AN EVALUATION OF SOCIAL COGNITION AND SOCIAL EMOTIONAL OUTCOMES FOLLOWING PEDIATRIC STROKE

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Abstract

Following stroke, children experience cognitive sequelae, which may have a consequential impact on a child's functional outcomes and quality of life. An under-appreciated element of pediatric stroke is its impact on social cognition and, in turn, social-emotional outcomes. Stroke characteristics have been reported to be associated with social cognitive ability and social functioning. Neurological factors and their effect on social cognition remain to be better characterized. The objectives of the present research are to assess the impact of these stroke characteristics on social-emotional outcomes and evaluate social cognition as a mediator of this association.

The study results indicate that having a left hemisphere stroke predicts the likelihood of a child experiencing poorer social-emotional functioning, and that this association is fully mediated through social cognition. This work signals the importance of evaluating stroke characteristics when attempting to develop recovery phenotypes and the value of assessing for social cognitive deficits following stroke.

Dedication

This work is dedicated to all of the children with stroke and their parents who contributed to this study in the hopes of developing a greater understanding and optimizing care for those with pediatric stroke in the future. Your resiliency is an inspiration, and I feel fortunate to have worked with each of you.

Acknowledgements

First and foremost, I wish to acknowledge the support and guidance of my supervisor Dr. Mary Desrocher. It is hard to circumscribe into words how dedicated you are to your students, the program, and to the greater good. I am grateful for your kindness, support, and incisive feedback, and look forward to learning from you in the years to come. I have also had the privilege of working at The Hospital for Sick Children under the supervision of Dr. Robyn Westmacott, a person whose generosity shows no bounds. Thank you, Robyn, for being so open and accepting of students and their ideas, and for your help in the conceptualization and feedback on these projects. I look forward to many more years of collaborating and learning from you as both a clinician and researcher. I am fortunate to have been able to continue to collect this data throughout the COVID-19 pandemic, and this project would not have been possible without the mentorship and support of my fellow lab mate, Claire Champigny. Thank you for acting as the frontal lobes for this project, for your caring nature, your baking, and for the many things both big and small that you have done to help me throughout my master's degree. Thank you to my cohort and lab mates for their guidance throughout this degree, and to the faculty and Barb, Lori, and Freda for answering all questions with a friendly smile. Lastly, but certainly not least, thank you to my parents and my partner Michael. I truly feel that I have won the parent lottery. Thank you, mum and dad, for your endless support, love, and encouragement. It has made all of the difference and I wouldn't be where I am today without you. Mike, thank you for moving across the country so that I can pursue my goals, for making every day brighter, and for your love and support.

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Background

Pediatric stroke describes cerebrovascular infarction occurring in infants or children at any age. It includes a variety of mechanisms, including arterial ischemia, venous thrombosis, or cerebral hemorrhage. Its yearly incidence rate is estimated at 23-37 per 100,000 infants and 1-13 per 100,000 children (deVeber et al., 2017), qualifying it as an uncommon event. Pediatric stroke can be further sub-classified into development-specific categories of perinatal and childhood stroke according to the age at which the cerebrovascular event takes place. Perinatal stroke is defined as occurring between 20 weeks' gestation to 28 days after birth, while childhood stroke occurs between 1 month and 18 years of age (Westmacott et al., 2018). Despite being an uncommon condition in children, unfortunately, 50% to 80% of those affected by stroke experience long-term neurological sequelae (Anderson et al., 2014a; Felling et al., 2020; Kolk et al., 2011). Pediatric stroke impedes further childhood development and impacts both the quality of life of those children affected as well as their families (Malone & Felling, 2020). Sequelae can be broad, with impairments that can include language, motor, cognitive, emotional, and behavioural deficits (deVeber et al., 2017; Westmacott et al., 2009). While a majority of the research to date has focused on risk factors and mechanisms following pediatric stroke to prevent further events, understanding how stroke affects subsequent child developmental processes and brain-behaviour relationships has received less attention, and yet is of utmost importance to direct rehabilitation and optimize social function (Gordon et al., 2015).

Impact of Pediatric Stroke Characteristics on Post-Stroke Outcomes

The available literature suggests that there are stroke-related factors that interfere with the normative cognitive development of children in those who suffered a stroke. Those with perinatal stroke have greater overall intellectual ability impairments when compared to those

with childhood stroke (Allman & Scott, 2013; Westmacott et al., 2010, 2018), while those with childhood stroke are particularly susceptible to executive functioning deficits when compared to those with perinatal stroke (Long, Anderson, et al., 2011; Westmacott et al., 2018). Other contributing factors to post-stroke neuropsychological function in children include lesion location, affected hemisphere, stroke mechanism, and post-stroke seizure disorders (de Montferrand et al., 2019; Everts et al., 2008; Malone & Felling, 2020; Wagenaar et al., 2018; Westmacott et al., 2010; Yvon et al., 2018). Cognitive impairments following stroke have an extensive impact on a child's life, affecting academic, behavioural, and social function (Greenham et al., 2016). Academically, children with stroke are more likely to require accommodations at school and score significantly lower than peers across academic domains, including reading, reading comprehension, spelling, and math (Champigny et al., 2020). Behaviourally, children with stroke and associated cognitive impairment experience greater impulsivity (Blom et al., 2003), instability in mood (Eeg-Olofsson & Ringheim, 1983), and attention-deficit hyperactive disorder related symptoms than children within the general population (Everts et al., 2008). Such difficulties following stroke are reported to affect self-esteem and contribute to greater social problems (De Schryver et al., 2000; Everts et al., 2008). Understanding how various post-stroke neurological characteristics impact brain-behaviour relationships and subsequently influence long-term outcomes is essential for developing appropriate targets for rehabilitation on an individualized basis.

Social-Emotional Functioning Following Pediatric Stroke

An integral part of development during childhood is for a child to learn how to interact with others and develop social relationships beyond the immediate family unit. Normative brain maturation and function has clear associations with the development of social skills,

underscoring the importance of neural substrates in supporting the development of social behaviour (Stanley & Adolphs, 2013). Social skills are increasingly being recognized as particularly vulnerable following stroke, as these skills are developed throughout the gradual brain maturation from infancy to early adulthood and are shaped by social experiences and neurodevelopment (Greenham et al., 2018). Effective social skills influence positive social functioning, with vital downstream effects on academic and educational success and quality of life (Gordon et al., 2015; Greenham et al., 2016). Given the personal and societal importance of social-emotional functioning to post-stroke outcomes (Gomes et al., 2014), it is essential to better elucidate the determinants of social-emotional functioning following stroke. With such understanding, it can become possible to identify early impairment and risk factors, and thus direct early therapeutic interventions.

Social Cognition as a Potential Determinant of Social Emotional Functioning

One key potential determinant of social-emotional functioning following pediatric stroke is social cognition. Social cognition has been operationalized as the processes involved in recognizing, understanding, decoding, and responding to social information (May et al., 2017). Models of social cognition that underlie efficient social functioning include effectively processing social cues, possessing empathy in understanding another person's feelings and experience, as well as being able to understand the intentions of others (Adolphs, 2009; Milders, 2019; Ochsner, 2008). Models of social cognition often include two key domains: facial affect recognition and theory of mind. Facial affect recognition consists of perceiving facial features and categorizing the emotion based on the perceptual features that are detected (Rigon et al., 2018). Theory of mind refers to the ability to make inferences about the thoughts, intentions, and beliefs of others to help in understanding and predicting another's intentions and behaviours

(Muller et al., 2010; Saxe & Baron-Cohen, 2006). It is posited that impairments in either of these social cognitive domains is likely to result in poor social outcomes (Adolphs, 2009; Stanley & Adolphs, 2013).

Stroke Characteristics and their Impact on Social-Cognition

To date, very few studies have specifically evaluated social cognition following pediatric stroke. Greenham et al., (2018) provided a limited evaluation of social cognition in a pediatric stroke population, which was restricted to an evaluation of affect recognition. Theory of mind, the ability to understand the feelings and intentions of others, incorporates both affect recognition and affect processing. It represents an important dimension of social cognition that has only recently been first reported in a pediatric stroke population. Ryan et al. (2021), were the first to report on theory of mind in a pediatric stroke population. Relative to typically developing controls, their arterial ischemic stroke group performed significantly worse on measures of affect recognition and theory of mind, with impaired theory of mind associated with increased peer problems (Ryan et al., 2021). Furthermore, stroke characteristics including lesion size, lesion location, and the affected arterial territory were associated with performance levels on the theory of mind task. This study provides early evidence for measurable impairment of social cognition in a pediatric stroke sample and its potential downstream effects on social outcomes (Ryan et al., 2021). There are a number of considerations around the association between stroke characteristics, social cognition, and social-emotional outcomes that remain unaddressed. Ryan et al. (2021) included children with arterial ischemic stroke and limited their evaluation of stroke characteristics to lesion size, arterial territories affected, and lesion location, and opted to only use one assessment measure to quantify social cognitive ability. The extent to which social cognition mediates or fully accounts for the association between stroke characteristics and social

outcomes remains unexplored, and the question of whether social cognition impacts other aspects of social-emotional functioning such as emotion regulation (i.e., internalizing behaviours) remains unanswered.

The impact of different stroke mechanisms and stroke characteristics on social cognition also merits further research attention. Etiologically, the focus in pediatric stroke to date has been on ischemic stroke and has not included an evaluation of hemorrhagic stroke, yet it is estimated that hemorrhagic stroke accounts for approximately 50% of pediatric stroke injuries (Beslow et al., 2010; Lo, 2011; Yvon et al., 2018). Given the mechanistic differences in the type of brain injury they each produce, including both stroke types within pediatric stroke studies of social cognition is important (Fuentes et al., 2016; Yvon et al., 2018). Indeed, recent findings suggest that children with hemorrhagic stroke experience better motor and functional outcomes than their ischemic counterparts; however, it remains unclear whether hemorrhagic stroke patients experience better social-emotional outcomes as well (Blom et al., 2003; Yvon et al., 2018). In the adult stroke literature it has been well established that social cognition is impaired following stroke (Adams et al., 2019; Pluta et al., 2017; Yuvaraj et al., 2013); however, studies have concentrated on either assessed arterial ischemic stroke or have collapsed both arterial ischemic stroke and hemorrhagic stroke groups together (Nissje et al., 2019a, Nissje et al., 2019b, Sensenbrenner et al., 2020), leaving uncertain if there are differential effects of these mechanisms on social cognition.

Other stroke factors which can influence social cognition are lesion location and the hemisphere affected. A number of studies have recognized lesion location as a determinant of cognitive outcomes, with lesions within specific functional neuroanatomical areas mapping onto associated cognitive and behavioural processes (Bates et al., 2003; Biesbroek et al., 2015;

Fuentes et al., 2016; Zhao et al., 2018). For example, frontal lesion locations in pediatric stroke are associated with deficits on tests that evaluate cognitive and social-emotional processes aspects of executive functioning such as cognitive flexibility, emotional control, and goal setting (Long, Spencer-Smith, et al., 2011). Furthermore, children with frontal lobe lesions have significantly lower social competence when compared to those with more posteriorly located or non-frontal lesions (Trauner et al., 1996). The brain biological relationship of pre-frontal and lateral temporal cortical processes supporting social cognition would support the hypothesis that damage to the prefrontal and lateral temporal lobes following pediatric stroke is likely to negatively impact social cognition; however, this has not yet been tested and further exploration is warranted (Amodio & Frith, 2006).

The hemisphere affected by pediatric stroke may also be an important factor, given the evidence base that supports the important of the role of the right hemisphere in social information processing in children and adults (Adolphs, 2009; Saxe & Wexler, 2005) (Voeller, Hanson, & Wendt, 1998; Semrud-Clikeman, Fine, & Zhu, 2011). Within the adult stroke literature, greater impairments in social cognition have been noted for stroke lateralized to the right hemisphere compared to the left (Hewetson et al., 2021; Ross & Monnot, 2008; Yuvaraj et al., 2013). This has been further supported by studies in adult hemispherectomized patients, where right hemispherectomized patients showed the most severe impairments in social cognition, despite high levels of family support and social engagement. In contrast, left hemispherectomized patients displayed only mild social cognitive functioning difficulties, which were mostly attributed to language limitations (Fournier et al., 2008).

After stroke, children are reported to have greater social difficulties and psychological problems both in the short-term, and the long-term (Anderson et al., 2014b; Gordon et al., 2015;

Greenham et al., 2017). Notably, there is evidence that suggests children have a hard time connecting with friends and peers following stroke (Everts et al., 2008), experience more social rejection (Steinlin et al., 2004), and have poorer social participation (Anderson et al., 2014a; Greenham et al., 2017). Social difficulties impact a child's self-esteem and may lead to psychiatric issues and reduced quality of life (Max et al., 2002). Children with stroke are reported to experience greater rates of psychiatric issues (Max et al., 2002), making it critical to understand how to reduce their risk of adverse outcomes. Furthermore, increased psychiatric rates in children with stroke relative to other pediatric clinical conditions cannot be explained by differences in age, gender, SES, race, family psychiatric history, or the presence of a chronic medical condition (Max et al., 2002). Identifying how changes to social cognition in addition to stroke characteristics impacts social-emotional outcomes may provide greater insight as to how stroke leads to worse outcomes. In turn, it may signal the value of directed intervention strategies to help mitigate the impact of stroke on children's social and emotional outcomes.

Given the importance of social-emotional well-being to successful education, social functioning, quality of life, and mental health ascertaining its determinants following pediatric stroke and risk factors for its impairment represents an important unmet need for those individuals, families, and therapeutic communities. Therefore, this thesis research investigates whether distinct stroke characteristics (lesion location, affected hemisphere, and mechanism) are associated with impaired social cognition and whether social cognition is an important mediator of social-emotional outcomes.

Objectives and Hypotheses

Objectives

1) To evaluate social-emotional outcomes following pediatric stroke and their association to stroke characteristics including lesion location, affected hemisphere, and mechanism.
2) To evaluate measures of social cognition following pediatric stroke and their correlation with social-emotional outcomes.
3) To determine the mediating effect of social cognitive processes on the association between social-emotional outcomes and stroke characteristics.

Hypothesis 1: In pediatric stroke, lesion location, affected hemisphere, and mechanism are associated with social-emotional outcomes, with the direction of the associations as follows:

a) ***Lesion location:*** Anterior hemispheric injuries predominantly affecting the frontal and temporal lobe lobes within the territory of the anterior and middle cerebral arteries are associated with greater impairment on measures of social-emotional outcomes, than strokes outside this distribution.
b) ***Affected hemisphere.*** Right hemispheric stroke is associated with poorer social-emotional outcomes than left hemispheric stroke.
c) ***Stroke Mechanism.*** Arterial ischemic injury is associated with poorer social-emotional outcomes than hemorrhagic injury (hemorrhage and venous infarction).

Hypothesis 2: Social cognition can be impaired by pediatric stroke and when it is affected, performance on social cognitive tasks is correlated with social-emotional outcomes.

Hypothesis 3: Social-emotional outcomes are mediated through social cognitive processes which are affected by stroke characteristics including location, laterality of the affected hemisphere, and mechanisms.

Methods

Design

Cross-sectional study of social cognition in a cohort of children and young adults with a past history of arterial ischemic stroke, venous thrombosis, or cerebral hemorrhage.

Participants

A total of 42 youth participated in the current study at the Hospital for Sick Children (SickKids) in Toronto, Canada. There were three sources of recruitment for this cohort including those who were:

a) Previously enrolled in the hospital's Children's Stroke Program

b) Previously in the Canadian Ischemic Pediatric Stroke Registry (deVeber et al., 2017)

c) Previously registered in the outpatient clinic of the Department of Neurosurgery who were identified as having had pediatric stroke (Dr. Peter Dirks and his team).

Inclusion criteria were deliberately broad to capture the heterogeneity of the pediatric stroke population, as well as to capture common medical and psychiatric co-morbidities. Participants met the following inclusion criteria:

a) Chronic ischemic or hemorrhagic non-traumatic stroke: stroke event >6 months previously.

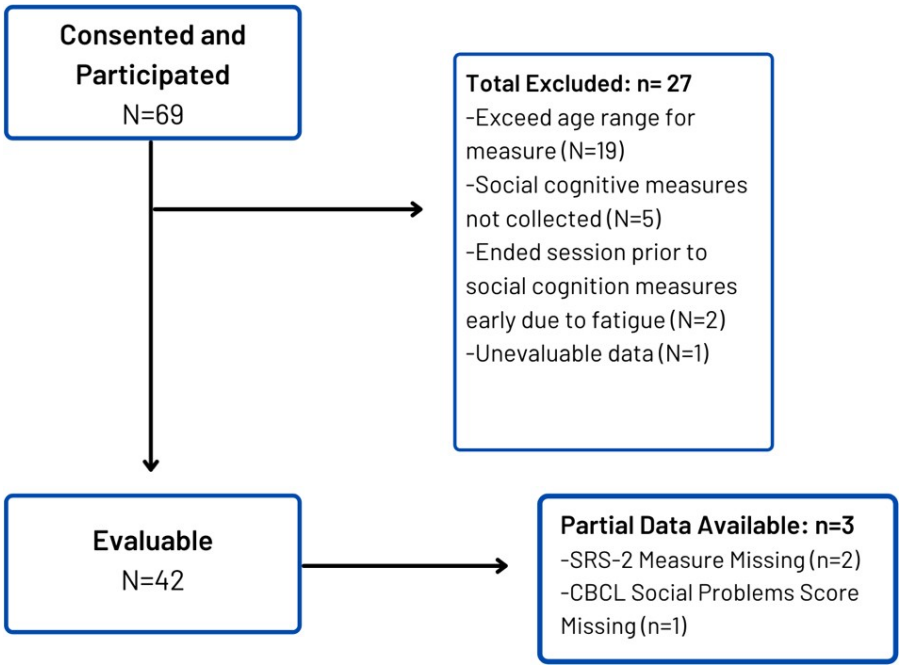
b) Diagnosis confirmed through review of hospital medical records and/or through a review of neuroradiological reports indicating features of ischemic stroke, venous thrombosis or cerebral hemorrhage.

c) Ages 6-25 years old.

d) Fluency in English of both the participant and caregiver/guardian. Those with ischemic stroke or hemorrhage associated with traumatic brain injury were excluded.

This research study was undertaken at the Hospital for Sick Children (SickKids) between January 2021 and June 2021 in the Psychology Department. Eligible participants from the databases were first sent a letter informing them of the study, and then were contacted by phone after two weeks by the research coordinator (C.C. or S.F.) to schedule a time to participate in the study. Informed consent was obtained from all individuals prior to participation in accordance with the declaration of Helsinki. Assent was obtained from children who were below the age of 16, consistent with Health Canada guidelines for research participation (Government of Canada, n.d.). The Hospital for Sick Children Research Ethics Board approved all aspects of the study design (REB Number: 1000070780) and confirmed study compliance with the Ontario Personal Health Information Protection Act (PHIPA), 2004. Approval for the present analyses were granted by both the Hospital for Sick Children and from the York University Ethics Review Board.

Figure 1: Participant Flow Through Study



As seen in Figure 1, there were 69 participants who were consented and went through study screening for inclusion. The 27 participants who were excluded from the current study either did not receive social cognitive measures that were needed for inclusion in the evaluable group or were beyond the age range of the social cognition measures included in the current research (ages 6-16). A total of 42 participants completed the study protocol and formed the fully evaluable study group that is reported. Of the participants who were included in the present study, two participants with evaluable data did not receive the SRS-2 measure, and one participant did not have a CBCL social problems standard score available for evaluation.
The present study was one half of a research project, where the other half of the study evaluated determinants of other aspects of cognition (i.e., attention and memory) following pediatric ischemic and hemorrhagic stroke.

Experimental Procedures

Measures

Neurological Features of Stroke Injury

Clinical diagnosis of pediatric stroke followed usual standards of hospital assessment and care. Cranial MRIs were performed at the time of participants admission to hospital with their cerebrovascular event. Reporting neuroradiologists within the Diagnostic Imaging Department at the Hospital for Sick Children evaluated the lesion characteristics including lesion location, arterial distribution (if applicable), affected hemisphere, and stroke mechanism. Infarcts were identified as hyperintense regions within the affected hemisphere on MRI with diffusion-weighted imaging. The radiological report for each participant was evaluated by S.F. on the SickKids internal online medical record system to code the following stroke characteristics: the lesion location (coded as either possessing frontotemporal involvement or no frontotemporal

involvement), affected hemisphere (coded as right or left hemispheric injury), and to confirm stroke mechanism (coded as hemorrhagic or ischemic). Participants provided consent for use of their clinical cranial MRIs within the current study.

Social Cognitive Measures

Developmental NEuroPSYchological Assessment – Second Edition (NEPSY) (Brooks et al., 2010)**.** The NEPSY is a developmentally-based standardized neuropsychological assessment normed for children between the ages of 3-16 (Davis & Matthews, 2010). The NEPSY contains two subtests of social cognition: affect recognition and theory of mind.

The affect recognition subtest evaluates how well a child can identify how other children might be feeling, and consists of both timed and untimed components. The task involves discriminating between a series of children's faces and identifying which two children are experiencing the same emotion based on facial expression. The child's sum of correct answers for the 34 items is converted to an age-based standard score for comparison across ages. A higher standard score is indicative of better performance (Brooks et al., 2010).

The theory of mind (ToM) subtest evaluates belief, intentions, deception, emotions and the ability to understand that others have their own thoughts, ideas, and feelings that may be different from one's own. Additionally, the ToM test evaluates the ability to understand how emotion relates to social context. During the test, the participant was read a series of social situations and stories, or was shown pictures of social scenes and was asked questions about the main intention and/or beliefs of the person in the story (Brooks et al., 2010). The child's sum of correct answers for the 28 items was converted to an age-based standard score for comparison across ages. Both subtests were given to all participants ages 6-16.

The Social Responsivity Scale—Second Edition (SRS) (Constantino & Gruber, 2012). The SRS is a standardized norm-referenced parent questionnaire which is used to evaluate social cognition and social behaviours across a variety of different settings in children ages 4-18 years of age (Bruni, 2014). The questionnaire consists of 65 items, with Likert-scale response options asking about a child's behaviour over the past six months. The response options range from 0 (not true of my child's behaviour) to 3 (almost always true of my child's behaviour). Raw scores for all of the items will be summed and converted to standardized scores, with a higher standardized score being indicative of more severe social impairment. Five subscale scores are provided: social awareness, social cognition, social communication, social motivation, and restricted interest. The only scale used in statistical analyses is the social cognition subscale, however, the other scores are located in the supplementary materials (refer to Supplementary Table 1). The questionnaire was administered to all parents with children ages 6-18.

Social Emotional Functioning

Achenbach Child Behaviour Checklist (CBCL) (Achenbach, 1991). The CBCL is a one of the most widely used standardized norm-referenced parent report forms used to assess emotional, behavioural, and social functioning (Saad et al., 2017). The form was given to parents of children 6-18 years of age. The checklist has previously been used to evaluate social and emotional difficulties in a pediatric stroke population (Trauner et al., 2001; Williams et al., 2019). The form consists of 111 items which query difficulties with emotion regulation and behavioural functioning over the past 6 months. The response options range from 0 (not true of my child's emotions and behaviour) to 3 (very true or often true of my child's emotions and behaviour). Raw scores for all items will be summed and converted to standardized scores, where a higher score is indicative of greater social and emotional functional problems. Eight

subscale scores are provided: withdrawn, somatic complaints, anxious/depressed, social problems, thought problems, attention problems, delinquent behaviour, and aggressive behaviour. Three additional symptom scales are available, which include: internalizing symptoms, externalizing symptoms, and total problems. For the purposes of the present research and its objectives, social problems, internalizing, and total problems will be evaluated within the statistical analyses as they most directly assess social functioning and symptoms related to anxiety and depression. Internalizing behaviours such as anxiety and depressive symptoms are characterized by social withdrawal and have associations with the understanding of other's emotions in typically developing youth, making it a relevant outcome measure worthy of evaluation (Göbel et al., 2016).

Experimental Session

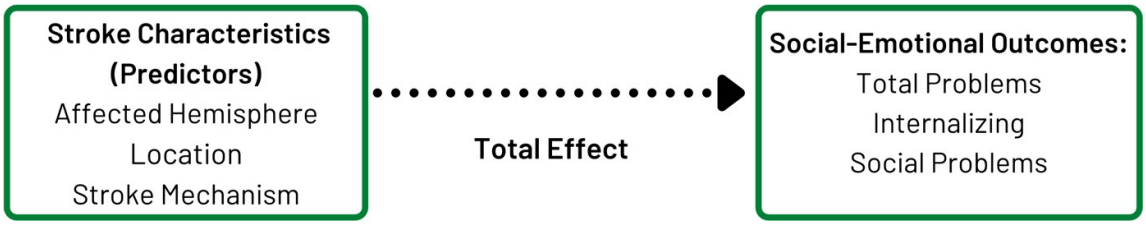
Participants completed the social cognition neuropsychological assessment (NEPSY) at SickKids over the course of one hour and parents completed the questionnaires (SRS and CBCL) while the participant was completing testing. At the end of the assessment period, the assessor (S.F. or C.C.) followed up with parents to answer clarification questions around any of the questionnaire items.

Data Analysis Plan

To assess social cognition using the NEPSY and SRS as potential mediators of the relationship between neurological features of stroke injury and social-emotional outcomes, mediation analysis was performed using the model described by Baron and Kenny (Baron & Kenny, 1986). As a first step, neurological variables which significantly predicted the outcome, were determined. This is referred to as the total effect. Univariate multiple linear regressions were evaluated with stroke mechanism (hemorrhagic or ischemic), affected hemisphere (right or

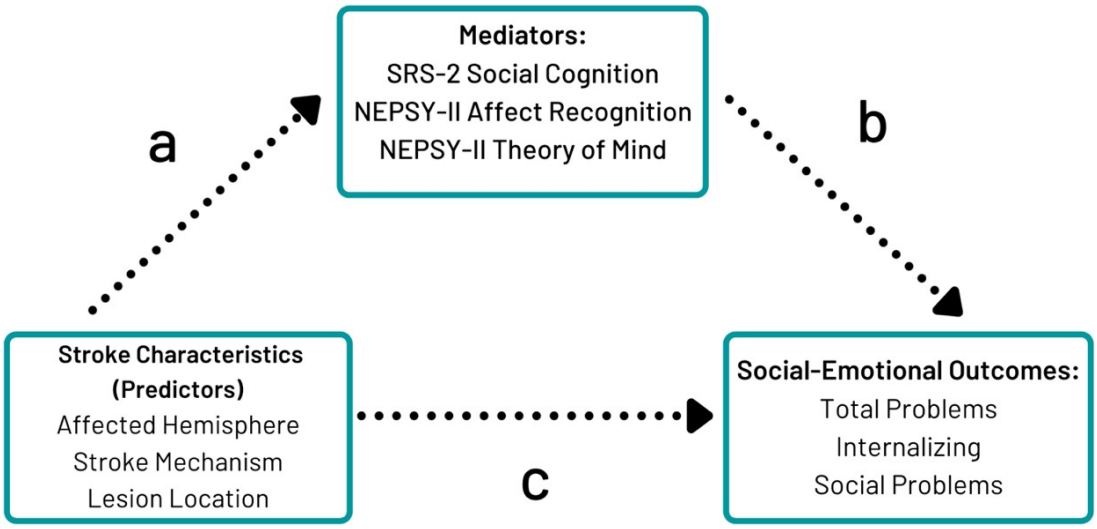
left), and lesion location (fronto-anterior temporal involvement or no fronto-anterior temporal involvement) regressed onto each of the social-emotional outcome variables (CBCL total problems, CBCL internalizing, and CBCL social problems) (Refer to Figure 2). Consistent with the Baron and Kenny model, only significant predictors of social-emotional outcomes were considered within subsequent mediation analyses (Baron & Kenny, 1986).

Figure 2: Univariate linear regressions



Indirect associations were subsequently evaluated to determine whether social cognition (NEPSY affect recognition, NEPSY theory of mind, and the SRS social cognition subscale), mediates the relationship between the stroke characteristics (location, affected hemisphere, and mechanism) and the social emotional outcome variables (internalizing, social problems, and total problems). Figure 3 illustrates the hypothetical mediation model where stroke characteristics predict social cognition and where social cognition, the mediator, in turn determines social-emotional outcomes, following pediatric stroke. Three mediation models are evaluated, with each mediation model only including one social-emotional outcome variable in each model.

Figure 3: Mediation Analysis



Note. Three pathways were tested: the association between stroke characteristics with social-emotional outcomes (path c), the association of stroke characteristics with social cognition (path a), and the association of social cognition with social-emotional outcomes (path b) (Figure 2).

Structural equation modelling (SEM) was conducted using the Lavaan package version 0.6-7 of R statistical software version 1.3.1093 to assess the significance of the indirect effects at an α of 0.05 (Rosseel, 2012). Direct and indirect associations were examined between affected hemisphere and the three CBCL outcome measures (total problems, internalizing, and social problems); this was done using the product of coefficients method with bootstrapping 1000 times to obtain 95% confidence intervals of the mediated effect (Mackinnon, Lockwood, Hoffman, West & Sheets, 2002). Statistical assumptions of normality, homoscedascity, and linearity were inspected for each regression model.

Results

Table 1: Participant Demographics (N=42 participants)

Age	
Mean + SD	10.89 + 3.065
Range	6.01-16.36
Sex	
Females	N= 18 (43%)
Males	N= 24 (57%)
Affected hemisphere	
Right hemisphere	N= 17 (41%)
Left hemisphere	N= 25 (59%)
Stroke Type	
Arterial Ischemic	N= 29 (69%)
Hemorrhagic	N= 13 (31%)
Imaging Classification	
Frontal or temporal or multiple	N= 21 (50%)
Outside of frontal temporal	N= 21 (50%)
Stroke Onset	
Neonatal	N= 21 (50%)
Childhood	N= 21 (50%)
FSIQ	
Mean + SD, (P.R.)	88.33 + 21.072, (21st)
Range	45.00-124.00, (<0.1-95th)
NEPSY – Affect Recognition	
Mean + SD, (P.R.)	95.24 +15.88, (37th)
Range (P.R.)	65.00-125.00, (1st-95th)
NEPSY—Theory of Mind	
Mean + SD, (P.R.)	90 + 16.52, (25th)
Range (P.R.)	64.00-117.00, (1st-87th)
SRS	
Mean + SD, (P.R.)	107.03+13.62, (68th)
Range (P.R.)	85.00-138.00, (16th-99th)
CBCL Total Problems	
Mean + SD, (P.R.)	106.50 + 16.25, (66th)
Range (P.R.)	63.00-138.00, (1st-99th)
CBCL Internalizing	
Mean + SD, (P.R.)	106.55 + 17.42, (66th)
Range (P.R.)	78.00-135.00, (7th-99th)
CBCL Social Problems	
Mean + SD, (P.R.)	110.78 + 11.92, (75th)
Range (P.R.)	100.00-148.00, (50th-99.9th)

Note. P.R. stands for percentile rank**.**

Table 2: Participant Demographics Organized by Stroke Mechanism (N=42 participants)

	Arterial Ischemic Stroke (N=29)	**Hemorrhagic Stroke or Venous Infarction (N=13)**
Age	**Mean + SD:** 10.87+ 2.744	**Mean + SD:** 10.93+3.80
Sex		
Female	N= 10	N= 8
Male	N= 19	N= 5
Affected Hemisphere		
Right	N= 18	N= 7
Left	N= 11	N= 6
Imaging Classification		
Frontal/Temporal or Multiple	N= 16	N= 8
Outside Frontal/Temporal	N= 13	N= 5
Stroke Onset		
Neonatal	N= 14	N= 7
Childhood	N= 15	N= 6
FSIQ		
Mean + SD	87.75+19.46	89.61+25.12
P.R.	19th	23rd
NEPSY – Affect Recognition		
Mean + SD	98.27+ 15.08	88.461+16.12
P.R.	45th	21st
NEPSY—Theory of Mind		
Mean + SD	91.62 + 15.90	86.38 + 17.96
P.R.	27th	18th
SRS		
Mean + SD	106.82 + 14.49	107.50 + 11.91
P.R.	66th	68th
CBCL Total Problems		
Mean + SD	108.28 + 18.00	102.54 + 11.00
P.R.	70th	55th
CBCL Internalizing		
Mean + SD	107.55 + 20.33	104.30 + 8.00
P.R.	68th	61st
CBCL Social Problems		
Mean + SD	113.36 + 13.01	105.23 + 6.60
P.R.	81st	63rd

Note. P.R. stands for percentile rank.

Table 3: Participant Demographics Organized by Affected Hemisphere (N=42 participants)

	Left Hemisphere (N=25)	Right Hemisphere (N=17)
Age		
Mean + SD	11.08 + 2.97	10.60 + 3.26
Sex		
Females	N= 10	N= 8
Males	N= 15	N= 9
Imaging Classification		
Frontal/Temporal or Multiple	N=11	N= 7
Outside Frontal/Temporal	N= 14	N=10
Stroke Onset		
Neonatal	N= 15	N= 6
Childhood	N= 10	N= 11
FSIQ		
Mean + SD (P.R.)	85.40 + 21.90, (16th)	92.65 + 19.63 (30th)
NEPSY – Affect Recognition		
Mean + SD (P.R.)	96 + 15.48, (40th)	94.11 + 16.89, (34th)
NEPSY—Theory of Mind		
Mean + SD (P.R.)	87.76 + 14.85, (19th)	93.29 + 18.69, (32nd)
SRS		
Mean + SD (P.R.)	112.04 + 11.72, (79th)	99.5 + 13.08, (47th)
CBCL Total Problems		
Mean + SD (P.R.)	113 + 14.43, 81st	96.94 + 14.18, (40th)
CBCL Internalizing		
Mean + SD (P.R.)	111.32 + 16.51, (77th)	99.53 + 16.74, (47th)
CBCL Social Problems		
Mean + SD (P.R.)	115.17 + 13.16, (84th)	104.59 + 6.03, (61st)

Note. P.R. stands for percentile rank.

Table 4: Participant Demographics Organized by Lesion Location (N=42 participants)

	Frontotemporal Involvement (N=21)	Non-frontotemporal Involvement (N=21)
Age		
Mean + SD	10.99 + 3.06	10.79 + 3.14
Sex		
Females	N= 14	N= 11
Males	N= 7	N= 10
Stroke Onset		
Neonatal	N= 9	N= 12
Childhood	N= 12	N= 9
FSIQ		
Mean + SD (P.R.)	85.10 + 23.32, (16^{th})	91.57 + 18.56, (27^{th})
NEPSY – Affect Recognition		
Mean + SD (P.R.)	95.48 + 17.24, (37^{th})	95.00 + 14.83, (37^{th})
NEPSY—Theory of Mind		
Mean + SD (P.R.)	87.71 + 15.17, (19^{th})	92.29 + 17.85, (30^{th})
SRS		
Mean + SD (P.R.)	109.85 + 13.64, (73^{rd})	104.20 + 13.34, (61^{st})
CBCL Total Problems		
Mean + SD (P.R.)	104.86 + 19.25, (61^{st})	108.14 + 12.84, (70^{th})
CBCL Internalizing		
Mean + SD (P.R.)	103.67 + 18.77, (58^{th})	109.43 + 15.89, (73^{rd})
CBCL Social Problems		
Mean + SD (P.R.)	109.86 + 9.99, (73^{rd})	111.75 + 13.86, (77^{th})

Note. P.R. stands for percentile rank.

Relationship between Stroke Characteristics and Social-Emotional Outcomes

For all regression models, diagnostic analyses confirmed there was no collinearity among non-interaction variables. Model residuals were approximately normally distributed. Plots of the residuals against fitted values did not suggest violation of homoscedascity or linearity. Cook's distance did not indicate the presence of influential observations.

To estimate the total effect of lesion location, affected hemisphere, and stroke mechanism with social-emotional outcomes, three separate multiple linear regression models were

performed with the aforementioned stroke characteristics as the predictors in all three models with one social-emotional outcome variable (CBCL total problems, CBCL internalizing, CBCL social problems) included as the dependent variable in each model. Affected hemisphere was a significant predictor of social-emotional outcomes in all three models (Total Problems: b=-16.62, p<0.05, Internalizing: b=-12.731, p<0.05, and Social Problems: b=-10.937, p<0.05). Stroke mechanism was only a significant predictor of CBCL social problems (b=-8.321, p<0.05). Lesion location did not significantly predict any of the social emotional outcomes. Consequently, analysis of the significance of the indirect effects was only performed with the significant predictors affected hemisphere (all three mediation models), and stroke mechanism (one mediation model where CBCL social problems is the outcome variable).

Table 5

Multiple regression model – Stroke characteristics and CBCL Total Problems

Effect	Estimate	SE	95% CI		*p*
			LL	UL	
Intercept	118.130	4.128	109.773	126.486	0.000**
Stroke mechanism	-5.447	4.791	-15.145	4.251	0.263
Affected hemisphere	-16.616	4.506	-25.737	-7.494	0.000**
Lesion Location	-6.438	4.464	-15.474	2.599	0.157

Note. *p <0.05 (one-tailed), **p<0.01 (two-tailed).

Table 6

Multiple regression model – Stroke characteristics and CBCL Internalizing

Effect	Estimate	SE	95% CI		*p*
			LL	UL	
Intercept	116.843	4.806	107.112	126.572	0.000**
Stroke mechanism	-3.549	5.578	-14.841	7.743	0.529
Affected hemisphere	-12.731	5.246	-23.351	-2.110	0.020*
Lesion Location	-8.089	5.197	-18.609	2.434	0.128

Note. *p <0.05 (one-tailed), **p<0.01 (two-tailed).

Table 7

Multiple regression model – Stroke characteristics and CBCL Social Problems

Effect	Estimate	SE	95% CI		*p*
			LL	UL	
Intercept	120.547	3.102	114.262	126.831	0.000**
Stroke mechanism	-8.321	3.470	-15.352	-1.290	0.022*
Affected hemisphere	-10.937	3.275	-17.573	-4.301	0.002**
Lesion Location	-5.063	3.271	-11.690	1.565	0.130

Note. *p <0.05 (one-tailed), **p<0.01 (two-tailed).

Relationship between Social Cognitive Measures and Social-Emotional Outcomes

Table 2 presents the correlations evaluated between the social cognitive measures, and social-emotional outcome measures. Significant positive correlations were established between the SRS-2 and CBCL Total Problems, $r(38)= 0.58$, $p=0.000$, CBCL Internalizing, $r(38)=0.47$, $p=0.002$, and CBCL Social Problems $r(38)=0.58$, $p=0.000$. Additionally, a significant correlation

between was identified between NEPSY Theory of Mind and CBCL Social Problems, $r(38)=-0.40$, $p=0.010$.

Table 8

Bivariate correlations between social cognition measures and social-emotional outcomes

	CBCL Total Problems	CBCL Internalizing	CBCL Social Problems
1.NEPSY Affect Recognition	0.068	0.212	-0.173
2. NEPSY Theory of Mind	-0.099	0.058	-0.397**
3. SRS-2	0.578**	0.465**	0.576**

Note. *p <0.05 (one-tailed), **p<0.01 (two-tailed).

Relationship between stroke characteristics and social cognitive measures

Multiple linear regression analysis performed to predict social cognitive assessment scores revealed that affected hemisphere significantly predicted social cognitive scores indexed by the SRS social cognition subscale (b= -11.819, p <0.05). Conversely, lesion location and stroke mechanism were not predictive of any of the scores on any of the three social cognition measures, and none of the neurological variables were predictive of NEPSY affect recognition or NEPSY theory of mind scores.

Mediation of association between affected hemisphere and social-emotional outcomes

Given that affected hemisphere was a significant predictor (left hemisphere being worse than right) of both social cognition and social emotional outcomes, mediation analyses were conducted to evaluate the potential indirect effect of social cognition on the association between affected hemisphere and social-emotional outcomes. Diagnostic analyses confirmed that none of

the assumptions of linear regression were violated (normality, homoscedascity, linearity, influential cases, independence of observations, and collinearity). There was a significant indirect effect of affected hemisphere on CBCL total problems through the mediating variable of SRS social cognition (z=-2.25, p<0.05) (Refer to Table 5). Further, affected hemisphere was no longer associated with SRS social cognition (z=-1.734, p=0.083), suggesting that the effect of affected hemisphere on CBCL total problems was fully mediated by social cognition as indexed by the SRS. Consistent with the first mediation model, indirect effects testing within a second mediation model indicated that SRS social cognition significantly and fully accounted for the effect of affected hemisphere on CBCL internalizing through SRS social cognition (z=-2.115, p<0.05) (Refer to Table 5). The third mediation model evaluating social cognition as a mediator of the relationship between affected hemisphere and CBCL social problems indicated that affected hemisphere no longer predicted CBCL social problems, which possibly suggests full mediation, however the p-value for the indirect effect is not significant (z=-2.115, p=0.097) (Refer to Table 5). It would be worthwhile confirming this mediation finding further in a larger sample.

Mediation of the association between stroke mechanism and social-emotional outcomes

Mediation analysis evaluated the effect of stroke mechanism on CBCL social problems as mediated by social cognition and indicated that stroke mechanism is predictive of CBCL social problems (z=-2.98, p<0.05) consistent with the previous analyses (Refer to Table 9). Stroke mechanism did not predict social cognition, nor is the relationship between stroke mechanism and CBCL social problems mediated through social cognition.

Exploratory Analysis: Mediation of the association between lesion location and social-emotional outcomes

Lesion location is a significant predictor of CBCL total problems (z=-2.164, p<0.05), internalizing (z=-2.508, p<0.05), and social problems (z=-2.138, p<0.05) once taking into account the mediators. As an exploratory evaluation and a deviation from the Baron and Kenny model of mediation analysis, indirect effects were subsequently considered to determine whether the association between location and social-emotional outcomes is mediated through social cognition. The results of the mediation analyses suggest that social cognition did not mediate the effect of lesion location on social-emotional outcomes.

Table 9

Results from Mediation Models

Indirect Effects	**Estimate**	**SE**	**95% CI**		***p***
			LL	**UL**	
Affected Hemisphere→SRS→Total Problems	-9.039	4.098	-18.353	-2.324	0.027*
Affected Hemisphere→SRS→Internalizing	-10.552	4.990	-21.949	-2.594	0.034*
Affected Hemisphere→SRS→Social Problems	-4.281	2.581	-10.367	-0.622	0.097
Stroke Mechanism →SRS→ Social Problems	0.630	1.668	-2.090	4.793	0.706
Effects					
Affected Hemisphere→ Total Problems	-8.654	4.989	-18.768	1.009	0.083
Affected Hemisphere→ Internalizing	-3.383	6.255	-16.259	7.408	0.540
Affected Hemisphere→ Social Problems	-5.762	3.539	-13.005	0.856	0.104
Stroke Mechanism→ Total Problems	-5.510	4.771	-15.469	3.450	0.248
Stroke Mechanism→ Internalizing	-1.972	5.151	-12.679	7.920	0.702

Stroke Mechanism➔ Social Problems	-10.222	3.436	-17.510	-4.445	0.003
Lesion Location ➔ Total Problems	-9.303	4.299	-17.425	-0.748	0.030
Lesion Location ➔ Internalizing	-11.211	4.470	-19.654	-2.334	0.012
Lesion Location ➔ Social Problems	-7.525	3.519	-14.809	-1.065	0.032

Discussion

This research investigates the impact of pediatric stroke on social cognition and social-emotional outcomes and the extent to which the impact of stroke characteristics on social-emotional outcomes can be explained by social cognitive ability. There is limited knowledge of the effect of pediatric stroke injury on social cognitive functions. The current study is one of the first to evaluate whether pediatric arterial ischemic and hemorrhagic stroke impact social cognitive processes, such as affect recognition and theory of mind, and explore whether social cognition mediates the association between stroke characteristics and social-emotional outcomes. Distinct predictive stroke characteristics emerged, including affected hemisphere, which influences social-emotional outcomes; with the association between affected hemisphere and social-emotional outcomes being fully mediated by social cognition. The current study allowed for comparison of outcomes following arterial ischemic stroke and hemorrhagic stroke in terms of social cognition and social-emotional outcomes in a sample deemed relatively large, given the rare nature of this clinical population. This research also contributes to the pediatric hemorrhagic stroke literature, which is an underappreciated group, as few studies have evaluated outcomes following hemorrhagic stroke compared to ischemic stroke in pediatric samples (Yvon et al., 2018).

Predicting Social-Emotional Outcomes from Stroke Characteristics

Consistent with previous literature, this cohort had greater social-emotional difficulties following pediatric stroke when compared to normative data (Gomes et al., 2014), as characterized by the three CBCL subscales: total problems, internalizing symptoms, and social problems. In particular, the mean standard score on social problems is at the 75th percentile, suggesting that parents of children in this pediatric stroke cohort report more social problems than 75% of other children, as per the normative data. Poorer social-emotional outcomes were predicted by lesion laterality across all three subscales of the CBCL, and by stroke type on the CBCL social problems subscale.

Contrary to hypothesis 1a, children with right hemisphere stroke reported significantly fewer social-emotional difficulties when compared to those with left hemisphere stroke. It was anticipated that right hemisphere strokes would impact social-emotional functioning to a greater extent than left hemisphere strokes, given the high prevalence rates of changes in social participation (94.4%) and social problems following right hemisphere stroke in adults (Hewetson et al., 2021). Furthermore, prior reports of adults with right hemisphere stroke indicate that they exhibit greater social cognitive difficulties (Hewetson et al., 2021). This is one of the first studies within the current literature to look at hemispheric differences in relation to social-emotional outcomes in pediatric stroke. These novel findings suggest that lesion characteristics, particularly laterality, differentially affect children whose brains are still developing compared to adults whose brain development is comparatively slower. Regions that are known to support social cognitive processes, such as the right medial prefrontal and lateral temporal cortices, undergo rapid maturation in children, and are less functionally distinct than within the adult brain, indicating that other networks may be involved in social cognitive processes during development

(Ryan et al., 2021). It may be the case that children with left hemisphere stroke experience greater disruption of networks central to language than children with right hemisphere stroke, given that language is lateralized to the left in many people from a very young age (Gazzaniga, 2000; Geschwind et al., 2002). This disruption would be especially detrimental to social cognitive development, as language is essential to the development of social cognitive skills such as theory of mind (Garfield et al., 2001). Functionally, this may be due to the lack of input from the left hemisphere from the stroke injury impacting the subsequent development of interhemispheric communication between language-specific regions and the right frontotemporal cortex; this may mean that the information processed in language centres is unable to the reach right hemisphere to aid in social emotion processing. The corpus callosum provides relevant verbal input to the right hemisphere, whose role may be to contextualize the information to initiate an action or generate a response; thus, damage to the left hemisphere may affect language information from being passed from the left to right hemisphere (Ferre et al., 2020). Language provides the basis for beginning to understand the inner thoughts and intentions of others through social interactions, which provides the opportunity to develop social knowledge and awareness (Garfield et al., 2001). Understanding and successfully interpreting theory of mind-related tasks in children, such as the false-belief task, correlates with language abilities (de Villiers, 2007; Milligan et al., 2007). Overall, the finding that left hemispheric stroke leads to worse social-emotional outcomes may be related to language-network dysfunction by adversely affecting the degree to which a child engages in social interactions, and subsequently disrupting the development of social cognitive skills and social-emotional well-being.

In line with hypothesis 1c, results indicate that arterial ischemic stroke is predictive of greater social problems when compared to hemorrhagic stroke. This finding is in concordance

with the current body of literature suggesting that children and adults with arterial ischemic stroke tend to experience worse outcomes than their hemorrhagic stroke counterparts (Paolucci et al., 2003). Better motor, cognitive, and functional outcomes have been reported in hemorrhagic stroke than in arterial ischemic stroke (Yvon et al., 2018), and the current study suggests that children with hemorrhagic stroke are more likely to experience fewer social problems as well. It remains unclear as to why stroke mechanism (ischemic compared to hemorrhagic) was not predictive of internalizing behaviours and total problems. This may result from the small sample size, or the fact that the subscales are measuring different constructs related to emotion regulation (i.e., gets in fights a lot, in the case of social problems, and feels worthless or inferior, in the case of internalizing). Further research in a larger sample is needed to confirm that stroke mechanism does not differentially affect the development of internalizing symptoms following pediatric stroke.

Associations between social cognition and social-emotional outcomes

The second aim of this study was to assess whether measures of social cognition were correlated with social-emotional outcomes. The correlational analyses revealed that scores on the theory of mind measure were associated with one of the social-emotional outcome measures (CBCL social problems) and that social cognition as measured by the SRS was associated with all three social-emotional outcome measures. Basic facial emotion processing measured using the NEPSY affect recognition subtest does not appear to be associated with, or predictive of, social-emotional outcomes. By contrast, scores on the SRS, which evaluates higher-order and more complex social cognitive skills such as theory of mind, are predictive of social-emotional outcomes (Ryan et al., 2021). These findings are consistent with the notion that theory of mind involves network-based activity to support complex social-cognitive abilities, requiring input

from multiple brain regions to process information within the developing brain. Affect recognition requires less integration of information and is a skill that is acquired earlier on than theory of mind. The fusiform face area (FFA), is a highly specialized region present bilaterally within the lateral portion of the posterior fusiform gyrus (Scherf et al., 2007). Functional neuroimaging studies indicate that the FFA shows bilateral activation in response to faces as early as two months of age, and the development of face processing systems is suggested to take place largely within the first year of life (Johnson et al., 2005; Scott et al., 2006; Tzourio-Mazoyer et al., 2002). As such, it may be that theory of mind is more likely to be disrupted during development due to multiple modal processing requirements across hemispheres, whereas identification of faces and emotion recognition may already be relatively established within both hemispheres, allowing for redundancy if stroke impacts the one of the emotion recognition networks.

An important distinction between the social cognitive measures used in this study is that the SRS is a parent-report questionnaire, and the NEPSY subtests (affect recognition and theory of mind) are neuropsychological assessment measures. The SRS was the only social cognitive measure predictive of all social-emotional outcome measures, and it was itself predicted by two of the three stroke characteristics. Conversely, the NEPSY affect recognition and NEPSY theory of mind measures were not predicted by any of the three stroke characteristics and only NEPSY theory of mind was predictive of one of the social-emotional outcome measures. This suggests that the parent report measure was more sensitive than formal neuropsychological assessment measures of social cognition, suggesting that development of a more sensitive neuropsychological assessment measure of social cognition incorporating parent report is possible. It also may be the case that the questionnaires tend to be better correlated with one

another, as previous research in executive functioning indicates that questionnaires are more likely to be correlated with one another than assessment measures and questionnaires (Toplak, 2013).

Social cognition as a mediator of the association between stroke characteristics and social-emotional outcomes

Mediation analyses revealed that social cognition, as indexed by the SRS, fully accounted for the association between the affected hemisphere and social-emotional outcomes (total problems and internalizing), such that difficulties in social cognitive processes and behaviours lead to a greater number of internalizing behaviours and total problems. This result is in line with hypothesis three: the impact of stroke on social cognition underpins the relationship between stroke characteristics and social-emotional outcomes. Social cognitive impairments have been linked to less prosocial behaviour and more peer problems (Ryan et al., 2021), and stroke characteristics have been shown to predict these outcomes; however, this is the first study to provide evidence that social cognition may be the mechanism through which the two are related. The current finding emphasizes the importance of evaluating social cognition, in the hopes of identifying those who are at risk for worse social-emotional outcomes. Following on the observation of left hemispheric stroke being associated with worse social emotional outcomes, more detailed evaluation of the role and contribution of language impairment would also be in order.

Limitations

There are a number of limitations in the current project. The study design was cross sectional within a trajectory of brain development that is ongoing. While the findings are meaningful in the current moment, their predictive validity requires longitudinal evaluation to

ascertain the stability and persistence of the social cognitive scores and social-emotional outcomes. The purpose of this study was to look at chronic effects of stroke characteristics, social cognition, and social-emotional well-being, and was not designed to look at early effects in the aftermath of acute stroke. The findings do suggest that early evaluation of social cognition and social emotional functioning would potentially be important as a baseline for longer term follow-up, to help drive awareness of areas of impairment and the development of potentially helpful early intervention programs.

In the current study, affected hemisphere, lesion location, and stroke mechanism were evaluated as the stroke characteristic measures. Although these measures have a theoretical basis for being associated with social-emotional outcomes, there are some notable variables that also have a strong research base that were not examined or prioritized in our multiple regression and mediation models. Some studies evaluating post-stroke outcomes in pediatric stroke have highlighted a clear association between combined cortical and subcortical lesions compared to cortical or subcortical only and cognitive, social-emotional, and social cognitive outcomes. Ryan et al. (2021) report associations with combined cortical-subcortical pathology and theory of mind processing, in addition to greater social problems, so it would be of interest for future research to investigate whether social cognition mediates the association between combined lesion pathology and social-emotional outcomes. In this study, those with cortical and subcortical locations were not distinguished as separate groups for analysis. Another feature that has been previously evaluated includes quantitative volumetric analysis of stroke, which was not available for these data. While more variables would have been of interest to explore, the three stroke characteristics chosen for this study had a solid theoretical basis (i.e., directly relevant to social cognition processes), with fewer predictors allowing for the reduction in risk of a type I error.

When reporting comparisons of the stroke group to controls, the mean standard scores of the stroke group relative to the standardization (normed) sample of the test were reported. The decision to evaluate the sample in this way was due to the limitation of collecting a contemporaneous control sample during this study which was undertaken during the COVID-19 pandemic. However, the comparison of the current sample to a normed sample for the NEPSY, CBCL, and SRS helps establish that the variance of these measures in the current study population approximates the larger population sample that is used for the normative scores (range of n=1000-1800) (Achenbach, 2001; Brooks et al., 2010; Bruni, 2014). We are thus not able to provide a comparison to age-matched controls, which would allow for a stronger exploration of group differences.

Implications and Future Directions

A key clinical challenge in pediatric stroke rehabilitation is understanding the long-term sequelae of stroke and where intervention programs may have significant impact. Social-emotional outcomes with their impact on behavior, socialization and vocation likely represents an overlooked and significant source of disability and function. Recognizing that social cognition is a mediator of such social emotional outcomes provides an avenue for assessment and potential for measuring treatment response. The research presented in this thesis contributes to a new line of inquiry investigating social cognition following pediatric stroke, and provides further evidence for its importance in predicting social-emotional outcomes.

Many questions related to the effect of stroke on social-cognitive function remain unanswered with potentially promising avenues of investigation available. Diffusion tensor imaging and functional magnetic resonance imaging hold the potential to understand the impact of stroke on functional networks which support social cognitive skills. An evaluation of

structural connectivity and disruptions after stroke will permit a greater understanding of the diffuse networks that support social cognitive skills, and how networks shift or recover over time in the developing brain to support new social cognitive processes. A more detailed examination of the role of language in supporting social cognition will add to the understanding of the impact of left hemisphere stroke and its associations with worse social cognitive outcomes. Finally, it would appear that current neuropsychological assessment measures used to evaluate social cognition in children may not be sensitive in identifying deficits. There are few social cognitive measures that have been normed and standardized for children, and the development of more social cognitive neuropsychological batteries for children incorporating child and family input is warranted.

Conclusions

The aim of the present thesis was to explore the contribution of social cognition in mediating the association between pediatric stroke characteristics and social-emotional outcomes. Children who experience left hemisphere stroke are more likely to experience social cognitive difficulties, which affect social-emotional outcomes. Social-emotional well-being is paramount in a person's development and is important in shaping a child's relationships, achievement, and self-sufficiency into adult life. Evidence from this work signals the importance of evaluating social cognition following pediatric stroke, to help identify those who may be at risk of poorer social-emotional outcomes; with the ability to predict these outcomes, clinicians can intervene earlier to guide children on a path to healthy social-emotional well-being and stroke recovery.

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Appendix A

Participant Demographics Organized Stroke Mechanism

ParticipantNumber	Stroke Mechanism	Age	Sex	Stroke Onset	Lesion Laterality	Lesion Location	FSIQ	CBCL Social Problems Standard Score	CBCL Internalizing Standard Score	CBCL Total Problems Standard Score	NEPSY Affect Recognition Standard Score	NEPSY Theoryof Mind Standard Score	SRS: Social Cognition Standard Score
A013	Ischemic	13.54	F	Neonatal	Left	Non-Frontotemporal	92	128	133	128	105	86	
A019	Ischemic	11.73	F	Neonatal	Left	Non-Frontotemporal	85		124	114	105	86	108
A023	Ischemic	14.81	M	Neonatal	Left	Non-Frontotemporal	84	130	131	131	85	96	128
A029	Ischemic	13.16	M	Childhood	Left	Non-Frontotemporal	85	129	113	109	75	64	114
A057	Ischemic	10.05	M	Neonatal	Left	Non-Frontotemporal	87	113	124	118	105	117	98
A065	Ischemic	13.16	M	Neonatal	Left	Non-Frontotemporal	84	148	125	116	95	79	110
A018	Ischemic	10.2	M	Neonatal	Left	Frontotemporal Involvement	79	135	116	135	70	65	138
A026	Ischemic	10.15	M	Childhood	Left	Frontotemporal Involvement	104	113	98	100	95	95	98
A027	Ischemic	9.43	M	Neonatal	Left	Frontotemporal Involvement	45	130	135	138	90	80	123
A028	Ischemic	6.01	M	Neonatal	Left	Frontotemporal Involvement	93	100	93	101	90	85	95
A031	Ischemic	6.33	M	Neonatal	Left	Frontotemporal Involvement	108	109	100	116	100	105	106
A038	Ischemic	11.2	F	Neonatal	Left	Frontotemporal Involvement	121	114	131	128	110	105	120
A041	Ischemic	12.17	F	Childhood	Left	Frontotemporal Involvement	81	106	114	118	105	96	108
A046	Ischemic	11.28	M	Childhood	Left	Frontotemporal Involvement	76	125	133	124	115	86	120
A049	Ischemic	16.36	F	Childhood	Left	Frontotemporal Involvement	75	101	84	88	105	86	93
A050	Ischemic	11.07	F	Childhood	Left	Frontotemporal Involvement	83	114	125	120	115	105	129
A056	Ischemic	13.04	M	Childhood	Left	Frontotemporal Involvement	47	113	85	95	80	73	108
A059	Ischemic	8.33	M	Childhood	Left	Frontotemporal Involvement	115	113	86	108	115	95	100
A017	Ischemic	12.08	F	Neonatal	Right	Non-Frontotemporal	92	101	90	91	110	95	90
A021	Ischemic	7.66	F	Neonatal	Right	Non-Frontotemporal	105	101	98	111	100	105	93
A054	Ischemic	7.97	M	Childhood	Right	Non-Frontotemporal	68	105	76	90	65	67	128
A060	Ischemic	9.61	F	Childhood	Right	Non-Frontotemporal	102	102	113	101	115	117	95
A063	Ischemic	13.82	M	Childhood	Right	Non-Frontotemporal	88	124	120	116	95	72	105
A064	Ischemic	13	M	Childhood	Right	Non-Frontotemporal	74	100	76	93	100	95	85
A069	Ischemic	8.76	M	Childhood	Right	Non-Frontotemporal	124	105	115	105	115	117	92
A039	Ischemic	6.17	M	Neonatal	Right	Frontotemporal Involvement	118	101	76	76	100	100	91
A051	Ischemic	14.48	M	Childhood	Right	Frontotemporal Involvement	67	113	130	121	90	73	124
A058	Ischemic	7.69	F	Neonatal	Right	Frontotemporal Involvement	71	100	75	63	75	95	98
A067	Ischemic	11.93	M	Childhood	Right	Frontotemporal Involvement	92	101	100	86	125	117	94
A016	Hemorrhagic	6.29	M	Neonatal	Left	Non-Frontotemporal	71	125	113	130	65	65	120
A022	Hemorrhagic	11.83	M	Neonatal	Left	Non-Frontotemporal	80	103	100	105	95	95	109
A025	Hemorrhagic	7.29	F	Neonatal	Left	Non-Frontotemporal	120	102	102	90	95	95	105
A061	Hemorrhagic	7.69	F	Childhood	Left	Non-Frontotemporal	49	110	102	101	95	67	120
A062	Hemorrhagic	15.73	F	Neonatal	Left	Non-Frontotemporal	119	101	121	118	115	105	102
A032	Hemorrhagic	15.3	F	Childhood	Left	Frontotemporal Involvement	98	101	102	99	110	96	114
A055	Hemorrhagic	10.93	M	Neonatal	Left	Frontotemporal Involvement	54	101	93	95	65	67	123
A030	Hemorrhagic	6.74	F	Childhood	Right	Non-Frontotemporal	105	102	100	95	85	105	86
A034	Hemorrhagic	6.44	F	Neonatal	Right	Non-Frontotemporal	106	106	113	109	95	115	108
A066	Hemorrhagic	15.13	F	Childhood	Right	Non-Frontotemporal	103	100	109	100	80	95	88
A014	Hemorrhagic	13.75	M	Neonatal	Right	Frontotemporal Involvement	54	106	106	100	65	65	
A043	Hemorrhagic	9.52	M	Childhood	Right	Frontotemporal Involvement	98	105	102	98	95	86	114
A052	Hemorrhagic	15.47	F	Childhood	Right	Frontotemporal Involvement	108	106	93	93	90	67	101

Participant Demographics Organized by Affected Hemisphere

Participant Number	Lesion Laterality	Stroke Mechanism	Age	Sex	Stroke Onset	Lesion Location	FSIQ	CBCL Social Problems Standard Score	CBCL Internalizing Standard Score	CBCL Total Problems Standard Score	NEPSY Affect Recognition Standard Score	NEPSY Theoryof Mind Standard Score	SRS: Social Cognition Standard Score
A013	Left	Ischemic	13.54	F	Neonatal	Non-Frontotemporal	92	128	133	128	105	86	
A019	Left	Ischemic	11.73	F	Neonatal	Non-Frontotemporal	85		124	114	105	86	108
A023	Left	Ischemic	14.81	M	Neonatal	Non-Frontotemporal	84	130	131	131	85	96	128
A029	Left	Ischemic	13.16	M	Childhood	Non-Frontotemporal	85	129	113	109	75	64	114
A057	Left	Ischemic	10.05	M	Neonatal	Non-Frontotemporal	87	113	124	118	105	117	98
A065	Left	Ischemic	13.16	M	Neonatal	Non-Frontotemporal	84	148	125	116	95	79	110
A018	Left	Ischemic	10.2	M	Neonatal	Frontotemporal Involvement	79	135	116	135	70	65	138
A026	Left	Ischemic	10.15	M	Childhood	Frontotemporal Involvement	104	113	98	100	95	95	98
A027	Left	Ischemic	9.43	M	Neonatal	Frontotemporal Involvement	45	130	135	138	90	80	123
A028	Left	Ischemic	6.01	M	Neonatal	Frontotemporal Involvement	93	100	93	101	90	85	95
A031	Left	Ischemic	6.33	M	Neonatal	Frontotemporal Involvement	108	109	100	116	100	105	106
A038	Left	Ischemic	11.2	F	Neonatal	Frontotemporal Involvement	121	114	131	128	110	105	120
A041	Left	Ischemic	12.17	F	Childhood	Frontotemporal Involvement	81	106	114	118	105	96	108
A046	Left	Ischemic	11.28	M	Childhood	Frontotemporal Involvement	76	125	133	124	115	86	120
A049	Left	Ischemic	16.36	F	Childhood	Frontotemporal Involvement	75	101	84	88	105	86	93
A050	Left	Ischemic	11.07	F	Childhood	Frontotemporal Involvement	83	114	125	120	115	105	129
A056	Left	Ischemic	13.04	M	Childhood	Frontotemporal Involvement	47	113	85	95	80	73	108
A059	Left	Ischemic	8.33	M	Childhood	Frontotemporal Involvement	115	113	86	108	115	95	100
A016	Left	Hemorrhagic	6.29	M	Neonatal	Non-Frontotemporal	71	125	113	130	65	65	120
A022	Left	Hemorrhagic	11.83	M	Neonatal	Non-Frontotemporal	80	103	100	105	95	95	109
A025	Left	Hemorrhagic	7.29	F	Neonatal	Non-Frontotemporal	120	102	102	90	95	95	105
A061	Left	Hemorrhagic	7.69	F	Childhood	Non-Frontotemporal	49	110	102	101	95	67	120
A062	Left	Hemorrhagic	15.73	F	Neonatal	Non-Frontotemporal	119	101	121	118	115	105	102
A032	Left	Hemorrhagic	15.3	F	Childhood	Frontotemporal Involvement	98	101	102	99	110	96	114
A055	Left	Hemorrhagic	10.93	M	Neonatal	Frontotemporal Involvement	54	101	93	95	65	67	123
A017	Right	Ischemic	12.08	F	Neonatal	Non-Frontotemporal	92	101	90	91	110	95	90
A021	Right	Ischemic	7.66	F	Neonatal	Non-Frontotemporal	105	101	98	111	100	105	93
A054	Right	Ischemic	7.97	M	Childhood	Non-Frontotemporal	68	105	76	90	65	67	128
A060	Right	Ischemic	9.61	F	Childhood	Non-Frontotemporal	102	102	113	101	115	117	95
A063	Right	Ischemic	13.82	M	Childhood	Non-Frontotemporal	88	124	120	116	95	72	105
A064	Right	Ischemic	13	M	Childhood	Non-Frontotemporal	74	100	76	93	100	95	85
A069	Right	Ischemic	8.76	M	Childhood	Non-Frontotemporal	124	105	115	105	115	117	92
A039	Right	Ischemic	6.17	M	Neonatal	Frontotemporal Involvement	118	101	76	76	100	100	91
A051	Right	Ischemic	14.48	M	Childhood	Frontotemporal Involvement	67	113	130	121	90	73	124
A058	Right	Ischemic	7.69	F	Neonatal	Frontotemporal Involvement	71	100	75	63	75	95	98
A067	Right	Ischemic	11.93	M	Childhood	Frontotemporal Involvement	92	101	100	86	125	117	94
A030	Right	Hemorrhagic	6.74	F	Childhood	Non-Frontotemporal	105	102	100	95	85	105	86
A034	Right	Hemorrhagic	6.44	F	Neonatal	Non-Frontotemporal	106	106	113	109	95	115	108
A066	Right	Hemorrhagic	15.13	F	Childhood	Non-Frontotemporal	103	100	109	100	80	95	88
A014	Right	Hemorrhagic	13.75	M	Neonatal	Frontotemporal Involvement	54	106	106	100	65	65	
A043	Right	Hemorrhagic	9.52	M	Childhood	Frontotemporal Involvement	98	105	102	98	95	86	114
A052	Right	Hemorrhagic	15.47	F	Childhood	Frontotemporal Involvement	108	106	93	93	90	67	101

Participant Demographics Organized by Location

ParticipantNumber	Lesion Location	Lesion Laterality	Stroke Mechanism	Age	Sex	Stroke Onset	FSIQ	CBCL Social Probe	CBCL Internalizing Standard Score	CBCL Total Problems Standard Score	NEPSY Affect Recognition Standard Score	NEPSY Theoryof Mind Standard Score	SRS: Social Cognition Standard Score
A018	Frontotemporal Involvement	Left	Ischemic	10.2	M	Neonatal	79	135	116	135	70	65	138
A026	Frontotemporal Involvement	Left	Ischemic	10.15	M	Childhood	104	113	98	100	95	95	98
A027	Frontotemporal Involvement	Left	Ischemic	9.43	M	Neonatal	45	130	135	138	90	80	123
A028	Frontotemporal Involvement	Left	Ischemic	6.01	M	Neonatal	93	100	93	101	90	85	95
A031	Frontotemporal Involvement	Left	Ischemic	6.33	M	Neonatal	108	109	100	116	100	105	106
A038	Frontotemporal Involvement	Left	Ischemic	11.2	F	Neonatal	121	114	131	128	110	105	120
A041	Frontotemporal Involvement	Left	Ischemic	12.17	F	Childhood	81	106	114	118	105	96	108
A046	Frontotemporal Involvement	Left	Ischemic	11.28	M	Childhood	76	125	133	124	115	86	120
A049	Frontotemporal Involvement	Left	Ischemic	16.36	F	Childhood	75	101	84	88	105	86	93
A050	Frontotemporal Involvement	Left	Ischemic	11.07	F	Childhood	83	114	125	120	115	105	129
A056	Frontotemporal Involvement	Left	Ischemic	13.04	M	Childhood	47	113	85	95	80	73	108
A059	Frontotemporal Involvement	Left	Ischemic	8.33	M	Childhood	115	113	86	108	115	95	100
A032	Frontotemporal Involvement	Left	Hemorrhagic	15.3	F	Childhood	98	101	102	99	110	96	114
A055	Frontotemporal Involvement	Left	Hemorrhagic	10.93	M	Neonatal	54	101	93	95	65	67	123
A039	Frontotemporal Involvement	Right	Ischemic	6.17	M	Neonatal	118	101	76	76	100	100	91
A051	Frontotemporal Involvement	Right	Ischemic	14.48	M	Childhood	67	113	130	121	90	73	124
A058	Frontotemporal Involvement	Right	Ischemic	7.69	F	Neonatal	71	100	75	63	75	95	98
A067	Frontotemporal Involvement	Right	Ischemic	11.93	M	Childhood	92	101	100	86	125	117	94
A014	Frontotemporal Involvement	Right	Hemorrhagic	13.75	M	Neonatal	54	106	106	100	65	65	
A043	Frontotemporal Involvement	Right	Hemorrhagic	9.52	M	Childhood	98	105	102	98	95	86	114
A052	Frontotemporal Involvement	Right	Hemorrhagic	15.47	F	Childhood	108	106	93	93	90	67	101
A013	Non-Frontotemporal	Left	Ischemic	13.54	F	Neonatal	92	128	133	128	105	86	
A019	Non-Frontotemporal	Left	Ischemic	11.73	F	Neonatal	85		124	114	105	86	108
A023	Non-Frontotemporal	Left	Ischemic	14.81	M	Neonatal	84	130	131	131	85	96	128
A029	Non-Frontotemporal	Left	Ischemic	13.16	M	Childhood	85	129	113	109	75	64	114
A057	Non-Frontotemporal	Left	Ischemic	10.05	M	Neonatal	87	113	124	118	105	117	98
A065	Non-Frontotemporal	Left	Ischemic	13.16	M	Neonatal	84	148	125	116	95	79	110
A016	Non-Frontotemporal	Left	Hemorrhagic	6.29	M	Neonatal	71	125	113	130	65	65	120
A022	Non-Frontotemporal	Left	Hemorrhagic	11.83	M	Neonatal	80	103	100	105	95	95	109
A025	Non-Frontotemporal	Left	Hemorrhagic	7.29	F	Neonatal	120	102	102	90	95	95	105
A061	Non-Frontotemporal	Left	Hemorrhagic	7.69	F	Childhood	49	110	102	101	95	67	120
A062	Non-Frontotemporal	Left	Hemorrhagic	15.73	F	Neonatal	119	101	121	118	115	105	102
A017	Non-Frontotemporal	Right	Ischemic	12.08	F	Neonatal	92	101	90	91	110	95	90
A021	Non-Frontotemporal	Right	Ischemic	7.66	F	Neonatal	105	101	98	111	100	105	93
A054	Non-Frontotemporal	Right	Ischemic	7.97	M	Childhood	68	105	76	90	65	67	128
A060	Non-Frontotemporal	Right	Ischemic	9.61	F	Childhood	102	102	113	101	115	117	95
A063	Non-Frontotemporal	Right	Ischemic	13.82	M	Childhood	88	124	120	116	95	72	105
A064	Non-Frontotemporal	Right	Ischemic	13	M	Childhood	74	100	76	93	100	95	85
A069	Non-Frontotemporal	Right	Ischemic	8.76	M	Childhood	124	105	115	105	115	117	92
A030	Non-Frontotemporal	Right	Hemorrhagic	6.74	F	Childhood	105	102	100	95	85	105	86
A034	Non-Frontotemporal	Right	Hemorrhagic	6.44	F	Neonatal	106	106	113	109	95	115	108
A066	Non-Frontotemporal	Right	Hemorrhagic	15.13	F	Childhood	103	100	109	100	80	95	88