road settings. The current study focused on behaviour at intersections, because of the known complexity of safely navigating through intersections during real-world driving. Conclusions about deviations in brain activation patterns during sudden, unexpected events where a rapid response would be required, or during prolonged driving such as highway driving where stroke-related fatigue may factor into performance. Future work should aim to measure brain activation using a more diverse set of driving tasks. Further research should also compare the activation patterns of patients who perform well, and patients who demonstrate poorer performance to determine if the degree of network reorganization observed in stroke patients leads to impairments in driving performance.
5.1 Unifying Discussion

This brief, final discussion is meant to unify the findings in Chapters 3 and 4 in the context of the overall themes addressed throughout this thesis. The heterogeneous nature of stroke with respect to lesion location, size and severity and recovery trajectories renders it difficult to draw relationships between clinical presentation and driving behaviour. Despite this variability in outcome, significant overall changes in specific behavioural measures of driving were observed in Chapter 3. In particular, stroke patients demonstrated impairment when navigating intersection turns, especially when making left-hand turns with oncoming traffic. In addition, stroke patients committed more hazardous-type errors. When subgroups were assessed separately, the SAH patients were more impaired than the IS on the driving assessment as the IS group did not show significant differences in performance relative to the healthy controls, possibly due to increased variability in performance. In Chapter 4, consistent activation in the same “core” driving network of occipital, parietal and superior frontal regions was observed in both the IS patient and control groups during all turning tasks, although the patient group to a lesser extent. An increase in activation was observed for the control group when comparing right turns, to left turns, to left turns with traffic, but this increase was not observed in the patient group where the group-level activation pattern became less extensive during the most complex task, the left turn with oncoming traffic.

Previous findings by Schweizer et al. (2013) demonstrated a task-related increase in neural activation as the task changed from right turns, to left turns, to left turns with oncoming traffic. Using these findings as a framework for understanding the mental workload associated with these tasks, we can draw a relationship between the increasing complexity of the task, and the behavioural impairments observed in the stroke patients. This relationship supports the finding that in general, stroke patients committed more errors during the most complex driving task. Furthermore, the observation that as task complexity increases, activation patterns of IS patients...
deviated from control activation patterns. Based on evidence describing widespread connectivity changes in areas remote from ischemic lesions, it seems reasonable to predict that the greater the recruitment required for the task, the greater the potential for disruptions in the pattern of activation (Grefkes & Fink, 2011). This is merely speculative as the empirical evidence of the effects of increased cognitive demand on functional network changes in stroke patients has not yet been established. Even still, the observation that the task-related increase observed between left turns and left turns with oncoming traffic in control participants was not present in the IS group may indicate inconsistency in the network activated for that task. This was perhaps a result of high heterogeneity in clinical presentation and driving performance of the patient group and a greater sample size may have provided the power necessary perform a more in-depth analysis of high and low performers. The behavioural results from the in-scanner driving performance also did not provide evidence of impaired behavioural performance, which may be attributable to the simplified nature of the driving tasks required for fMRI data acquisition. It is still unclear as to what type of activation changes could lead to behavioural impairment on an individual level, and future research is required to investigate the influence of lesion location on both activation patterns and behavioural performance.

A persistent point of emphasis throughout this thesis is the importance of assessing driving under standardized conditions with tasks that range in complexity. The stroke and driving literature contains multiple studies of on-road assessments measuring pass/fail rates with minimal indication of the specific aspects of driving that require improvement. The decision to investigate changes in driving performance and underlying brain activation patterns in stroke patients in comparison to age-matched controls has yielded new information regarding the types of driving errors committed, the driving situations where more errors are committed, and differences in performance between stroke subtypes. This information is helpful for targeting areas for driving assessment and rehabilitation.

Aiming to understand changes in activation patterns during driving tasks as a result of ischemic lesions was a novel, but difficult undertaking. Stroke is highly variable in presentation, which creates a challenge in the interpretation and generalization of group-level differences. A larger
sample size with more homogeneous lesion locations would allowed stronger inferences into the relationship between driving performance, lesion location and changes in brain activation. A focus of future studies in driving simulation and neuroimaging of driving in stroke patients should aim to recruit larger samples of patients to identify patterns that emerge with specific lesion location, as well as cognitive correlates of impaired performance. Although the UFOV-DA task was shown here as a potential correlate of more hazardous driving errors, further research using more comprehensive neuropsychological test batteries is required to characterize the cognitive correlates of different driving behaviours.

Exploring the functional status and source of patient recruitment is another essential aspect to the interpretation and application of the results. Based on previous literature, it was hypothesized that stroke patients would commit more driving errors than control participants in all driving scenarios. However, this hypothesis was based on findings of patients who had been referred for a driving assessment, whereas the patients recruited in the present study were not. The patients who participated were functionally independent, although this does not preclude cognitive impairment. It is not surprising then that the patients performed better on the driving tasks relative to control participants than in previous studies. The applicability of the findings therefore extends to patients living independently in the community where driving has not been identified as a specific concern. These results are important in the context of the large-scale crash data, which suggest that chronic stroke patients experience a higher rate of MVCs. In general, the results highlight the importance of addressing driving in the years following stroke, as even subtle cognitive impairments may lead to challenges performing a task as complex as driving a motor vehicle. In an effort to avoid alarmist conclusions, it is also important to emphasize that many aspects of driving performance in this sample were preserved, and it is not the case that the loss of driving privileges would be appropriate in these patients.
5.2 Future Directions

*Translation into Real-World Settings*

Driving simulators provide a valuable tool with which researchers can study complex driving behaviours in neurological populations in a safe and controlled environment, but further work is required to determine how the behavioural impairments observed on the simulator translate into on-road driving performance. An important next step is a large-scale study of driving behaviour during on-road driving, in relation to the findings obtained using VR technology. One methodology to approach this question would be the use of population-based databases of collision data to determine the characteristics of MVCs in stroke patients. The feasibility of such studies has previously been established in a study of collisions in individuals with traumatic brain injury (TBI) (Neyens & Boyle, 2012). Using a combination of the Iowa Department of Transportation’s detailed collision records and the state’s Brain Injury Registry, Neyens & Boyle, (2012) discovered that in a sample of 1583 crashes involving drivers with a history of TBI, individuals were more likely to be involved in MVCs where they had passengers in the car, were not wearing a seatbelt and when driving at night compared to a control group with no history of TBI. They conclude that the findings generate a more comprehensive understanding of the challenges surrounding driving after TBI and suggest that this type of data is important for the development of driver evaluation and rehabilitation programs. One hypothesis related to stroke patients based on the results presented here would predict stroke patients to be involved in more accidents involving intersections, particularly when turning left in heavy traffic situations where the situation is both perceptually and cognitively demanding. Investigating the impact of having passengers in the vehicle or driving in adverse weather conditions would also provide additional information that is difficult to collect in a brief on-road or simulated driving assessment.

Another method to confirm the validity of the findings collected from driving simulation could involve the long-term observation of on-road driving performance in stroke patients by installing data-recording instruments such as cameras, accelerometers, and Global Positioning Systems into the vehicles of stroke patients and matched controls. Drawbacks to conducting research studies using an on-road or simulator-based assessment include the brevity in duration of the
assessment and susceptibility to observer effects. By observing driving performance over an extended duration (days to months rather than minutes to hours), and without the perceived threat of being scrutinized, the driver behaves as they normally would, and the researcher is able to gain an indication of driving habits with higher ecological validity. Although this methodology would only apply to patients who have been deemed to safely return to driving after stroke and not for the assessment of readiness to drive after stroke, it would generate novel information about how post-stroke drivers are handling complex driving situations and what restrictions or self-regulations they may impose on themselves. The feasibility of such a study has previously been established by the 100-Car Naturalistic Driving Study in healthy adults (Dingus, Klauer, & Neale, 2006) and the Naturalistic Teenage Driving Study in novice adolescent drivers (S. Lee, Simons-Morton, Klauer, Ouiment, & Dingus, 2011). Using in-vehicle data, these studies were able to overcome a major limitation of studying behaviour based on collision risk alone by also quantifying “near-crashes”, gaining greater insight into the behaviours or situations that may precede collisions. Combining these datasets, Klauer et al., (2014) reported that the risk of a collision, or near collision among novice drivers increased significantly when they were seen performing secondary tasks such as texting or eating. Although this investigation would require substantial resources, a study of this nature would provide valuable insight into how the naturalistic driving behaviours of stroke patients are different than their healthy, age-matched counterparts.

**Tracking Recovery of Driving Ability**

One major outstanding question regarding driving after stroke is the trajectory in the recovery of driving abilities and at what point is it safe for the patient to return to driving. Impairments in driving ability detected on a simulator have been identified in patients less than 7 days post-stroke (Hird et al., 2015) and in patients between 7-14 days post stroke (Kotterba, Widdig, Brylak, & Orth, 2005) but longitudinal studies of driving performance have not been published. Early identification of deficits and initiation of targeted rehabilitation strategies is known to maximize the recovery process to minimize persistent functional disability in stroke patients (Duncan et al., 2005). By studying the dynamic changes in driving ability and their cognitive correlates, better tools can be developed to assist in the clinical decision of a patient’s readiness
to return to drive. A large-scale study collecting simulated driving data, cognitive data, and functional measures at multiple time points (e.g. at one month, 3 months, 1 year, 5 years and 10 years) would inform the development of office-based assessments for determining if more comprehensive driving assessments are needed.

As a complement to longitudinal, simulator-based studies of driving ability, the neuroimaging methods discussed here may also assist in the evaluation of recovery in driving ability. Changes in functional connectivity are known to occur rapidly immediately following stroke but still fluctuate in the following months up to a year (Wang et al., 2010). Alterations in activation patterns in response to driving tasks of increasing complexity were present in IS patients who were, on average, greater than one year post-stroke. Using a longitudinal study design to assess changes in brain activation patterns at multiple time points in combination with behavioural and cognitive measures, a better understanding of when intervention can be introduced to maximize rehabilitation potential will be gained.

*Interventions to Improve Driving Ability*

Identifying difficulties with driving in complex driving situations such as navigating through busy intersections provides direction for developing context-specific intervention programs. As discussed in Section 1.4.3, cognitive and simulator training programs assessed through RCTs have shown little long-term success in improving the results of the on-road assessment. In clinical settings, driving lessons are the most common intervention to improve driving skills in stroke patients, yet no RCTs have reported on the success of these contextual approaches. By developing an intervention program that specifically trains the aspects of driving that were found to be impaired behaviourally (i.e. errors during intersection turns, hazardous errors including driving outside of the confines of the lane), performance can be assessed before and after the training protocol to determine if more emphasis on specific driving skills yields improvement in those aspects of driving.
The potential for functional neuroimaging to evaluate the impact of contextual interventions on the underlying neural activation patterns required to perform those tasks is another possibility for future study. Rehabilitation-induced changes in the fMRI BOLD signal with corresponding improvements in functional outcomes have been observed in recent task-based (Könönen et al., 2012) and RS-fMRI studies (Fan et al., 2015) evaluating motor function. A prospective, intervention-based study aimed to train stroke patients on complex driving maneuvers in combination with a task-based fMRI study of driving simulator performance could test the hypothesis that a specific training program increases the consistency in activation of the driving network that was observed such that IS patients more closely resembled the control activation patterns.

Expansion of fMRI Findings

The subgroup analysis presented in Chapter 3 indicated that SAH patients were more impaired on the complex aspects of the driving simulation than IS patients, but neuroimaging analysis of SAH patients is not presented in this thesis. This is due to time constraints, and the fact that many SAH patients treated with neurosurgical clips cannot be scanned, as these clips are often not MRI-compatible and may cause artifacts on the images that compromise the quality of the data. A logical next step would be to conduct a task-based fMRI study in SAH patients who are able to undergo fMRI to understand the impact of SAH on the brain activation patterns during the driving tasks in comparison to control participants, as well as IS patients. The literature on task-based fMRI studies in SAH is very limited, but a study of the Sternberg Search Task by Ellmore, Rohlffs, & Khursheed, (2013) found a widespread change in activation patterns during the task, and suggested that the more diffuse hemodynamic responses observed in SAH patients could result from subcortical disconnections resulting from the bleed that reduced the overall efficiency of cognitive processing. In the context of driving, working memory is reasonably required for monitoring the environment and executing goal-directed maneuvers such as overtaking another vehicle or turning at an intersection. Based on the findings of Ellmore, Rohlffs & Khursheed (2013), one might hypothesize that patients also exhibit a more diffuse, non-specific hemodynamic response when performing cognitively demanding driving tasks such
as left turns with oncoming traffic, which would help explain why a behavioural impairment was observed during this task.

The fMRI results presented here are still preliminary and the relationship between differences observed in the activation patterns and the behavioural consequences requires further study. In the months following stroke, network reorganization is an indication of the progress in functional recovery and may not necessarily be an indication of inferior task performance. However, the assessment of task-based activation patterns in stroke patients in more complex, real-world tasks such as driving is largely unstudied. Although changes in activation patterns in stroke patients performing a task signify recovery, it remains to be understood if this results in more inefficient networks or variability in the networks that may lead to impaired performance during the most complex tasks. To answer this question, comparisons of patients who exhibit poor performance on the driving tasks should be compared to patients with high levels of performance. Studies of this nature will also help answer the fundamental question of how changes in areas of activation or functional connectivity during stroke recovery are related to long-term functional recovery.
5.3 Conclusions

Stroke is one of the leading causes of disability worldwide and often leaves patients with impairments in vision, motor function, and cognition, all of which may impair the ability to drive safely. Driving is an important aspect of daily living for stroke patients, as it enables a sense of independence, and allows individuals to fulfil their professional and personal obligations. Sudden cessation of driving after stroke is known to precede declines in the quality of life, and may engender feelings of isolation that lead to increased rates of depression. Although many stroke patients suffer severe deficits such as visual field cuts, or paralysis that would render them unable to resume driving, the diagnosis of stroke is not a definitive contraindication to safe driving, and many high-functioning patients with minimal deficits do resume driving. Of the patients who do return to drive, there is evidence that the there is an increased risk of experiencing a MVC, which raises the concern that stroke-related deficits are contributing to unsafe driving.

On behavioural measures of simulated driving performance, stroke patients demonstrated impairments on some aspects, but not all. On overall measures of driving performance (i.e. total driving errors) stroke patients were not different from controls on the full scenarios requiring that participants drive through urban and rural driving scenery, and a construction zone task where participants must execute fine motor control to avoid obstacles. On a bus following task requiring sustained attention and error monitoring, patients did commit more driving errors but did not differ from control participants on measures of task adherence. Further investigation of driving performance during the full scenarios indicated that stroke patients committed more driving errors than controls during intersection turns and committed more hazardous type driving errors.

The current study also assessed differences in driving performance among two stroke subtypes and found that SAH patients demonstrated greater impairments on the measures shown to differ between the stroke and control group than IS patients. Although both groups were age-matched and composed of good outcome, functionally independent patients, the IS group was much
younger than the average IS patient, and might represent a more favorable outcome relative to the general population of interest than the SAH group who were more representative of the SAH population. The results of the behavioural driving investigation highlight the importance of studying driving performance during complex driving situations, and comparing the results of different stroke subtypes to better characterize the driving impairments observed in chronic stroke patients.

In an fMRI investigation of the neural activation patterns underlying driving tasks of increasing complexity in IS patients, it was found that patients recruited the same core network of activation for driving performance as control participants during simple right and left turns at intersections, although to a lesser extent. Furthermore, as task complexity increased from left turns to left turns with oncoming traffic, the task-related increase in the magnitude of activation observed in control participants was not observed in IS patients. One can speculate on the mechanism underlying this observation as resulting from increased BOLD-signal variability resulting from the variability in ischemic lesion location, but this needs further study. Future research should aim to characterize the extent to which deviations in expected activation patterns are related to impaired driving performance by comparing patients with preserved and impaired performance. These results also encourage future investigation of tasks with increasing mental workload in stroke patients and tasks with relevance to complex, real-world activities.

In conclusion, an objective analysis of driving performance in functionally independent, chronic stroke patients revealed that although many aspects of performance were preserved, patients showed impaired performance during the most complex aspects of driving, especially during left turns with oncoming traffic. Furthermore, SAH patients were more impaired on these measures than IS patients. Functional MRI data of IS patients performing driving maneuvers of increasing complexity demonstrated the least consistent BOLD signal change during the most complex driving task, which may be suggestive of increased BOLD signal variability as a result of functional changes associated with stroke recovery. The results highlight the importance of studying driving tasks of varying complexity, as well as performance in stroke subtypes. To that end, continuing to improve our understanding of driving behaviour after stroke and the neural
and cognitive correlates will inform the development of new guidelines, screening measures and rehabilitation programs that allow patients who have the capacity to drive safely to maintain their driving privileges.
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