Assessment of Social Cognition by Site of Lesion in Adults with Traumatic Brain Injury Using the Visual Social Inference Test

by

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A thesis submitted to the Department of Neuroscience

In conformity with the requirements for

The degree of Masters of Science

McMaster University

Hamilton, Ontario, Canada

(August, 2020)

Abstract

Individuals with Traumatic Brain Injury (TBI) exhibit impaired performance on social cognition and theory of mind (ToM) measures, like the Video Social Inference Test (VSIT). The frontal lobe, being the primary region involved in higher level cognitive functions mediates the neural mechanisms involved in social cognition and ToM abilities, according to studies on brain and behaviour. The goal of this study was to examine if individuals with TBI who did not damage their frontal lobe would perform differently on the VSIT than individuals with TBI who did. This study was a secondary analysis of documented imaging data and VSIT scores obtained from 51 adults with moderate-to-severe TBI (23 females). A comparison was made between scores obtained on the VSIT between participants with and without frontal lobe lesions. The results indicated that there was no significant difference between the two groups, in other words, site of lesion in participants with TBI did not predict performance on the VSIT. The results suggest that while the VSIT may yield critical information about social cognition, it is not sensitive to individual site of lesion. There is evidence that aspects of social cognition are impaired in this clinical population, however, most research in this area is obstructed by the complex nature of TBI neuropathology in addition to small heterogenous samples involved in studies. Further research in this area is required in order to reveal and enhance our understanding of social cognition deficits following TBI.

Keywords: social cognition, traumatic brain injury, theory of mind, frontal lobe lesions, video social inference test

Acknowledgements

I would like to thank Dr. Lyn Turkstra for her unwavering support, patience and guidance through these two years, she has been a great role model and mentor for me. I would also like to thank Dr. John Connolly, Dr. Victor Kuperman, Dr Karin Humphreys and members of the Turkstra Lab for assisting me throughout my graduate studies and providing me with valuable insight and encouragement . I would not have been able to do this without any of you.

I also thank my family for never allowing me to give up and always being there for me when I needed them. Your unconditional love and support are what allowed me to excel during my graduate studies.

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A traumatic brain injury (TBI) is caused by a sudden bump, blow, or jolt to the head that disrupts the normal function of the brain (Centers for Disease Control and Prevention, 2019). Every year in Canada more than 165,000 people suffer a serious brain injury. A majority of those people develop a partial or permanent disability and more than 11,000 Canadians die (Northern Brain Injury Association, 2020). In 2014, there were 2.87 million TBI-related hospitalizations in the United States alone. TBI contributed to the death of 56,800 of those people, and the death of 2,595 children (Centers for Disease Control and Prevention, 2019). According to the Centers for Disease Control and Prevention, falls and motor vehicle accidents are the first and second leading causes of all TBI-related accidents. In Canada, each severe TBI can cost the medical system up to a million dollars at the time the injury occurs (Northern Brain Injury Association, 2020).

A TBI is graded as mild, moderate, or severe based on the individuals level of consciousness following a blow or jolt to the head or their Glasgow Coma Scale (GCS) score after resuscitation (Ghajar, 2000). A mild TBI (GCS 13-15) is commonly referred to as a concussion. Someone with a mild TBI may experience a brief change in mental status or consciousness (Ghajar, 2000). While most mild TBI patients gain full neurological recovery, others may have short-term memory problems and concentration difficulties throughout life (Ghajar, 2000). The term moderate TBI (GCS 9-13) is used when the blow or jolt to the head changes brain function for longer than a few minutes (Ghajar, 2000). A patient with moderate TBI can be described as lethargic or stuporous (i.e., not quite fully conscious). In a severe TBI (GCS 3-8) the patient is said to be comatose, not able to open their eyes or follow directions (Ghajar, 2000). Common cognitive problems following a TBI include memory impairments,

difficulty in thinking, impairments in language comprehension, reasoning, behavioural and psychosocial changes, social inappropriateness, depression and anxiety (Centers for Disease Control and Prevention, 2019).

The feeling of being socially isolated has profoundly changed and shaped the lives of individuals with TBI (Salas, Casassus, Rowlands, Pimm, & Flanagan, 2018). There is well documented literature revealing that, in the long term, people with TBI are not as involved in social and recreational activities, have a fewer number of friends, and less social contact (McDonald, 2013; McDonald & Flanagan, 2004; Salas et al., 2018). Previous research also indicates that there is a positive correlation between life satisfaction and a negative correlation with emotional distress in adults with TBI who are socially involved and integrated in their community (McDonald & Flanagan, 2004; Salas et al., 2018). Community integration, defined as the extent in which an individual is able to stay socially connected to the people in their social circle, has also been linked to development of self-concept after a TBI (Douglas, 2013).

Existing literature on TBI reveals several factors that contribute to social isolation, including impaired social skills and social judgement, problems in communication pragmatics, impairment in initiation and impulse control, and reduced sensitivity to social cues (McDonald, 2013; McDonald & Flanagan, 2004; Turkstra, Norman, Mutlu, & Duff, 2018). People with TBI report having fewer close friends, difficulty maintaining contact with their old friends, struggle making new friends, engaging in a telephone conversation or attending any social events. This lifestyle pushes people with TBI to engage in only solitary activities (e.g. watching television or listening to music) (McDonald, 2013; McDonald & Flanagan, 2004; Turkstra et al., 2018). Inevitably, these social communication problems lead to the social isolation of adults with TBI because they prevent them from being able to carry out successful social interactions; thereby,

reducing their capacity to initiate or maintain social connections (McDonald & Flanagan, 2004; Salas et al., 2018). Over time, social isolation, diminished social support and loneliness has a negative impact on the psychological adjustment and wellbeing post-TBI. Decreased social support following TBI is also a predictor of psychological symptoms such as anxiety and depression (McDonald & Flanagan, 2004; Salas et al., 2018).

A factor that may contribute to social isolation and social communication problems in individuals with TBI is impairments in social cognition (McDonald, 2013). At base, social cognition is defined as the ability to understand and construct representations of the mental states of others (Adolphs, 2001). This includes their beliefs, feelings, experiences, and intentions, in relation to ourselves and making use of this knowledge by allowing it to shape and guide social behaviour (Adolphs, 2001). A fundamental component of social cognition that individuals with TBI struggle with is the ability to make social inferences (McDonald, 2013; Turkstra, 2008) . Social inferences guide our social behaviour and allows us to predict the behaviour of others by providing us with the ability to construct the beliefs, feelings, experiences, and intentions of others in relation to ourselves (McDonald, 2013; Turkstra, 2008).

As will be seen in the literature review that follows, the VSIT is one of many tests developed to measure social cognition and social inference (Turkstra, 2008). Although the VSIT in particular was developed to characterize performance of individuals with TBI and to capture social inference processes that take place during daily conversations (Turkstra, 2008) little is known about whether accuracy of performance differs by site of lesion. The aim of the proposed study is to address this gap in the literature, to better address the social challenges faced by adults with TBI.

The following sections review current literature on social cognition, social inference, and ToM in individuals with TBI. The review also discusses brain regions hypothesized to be involved in social cognition and how neuropsychological and neuroimaging studies have examined these regions in individuals with TBI.

Literature Review

Social Cognition and TBI. Social cognition involves the ability to understand and perceive the mental states of others (Adolphs, 2001). Moreover, it refers to one's ability of being able to combine their own knowledge and interpretation of social stimuli and prevents inappropriate behaviours, thoughts, and actions from being displayed or said (Adolphs, 2001; Turkstra, 2008). Impairments in social cognition are common in adults with moderate or severe TBI (McDonald, 2013). Social cognition impairments can prevent social reintegration after TBI, as they may keep individuals from being able to engage in successful social interactions (Johnson & Turkstra, 2012; McDonald, 2013). As a result, others may feel disinclined to initiate or maintain social contact with individuals who have TBI altogether (Johnson & Turkstra, 2012; McDonald, 2013).

Adolphs (2009) and McDonald (2013) identified three different levels of social cognitive processing: perception, evaluation and interpretation, and regulation. Social stimuli perception consists of both conscious explicit processing by the visual cortex, in addition to frequent implicit processing by the superior colliculi and or optic tectum (Adolphs, 2009; McDonald, 2013). Perceptual processes are specialized for some types of stimuli, including facial expressions, prosody, hand gestures and other body movements (Adolphs, 2009; McDonald, 2013). Evaluation and interpretation of social information appears to be mediated by a specialized system of interconnected networks involving the orbital and ventromedial prefrontal

cortex, cingulate cortex, and striatum, insula, and amygdala (McDonald, 2013). These structures orchestrate the automatic, often implicit, appraisal of emotionally salient information and mental states (Adolphs, 2009; McDonald, 2013). Finally, regulation of responses and contextualization related to memory are mediated by dorsal regions of the lateral and medial prefrontal cortex in concert with the hippocampus and temporo-parietal regions (Adolphs, 2009; Lieberman, 2007; McDonald, 2013). Unlike the preceding stages, regulation and contextualization are generic cognitive processes and not specific to social cognition (Adolphs, 2009; Lieberman, 2007; McDonald, 2013).

Previous studies on social cognition in people with TBI. McDonald (2013) reviewed a series of studies with the aim of critically evaluating the evidence for social cognition disorders following a TBI. In explaining social cognition, McDonald made a conceptional distinction between "hot" social cognition and "cold" social cognition. The term "hot" social cognition refers to emotion processing, including recognizing and being able to empathize with the emotional state of others' (McDonald, 2013). By contrast, "cold "social cognition refers to thinking about something from another person's point of view, including ToM abilities (McDonald, 2013). Affective empathy refers to the extent a person is able to resonate with the feelings of others' while recognizing that they are separate and distinct from their own and is an example of "hot" social cognition. It has been measured using self-report tools such as the Balanced Emotional Empathy Scale (Mehrabian, 1996). McDonald (2013) stated that results across different studies have found that between 60-70% of adults with severe TBI report feeling little to almost no emotional empathy towards others, vs. 30% of adults without TBI. Comparison of self-report measures across multiple different studies supported the notion that severe TBI patients experience similar deficits in empathy following their injury because they

score poorly on all the same areas as one another (McDonald, 2013). Data from self-report measures of empathy should be interpreted with caution, as they do not capture factors like attentional bias and cognitive impairments that influence higher-level functions of language processing and attention in the moment (McDonald, 2013). However, they are considered to be a valuable and valid tool for measuring empathy (McDonald, 2013).

McDonald (2013) also reviewed studies examining emotion perception in adults with TBI, another component of "hot" social cognition. Results of these studies indicated that adults with either acute or chronic severe TBI made errors in recognizing emotions from static photographs of facial expressions. In one meta-analysis of 296 adults with TBI across 13 different studies, 39% of patients with severe TBI showed impairments in emotion recognition (Babbage et al., 2011), again using static photographs. To improve ecological validity (i.e., making the task more like everyday life) a different study used dynamic images to determine if they can influence emotion perception abilities (Mcdonald & Saunders, 2005). The results indicated that the use of dynamic images made no difference and that people with TBI made errors in recognising emotions regardless (Mcdonald & Saunders, 2005). Overall, the findings from these different studies highlight cognitive and social deficits that are compromised in individuals with TBI. They demonstrate that impairments present in individuals with TBI are not task specific and that dynamic images may tap into and engage different brain systems in comparison to static. The proposed study will add to this literature by further examining the neural basis of these impairments.

Social Inference and TBI

Some of the cues that guide social behaviour cannot be perceived directly, but rather require the individual to use their knowledge of the social world in addition to information that

they infer from incoming stimuli (Adolphs, 2001). A fundamental component of social cognition is social inference, referring to the information that is not directly stated, but rather implied by the speaker or writer (Turkstra, 2008). An example of a social inference error that is commonly made by adults with TBI is misperceiving a speaker's intent, such as taking a sarcastic comment literally, or laughing at a comment or remark that was not intended to be a joke (Turkstra, 2008). Inference errors can be the root cause inappropriate behaviour or comments. Social inferences rely on individual social knowledge (Turkstra, 2008), which can be obtained via personal experience (e.g., that person was not interested in carrying a conversation with you last time) or social conventions (e.g., in general, forcing someone to talk to you will annoy them). In order to generate an inference, information from a variety of different sources and factors must be integrated (Johnson & Turkstra, 2012; Leinonen & Letts, 2001). Successful communication requires the understanding of inferences, as a person must be able to not only listen to and understand the message of a speaker, but also extrapolate information from the message by relating it to a relevant context (Leinonen & Letts, 2001).

Previous studies on social inference and TBI. Studies analyzing inference comprehension in adults with TBI typically assess how well individuals can detect sarcasm and irony in a conversation (Dennis Purvis, Barnes, Wilkinson, & Winner, 2001; Martin & McDonald, 2005; McDonald, 1999; L. Turkstra, S. McDonald, & R. DePompei, 2001). Findings across many of these studies have revealed no significant differences between adults with and without TBI in literal comprehension, and errors when inferences are required, such as interpreting exchanges as being sarcastic (McDonald, 1999). The main critique of many studies investigating inference comprehension in adults with TBI is that assessments involve scripted artificial laboratory tasks like short written vignettes (Johnson & Turkstra, 2012; Turkstra, 2008).

These tasks have the advantage of providing more time to process inferences than would actually be given during everyday real conversations, thus potentially underestimating everyday impairments (Johnson & Turkstra, 2012). The tests have also been criticized for either not being particularly designed for individuals with TBI or for solely focusing on inferences involving sarcasm and lies (Turkstra, 2008). To address these limitations, Turkstra (2008) developed the Video Social Inference Test (VSIT). The VSIT was specifically designed for adults with TBI and tests not only social inference in the context of sarcasm and irony but also general inferences in everyday conversations (Turkstra, 2008).

The VSIT includes a series of video clips depicting actors in a variety of social interactions. What makes the VSIT unique is its ability to provide information regarding different aspects of ToM (Turkstra, 2008). Amongst the different social inferences that can be made, the particular inference about what others are thinking and feeling is known as ToM (Turkstra, 2008). ToM is critical in social interactions because it provides individuals with the ability to make inferences regarding the mental states of others, in addition to making use of those inferences to explain and predict the behaviour of others (Perner, 1991). The VSIT video require participants to use a combination of mental state inferences (e.g., being able to pick up on the fact that the actors in the video are not getting along with one another) and use those inferences to make judgements regarding how the actors in the clip will behave in the future (e.g., they will not be hanging out with one another in the future) (Turkstra, 2008), both of which are fundamental to ToM (Turkstra, 2008). Participants also must focus their attention, make decisions, and access other processes supporting social cognition that may be engaged in everyday conversations (Turkstra, 2008). The VSIT is structured to manipulate working memory demands, as for some stimuli participants must hold, maintain, and update information in their

mind as social interactions between actors evolve over time (Turkstra, 2008). Higher scores on the VSIT also indicate a more accurate performance in identifying social relationships (Meulenbroek & Turkstra, 2016). In three previous studies using the VSIT, individuals with TBI scored significantly lower than typically developing adults (Meulenbroek & Turkstra, 2016; Turkstra, 2008; Turkstra et al., 2018), whether or not the scores obtained were influenced by site of lesion has never been investigated.

Turkstra et al., (2001) administered a precursor version of the VSIT to 60 typically developing adolescents and 10 adolescents with TBI. TBI group scores were significantly lower than the scores of typically developing adolescents. The researchers indicated that this was particularly the case on items in the VSIT which stimulated the use of second order ToM (e.g. what did she think about what he thought). The full version of the VSIT was created with the consensus that there are three main skills involved in social interactions: the ability to understand and interpret a situation (Turkstra, 2008) (e.g., to determine if this is a good time to ask someone for a favour), the ability to infer or understand what is being implied (Turkstra, 2008) (e.g., to understand whether they are okay with doing you a favour or not), and having knowledge regarding general social normal or rules specific to a particular culture (e.g., that asking someone you know well for a favour is acceptable). Social cognition is a requirement for the first two skills in particular, since they are not culture specific, therefore, assessment of the first two skills were selected to be the central focus during stimulus video development (Turkstra, 2008). Although previous studies using the VSIT have used it as a tool for measuring social inference amongst individuals with TBI, to date there has been no study examining whether individual site of lesion influences performance on the VSIT; the present study examines this. In the present

study, I compared participants' imaging data showing the site of lesions to VSIT scores, to determine if social cognitive deficits were linked to specific lesion sites.

Frontal Lobes and Social Cognition

Neuroanatomical and imaging studies do not, in isolation, illuminate whether observed social cognition deficits occur solely with damage to frontal lobe lesions as opposed to damage to other areas of the brain (Mazza et al., 2006; Rowe, Bullock, Polkey, & Morris, 2001). Nonetheless, these studies provide support for the view that this particular area does play a critical role (Mazza et al., 2006; Rowe et al., 2001). Frontal lobe damage is not only associated with impairment in higher-level cognitive functions, but also with impairments in social behaviour, personal memories, self-awareness, the ability to understand and appreciate humour, self-face recognition, and episodic memory (Stuss, Gallup, & Alexander, 2001). Different studies have revealed that damage to the left or right orbitofrontal/ventral medial areas repeatedly lead to changes in individual personality (Frith & Frith, 2003; Siegal & Varley, 2001; Stuss et al., 2001). These changes include, but are not limited to, impairments in social judgement, indifference, reduced emotional and empathetic responsiveness, impairments in pragmatics, diminished self-control, and inability to relate social situation to personal emotional and affective experiences (Stuss et al., 2001).

Previous studies on frontal lobe and social cognition. A clear role for a specific region of the frontal lobes in ToM can be expected based on correlation with impairments in social behaviour and altered personality changes (Stuss et al., 2001). Results across several different neuroimaging studies investigating ToM abilities indicate that it is mediated by the amygdala, the temporo-parietal junction, the orbital frontal cortex and the medial frontal lobes (Frith & Frith, 2003; Siegal & Varley, 2001). The data obtained from these studies indicate that in

comparison to other regions of the brain, the frontal lobes play a more critical role in mentalizing, and damage to this area suggests impairment in making mental state attributions (Frith & Frith, 2003; Siegal & Varley, 2001).

Fletcher et al. (1995) conducted a functional neuroimaging study with positron emission tomography (PET) in order to study the brain activity of normal participants while they performed story comprehensions tasks that required mental state attribution. When the stories required participants to consider the emotions, thoughts, and feelings of the characters, Fletcher and colleagues noted significant activation in the left medial frontal area (specifically Brodmann area 8) (Fletcher et al., 1995). The researchers emphasized that the same regions were not being activated during the control task, where the thoughts and feelings of the characters in the stories were irrelevant (Fletcher et al., 1995). A study by Goel, Grafman, Sadato, and Hallett (1995), also found PET activation in the left medial frontal lobe when inferential reasoning regarding the thoughts, beliefs, and intentions of others were required.

The inability to recognize emotions via static photographs has also been backed up by results obtained from different neuroimaging studies working with individuals who have TBI (Bigler & Maxwell, 2011; Mcdonald & Saunders, 2005). The findings from these studies indicate that the position of the ventral fronto-temporal lobes being located within the interior and middle fossa makes them that much more vulnerable and susceptible to TBI (Bigler & Maxwell, 2011; Mcdonald & Saunders, 2005). As a result of the focal pathology, disorders involving impairments in static expression recognition may be more common (Bigler & Maxwell, 2011; Mcdonald & Saunders, 2005). Results from one of the neuroimaging studies found that adults with TBI did not encounter as many difficulties perceiving emotions when presented with dynamic images, where facial movements could be directly observed and were

not static (McDonald & Saunders, 2005). Once again, given the focal pathology of the ventral fronto-temporal lobes, the researchers argued that obtaining such results are to be expected (McDonald & Saunders, 2005) .

Stuss et al. (2001) developed a study to examine ToM in patients with focal lesions in distinct frontal vs. non-frontal regions of the brain. The objective of their study was to determine whether the frontal lobes were uniquely related to ToM and if damage to the left, right or ventral medial regions within the frontal lobe influenced different processes related to ToM (Stuss et al., 2001). Participants were tested for visual perspective taking and detecting deception. Findings were similar to previous studies; participants with frontal-lobe lesions did not accurately infer mental states in others (Stuss et al., 2001). Their findings suggested that right frontal lobe lesions were also associated with diminished visual perspective taking and participants with medial frontal lesions, in particular right ventral, were unable to detect deception (Stuss et al., 2001). The medial prefrontal cortex is constantly activated when a participant is prompted to think about themselves either verbally, visually, emotionally, or spatially (Northoff et al., 2006) and when thinking about how other people may be similar to self (Mitchell, Banaji, & MacRae, 2005). The left posterior dorsal regions of the medial prefrontal cortex are also engaged when analyzing the psychological state of someone from a third person perspective (D'Argembeau et al., 2007). Finally, studies have shown activation in the left temporal pole when participants are prompted to engage in tasks requiring semantic processing or autobiographical recall, or when asked to sort incoming information into context (D'Argembeau et al., 2007; Frith & Frith, 2003). To summarize, attributing the mental states of others, perspective taking, in addition to other components of ToM and social cognition in general are mediated by a variety of neural processes

and networks. However, the frontal lobes do appear to be more critically involved in comparison to other regions.

TBI and Social Cognition Impairments

Structures underlying social cognition are vulnerable to TBI (Bigler, 2007; Bigler & Maxwell, 2011). Although TBI produces variable multifocal and diffuse neuropathology, typical damage occurs due to acceleration-deceleration forces that scrape the soft brain tissue across the bony floor of the anterior and middle fossae of the skull (Bigler, 2007; Bigler & Maxwell, 2011). The medial frontal brain surfaces are compressed against the dorsal bone and collide with the cerebral falx. These bumps and bruises lead to the disruption of medial regions and their connections, therefore the ventrolateral, medial, and orbital frontal lobes and the ventromedial temporal lobes are the are the brain regions most commonly impacted by TBI (Bigler, 2007; Bigler & Maxwell, 2011; McDonald & Flanagan, 2004). The connections between the subcortical and frontal systems are further disrupted by diffuse axonal injury to brainstem-cortical connections, the corpus callosum, as well as the gray-white matter junction of the cerebral cortex (McDonald & Flanagan, 2004).

Previous research on TBI and social cognition. Neural accounts of social cognition and ToM have been dominated by imaging research involving typically developing individuals or individuals with focal lesions (McDonald, 2013). There have been a few studies involving participants with TBI (Newsome et al., 2010; Schmitz, Rowley, Kawahara, & Johnson, 2006), however their validity has been questioned because the complex nature of TBI-related brain damage makes it difficult to extrapolate valid information using neuroimaging (McDonald, 2013). On the other hand, there have been some fruitful results obtained from some structural imaging studies examining brain-behaviour relations in TBI participants. In one study conducted

by Shamay-Tsoory and Aharon-Peretz (2007), ToM deficits were observed in participants with TBI with severe ventromedial lesions and dorsal lateral frontal pathology. While the findings of the study enhance our understanding of social cognition processes in patients with TBI, they cannot be generalized since the sample size only consisted of participants with severe TBI (Shamay-Tsoory & Aharon-Peretz, 2007). Similar findings on ToM abilities in studies involving patients with focal lesions were also obtained in a different study by Shamay-Tsoory (2011) with TBI participants. In both focal lesion and TBI participant population the ventral and dorsal regions within the medial prefrontal cortex were activated during cognitive processing of the self and others (Shamay-Tsoory, 2011). Emotional resonance, the ability to sympathize with the pain of others and feel inclined to help, also appears to be mediated by the anterior cingulate and the insula in combination with the amygdala in both clinical population (Shamay-Tsoory, 2011). There was no difference between participants with vs. without brain damage in their ability to sympathize with someone else's pain (Shamay-Tsoory, 2011). Problems in different aspects of social cognition are to be expected in individuals with TBI given how prone the ventromedial frontal lobes are to damage following a TBI (McDonald, 2013). Critical connections in circuits that support social cognition processes will be further compromised due to diffuse axonal injury, which is prevalent in TBI.

With respect to ToM abilities and other social cognitive processes, imaging studies have found activation in similar brain regions in participants with focal lesions and participants with TBI engaging in the same task (McDonald, 2013; Shamay-Tsoory, 2011; Shamay-Tsoory & Aharon-Peretz, 2007; Stuss et al., 2001). Several neuropsychological tests sensitive to TBI, such as The Awareness of Social Inference Test (TASIT) (McDonald, Flanagan, & Rollins, 2002) and the VSIT (Turkstra, 2008) have also been used repeatedly to predict functional deficits and

behavioural problems (McDonald, 2013). The VSIT in particular has been recognized for measuring social cognition in more real-life encounters (McDonald, 2013). Previous studies using the VSIT have found that individuals with TBI obtain much lower scores in comparison to the control groups (Turkstra, 2008; Turkstra et al., 2018). To date there has been no study that has investigated whether site of lesion in participants with TBI influences their performance on the VSIT. Addressing this would allow us to better understand if TBI participants are able to preserve social cognitive and ToM abilities if their injury does not cause any damage to the frontal lobes.

Study Hypothesis

The study hypothesis was that individuals with TBI who had frontal lobe lesions would obtain lower scores on the VSIT than individuals with TBI who did not have documented frontal lobe lesions. There were two main reasons for this hypothesis based on review of existing literature. First, damage to the frontal lobes has been found to disrupt social cognitive processes, including ToM (McDonald, 2013). Second, individuals with TBI and individuals with focal frontal lobe lesions both perform similarly on social cognition and ToM tasks (Shamay-Tsoory, 2011; Shamay-Tsoory & Aharon-Peretz, 2007). Therefore, a person who has a TBI where there was frontal lobe damage is expected to be less accurate on the VSIT when compared to someone who had a TBI with no documented damage to the frontal lobes.

Materials and Methods

Participants

This study was a secondary analysis of data from 51 adults with moderate-to-severe TBI (23 females), for whom imaging data were available. Participants had been recruited from community sources for two completed studies in the midwestern United States (Turkstra, 2008;

Turkstra et al., 2018), and a third study in Canada that was in progress but suspended because of pandemic precautions in March 2020. Injury severity for TBI participants was defined based on standard injury criteria (Malec, Testa, Rush, Brown, & Moessner, 2007): 1) loss of consciousness for at least 30 minutes, and 2) Glasgow Coma Scale full score in the first 24 hours of less than 13, or 13 or higher with evidence of brain lesions. In all three studies, participants were included if they were ages 18-65 years, self-identified as native English speakers, and provided confirmation that their TBI occurred at least 6 months prior to study participation. Demographic information and cognitive test scores for 13 participants from the study conducted by Turkstra (2008) are shown in Table 1. Demographic information and cognitive test scores for 34 participants from the study conducted by Turkstra et al. (2018) and 4 participants from the third study that was suspended due to pandemic precautions are shown in Table 2.

Table 1

TBI Participant Demographic Information and Test Scores obtained from Turkstra (2008)

	TBI (n = 13)	
	M	*SD*
Age in Years	32.85	15.48
Age Range	18-65	
Males: Females	5:8	
KBITIQ	86.78	16.70

Note. TBI = traumatic brain injury, *M* = mean, SD = standard deviation, KBIT IQ = Kaufman Brief Intelligence Test Intelligence Quotient.

Table 2

TBI Participant Demographic Information and Test Scores

	TBI (n = 38)	
	M	SD
Age in Years	41.32	12.06
Age Range	24-65	
Males: Females	16:22	
Years of Education	14.88	2.39
Trails A	-.5	1.29
Trails B	-1.82	3.40
WAIS-PSI	87.74	15.06
CVLT First Trial	5.69	1.89
CVLT Immediate	-.74	1.34
CVLT Delayed	-.86	1.44

Note. TBI = Traumatic Brain Injury group. *M* = mean, SD = standard deviation, CVLT = California Verbal Learning Test (Delis, Kramer, Kaplan, & Ober, 1987), Trails A: Trailmaking Test Part A, Trail B: Trailmaking Test Part B (Tombaugh, 2004), WAIS PSI = Wechsler Adult Intelligence Scale (Wechsler, 2008) Processing Speed Index. Sex is reported as male to female ratio. Age range is reported as youngest to oldest. Trails A and B scores are *z*-scores; CVLT, WAIS and PSI scores are scaled scores.

Table 3

Participant VSIT Scores by Site of Lesion

	TBI (n = 51)	
	Frontal Lesion (n = 33)	Other Lesion (n = 19)
Mean	88.28	86.84
SD	9.22	9.10

Note. TBI = Traumatic Brain Injury group, SD = standard deviation.

Measures

Informed Consent and Study Intake Form. In all three studies, participants were provided with an Ethics Committee-approved consent form outlining the purpose and procedure of the study, and risks and benefits. A study intake form was filled out by the researcher in collaboration with the participants. The intake form consisted of questions about participants' age, sex, race, years of education, and TBI history (See Appendix A).

Measures to Characterize the Sample. The Common Data Elements Committee (CDE) for TBI research (Wilde et al., 2010) recommended standardized tests that participants with TBI should complete, to characterize the sample and allow researchers to compare results obtained by different studies and publications. Per the CDE recommendations, participants completed the following tests: the California Verbal Learning Test (CVLT; Delis et al., 1987)**,** Wechsler Adult Intelligence Scales Processing Speed Index tests (WAIS-PSI; Wechsler, 2008) and Trails making Tests A and B (Trails A and B; Tombaugh, 2004).

Visual Social Inference Test (Turkstra, 2008) is a video test of social cognition that was designed to manipulate working memory as a construct factor and minimize it as a measurement factor (Turkstra et al., 2018). The full test development has been described in detail in a previous study (Turkstra, 2008). The VSIT was created based on the consensus that there are three primary skills that are essential in social interaction: the ability to 'read' a situation, the ability to understand implied meaning, as well as having knowledge and insight on social rules and culture (Turkstra, 2008). There are 16 pairs of videos in the test, each depicting two adolescent actors having conversations. To ensure that interactions between the actors in the video were as natural as possible, actors were not provided with a script or time to rehearse, they were instructed to improvise (Turkstra et al., 2018). Questions in the VSIT are in a yes or no

forced-choice format and displayed on the screen during the entire video and all language is at a third-grade level, to minimize potential confounds due to non-ToM measurement factors such as working memory or language level (Turkstra et al., 2018).

The same actors are used within each pair of videos. Whether or not a participant is able to answer the question asked in the second video correctly depends on if they understood the question being asked in the first video. For example, a question in the second video may ask the viewer if the request being made by one of the actors in the video is appropriate. In order to answer this question correctly, the participant would have had to remember his or her answer for the first video (e.g., Do they know each other well?). For 8 of the video pairs, the second video is immediately presented after the first video (Immediate Items); for the remaining 8 pairs, there is a 30-second distractor after the first video and then the second video in the pair is presented (Delayed Items). The distractor tasks are non-theory of mind tasks (e.g., listing all the foods you can think of beginning with the letter 'F') (Turkstra et al., 2018).

Order of video pairs was randomized then fixed. A practice item at the beginning of the task shows the distractor screen and demonstrates that the two videos in each pair are linked to one another, so participants are aware that they will have to hold information about the first video in working memory to answer a question in the second video. In a previous study (Turkstra, 2008), adults with TBI scored significantly lower on the VSIT than comparison group for the first video in each pair (First Items) as well as items in the two delayed conditions (effect sizes =.87 First Items, 1.00 Immediate Items, .54 Delayed Items) and Immediate Item scores were significantly correlated with scores on a WM test (r=.40). Results from the study demonstrated direct effects of working memory manipulation on theory of mind task performance. Other studies using the VSIT have obtained similar results (Turkstra et al., 2001;

Turkstra et al., 2018). Scores of all participants with TBI were lower on the delayed condition, supporting the task manipulation for people with or without TBI.

Procedure

In all three studies, participants were first provided with a consent form followed by an intake form. The consent process included a request for medical records, to provide information about site of brain damage. TBI participants in all three studies were then required to complete the Common Data Elements Committee tasks and other study tasks in randomized order. The following data were obtained for all three studies and sorted onto an excel sheet for further analysis: sex, age, cause of TBI, TBI severity, scores on the VSIT, and primary site of lesion on most recent MRI or CT scan.

Scoring and data analysis. The VSIT yields three sets of scores: (1) total correct for first items (i.e., number of correct social inferences on the first item in each pair; maximum =16) , (2) immediate Items (i.e., the number of correct inferences for the items requiring an immediate prediction; maximum = 8), and delayed Items (i.e., the number of correct inferences for items requiring a delayed prediction; maximum = 8). In order to obtain a full credit for the immediate and delayed prediction items for the videos in each pair, participants had to answer both videos correctly.

Site of lesion. For the purpose of this study participants were divided into two different categories based on whether the radiology report included unilateral or bilateral lesions in the frontal lobe (n = 33), or lesions in other brain regions excluding the frontal lobes (n= 19). This was determined using reports from neuroimaging completed either at the time of initial hospitalization or subsequent to that. Lesion analysis and categorization was determined following recommendations provided by Damasio and Damasio (1989). Most TBI participants

have lesion overlaps and secondary lesions, if the frontal lobe was one of the many lesions that the participant had, they were placed in the frontal lobe damage category. Based on recommendations provided by Damasio and Damasio (1989) cases involving deep frontal white matter and dorsal striatum were categorized as frontal lobe damage as well.

Results

We compared groups on their immediate, delayed, and first items scores on the VSIT using a one-way ANOVA, with the percent correct on the VSIT as the dependent variable, and site of lesion (Frontal vs. Other) as categorical between-group variables. There was no statistically significant difference between groups as determined by one-way ANOVA F (1,53) = 0.009, p = 0.93. Table 3 provides the descriptive statistics for the study.

Discussion

Individuals with TBI who did not have a frontal lobe lesion were no more likely to score higher on the VSIT than participants with TBI who did have a frontal lobe lesion. While the results obtained did not support the study hypothesis, they do contribute to literature in this area; shedding light on how difficult social cognition is to measure amongst the TBI population and how research results obtained are generally questionable due to the complex neuropathology associated with TBI. Moreover, the results do provide information regarding the use of the VSIT in that we now know it is not sensitive to site of lesion amongst participants with TBI. There is evidence indicating that participants with TBI perform more poorly than control participants on the VSIT. In the previous study by Turkstra et al. (2018) there was a significant difference between scores of control participants and participants with TBI on the VSIT first and Immediate items, t (245) = 2.9, $p < .005$. The aim of the study was to report behavioural data and site of

lesion was not considered in analysis, so the study did not advance understanding of mechanisms underlying the behavioural difference.

Previous studies have revealed links between ToM and frontal lobe damage (McDonald, 2013; Rowe et al., 2001; Stuss et al., 2001), but these have mostly been in patients with focal frontal lesions. Brain-behaviour relationships are much more difficult to establish in TBI because of the heterogeneity of brain damage across this population. In studies comparing ToM performance of adults with TBI and adults with focal lesions, differences have been marginal or insignificant (Ietswaart, Milders, Crawford, Currie, & Scott, 2008; McDonald & Flanagan, 2004). Other features of TBI complicate the picture. For example, slow processing speed and poor cognitive flexibility interfere on both static (Ietswaart et al., 2008) and dynamic (McDonald & Flanagan 2004) emotion perception tasks, and in one study (Ietswaart et al., 2008) entirely accounted for between-group differences. Injury severity also predicted poor performance (Ietswaart et al., 2008). Overall, the complex nature of a TBI in addition to the fact that patterns of neuropathology vary in severity from one patient to another, generally prevent researchers from being able to obtain clear results from structural imaging data or neuropsychological assessments.

This study had several limitations. I divided patients into two categories using structural imaging reports, following previous studies examining social cognition and the frontal lobes (Stuss et al., 2001). In focal lesion studies (Stuss et al., 2001), dividing participants into the two respective categories using imaging data is quite a straightforward process. It is based on the presents or absence of a lesions in a particular region. In my study, this was not as easy to do. As can be seen on Table 2 (Appendix A), almost all participants had injured more than one region of the brain. Medical notes for some reports included words like “could” or “may” when referring

to whether or not a lesion was present, so data may not be accurate. Some medical records included statements that a skull fracture, hematoma, contusion, excessive bleeding, or swelling prevented the ability to clearly see and pinpoint which areas had been damaged. Thus, clarity and resolution of CT and MRI scans also could have been compromised, depending on these complications and the severity and neuropathology of the injury. As a result, I could have easily miscategorized participants in regard to true pathology. This was one of the primary challenges in using imaging reports.

Another limitation was not being able to determine the length of time between the accident and when imaging data were acquired. As can be seen in Table 2 (Appendix A), reports for patients such as M4, M10, F5, and many others, indicated a hematoma, hemorrhage, contusion, or other acute process, suggesting that the scan may was acquired at the time of the accident. However, for patients like M22, M21, F19, there are no notes about acute processes, suggesting that those scans were in the chronic stage post-injury. Time between the accident and when the imaging scans were taken is critical because it influences whether or not the site of lesion for a particular patient is accurate. As one can imagine, the imaging data obtained at the time of accident is going to differ significantly from the imaging data obtained at a later day, week, month, or year when excessive bleeding and swelling has reduced, and function of some regions may have improved.

Site of lesion categorization was based on structural imaging. In general, structural imaging techniques like CT and MRI are used to obtain a visual of primary brain injury (Metting, Rödiger, De Keyser, & van der Naalt, 2007). Primary brain injury, like diffuse axonal injury, contusions and hematomas, are those that occur at the moment of impact as a results of external contact forces or from movement of the brain within the skull (Metting et al., 2007). In a

clinical setting, structural imaging provides a visualization of lesions and abnormalities that may need acute and or surgical interventions (Metting et al., 2007). In our study, the use of functional imaging techniques such as single photon emission computed tomography (SPECT), PET, functional magnetic resonance imaging (fMRI), may have provided better insight on brain-behaviour relationships. SPECT, PET, and fMRI are able to provide information on different activation patterns of localized brain functions and show cerebral abnormalities beyond the structural visualisation provided by CT and MRI (Metting et al., 2007). Studies using PET indicate that one third of anatomical lesions can be linked to more widespread metabolic abnormalities within the brain and that 42% of abnormalities detected using PET are not associated with any anatomical lesions(Alavi, 1989; Metting et al., 2007). The information that can be provided using different functional imaging techniques is not going to be the same as that provided by structural imaging. The former provides useful information on brain pattern activation and its metabolic state, while the latter provides an anatomical visualization of lesions.

Another major challenge in TBI research is that it is limited by small sample sizes. A small sample size restricts us from being able to analyze any relationship patterns. Severity varies from one patient to another and so does the neuropathology of the TBI, therefore, results cannot be generalized to the TBI population as a whole. A larger sample size consisting of an even number of moderate and severe participants with TBI would allow for more generalizable data analysis. Previous studies have recommended a minimum of 30 participants for each TBI severity group to obtain data with better precision and confidence (Babikian & Asarnow, 2009; Looi et al., 2020)

In TBI research, neuropsychological assessments have been adopted as a common approach to examine individual distinct functional units of the brain (McDonald, 2013). While

neuropsychological tests provide valuable insights, they have confounds of their own. For example, it is difficult to look at one region of the brain in isolation with respect to ToM, when most ToM tasks (e.g., stories, videos, photos) stimulate visual, auditory, attention, and language processes in different ways (McDonald, 2013). ToM tasks also vary in complexity because they tap into, engage, and rely on working memory, learning, abstract reasoning and flexibility, which are all cognitive resources that are often compromised following a TBI (McDonald, 2013).

Contradicting results have often been obtained when using neuropsychological assessments within the TBI population. In a study of school-aged children with TBI by Dennis, Agostino, Roncadin, and Levin (2009), cognitive inhibition and working memory deficits accounted for poor performance on ToM tasks. Based on these findings, the researchers concluded that ToM is not domain-specific (Dennis et al., 2009). Bibby and McDonald (2005), however, found different results in adults with TBI. These researchers found that ToM tasks that required participants to understand what another person thought (i.e., first-order ToM), did not require working memory or the capacity to make general inferences (Bibby & McDonald, 2005); whereas ToM tasks that required the participant with TBI to understand what one person thought about someone else's thoughts (i.e., second-order ToM) did require both working memory and general inference-making capacity (Bibby & McDonald, 2005). One way to answer this question would be to use non-mental inferencing tasks with similar working-memory demands as a control when examining ToM performance amongst TBI participants (McDonald, 2013).

In this study, the VSIT was used as a ToM and social cognition assessment amongst individuals with TBI. As the frontal lobe plays a critical role in social cognition, there was reason to hypothesize that adults with TBI who did not have frontal lobe lesions would perform better on a social cognition task like the VSIT. While this was a plausible hypothesis, supported by

previous research (Bibby & McDonald, 2005; McDonald, 1999, 2013; Rowe et al., 2001; Stuss et al., 2001; Turkstra, 2008; Turkstra et al., 2018), the relationship between these different components was not as expected. What this study emphasizes most is that social cognitive impairments are not a measure of brain damage. Adults with TBI participants can score poorly on social cognition tasks, but performance on those tasks does not necessarily indicate cortical damage and it should not be assumed that it would. With this in mind, when researchers are talking about TBI severity, it is critical for them to clarify whether they are referring to severity in terms of cognitive impairments or social impairments or brain damage.

Results of this study suggest that the site of lesion of participants with TBI does not explain performance on the VSIT. These results seem plausible given the complex neuropathology of a TBI. Our study shows that damage caused by a TBI is too widespread to investigate and isolate the impact caused by a specific lesion site. A next step would be to use functional imaging, rather than structural imaging, to obtain a better understanding of the neural substrate of social cognition impairments in participants with TBI. The former is often used in research settings to depict brain activity during different tasks and therefore can better indicate if site of lesion can influence performance on the VSIT in participants with TBI.

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Appendix A

TBI Participant Injury Data and VSIT Scores

ID	Age at Test	Severity	Injury Mechanism	Primary Site of Lesion (s) on Most Recent MRI or CT Scan	VSIT Score
M1	42	Moderate-Severe	Assault	Right basal ganglia infarct, prominent perivascular space	75
M2	50	Moderate-Severe	MVA	Right posterior frontal lobe lesion, deformity of front horn and body of right lateral ventricle, loss of right basal ganglia volume	87.5
M3	26	Moderate-Severe	MVA	Frontoparietal contusion with subarachnoid hemorrhage and subdural hematoma, right frontal subdural hematoma, general cerebral edema	100
M4	35	Moderate-Severe	MVA	Several small foci of petechial hemorrhage within the cerebral hemispheres at grey/white junction (most conspicuous in the posterior right frontal lobe, anterior left frontal lobe, and right temporal lobe)	87.5
M5	36	Moderate-Severe	Assault	Epidural and subdural hematoma	87.5
M6	26	Moderate-Severe	MVA	Intraparenchymal hemorrhage, subarachnoid hemorrhage, diffuse axonal injury, left frontal contusions, and a subdural hematoma	75
M7	59	Moderate-Severe	Fall	Parenchymal contusion and intraparenchymal hemorrhage within the medial right frontal lobe	87.5
M8	27	Moderate-Severe	MVA	Intraventricular hemorrhage and intraparenchymal hemorrhage	93.75
M9	44	Moderate-Severe	Other	Hemorrhages in the left frontal, bilateral posterior parietal and cerebral peduncles	87.5
M10	28	Moderate-Severe	MVA	Focal hematoma within the left thalamus, numerous scattered punctate high attenuation areas including deep posterior frontal lobes near the gray white interface	100
M11	48	Moderate-Severe	MVA	Hemorrhagic contusions within the body of the corpus callosum and the deep white matter of the posterior frontal lobe on the left	93.75
M12	64	Moderate-Severe	MVA	Obstructive hydrocephalus	93.75
M13	42	Moderate-Severe	MVA-Pedestrian	Left frontal lobe to occipital lobe subdural hematoma	87.5
M14	34	Moderate-Severe	MVA	Intracranial injury of other and unspecified nature	87.5
M15	33	Moderate-Severe	Fall	Left subdural hematoma and left frontal lobe hemorrhagic contusion	93.75
M16	53	Moderate/mild	Fall (1st), MVA (2nd)	Subarachnoid hemorrhage of right tentorium with extension into right middle cranial fossa	81.25
M17	36	Moderate-severe	Assault	Right epidural hematoma, large right temporal hemorrhagic contusion, inferior right posterior subdural hematoma	81.25
M18	65	Moderate-severe	Fall	Bilateral frontal and temporal lobes as well as subarachnoid hemorrhage within the bilateral sylvian cisterns	81.25
M19	55	Moderate-severe	MVA	Left frontal subarachnoid hemorrhage	93.75

M20	65	Moderate/moderate-severe	Fall	Subdural hematoma with left frontal focal density	68.75
M21	65	Moderate	MVA	Right temporal lobe	75.00
M22	20	Severe	MVA	Left frontal lobe	93.75
M23	39	Severe	MVA	Left frontal and temporal lobes, corpus callossum	75.00
M24	19	Severe	MVA	Multiple cortical and subcortical lesions, diffuse axonal injury left temporal lobe greater than right, shearing of corpus callossum	87.5
M25	18	Severe	MVA	Bilateral frontal lobes	87.50
M26	20	Severe	MVA	Diffuse axonal injury	87.50
M27	41	Severe	MVA	Left temporal lobe damage, left temporal hemorrhagic contusion	93.75
M28	43	Severe	MVA	Significant intracranial injuries, multiple small bifrontal cortical contusions, cortical contusions involving bilateral temporal and occipital lobes	93.75
F1	25	Moderate-Severe	MVA	Lateral left parietal lobe and medial right temporal lobe. Large contusion with a few patchy areas of pneumocephalus in the frontal lobe, above the anterior cranial fossa	87.5
F2	24	Moderate-Severe	MVA	Parietal lobe and right temporal lobe	100
F3	37	Moderate-Severe	MVA	Insults in the frontal lobes	93.75
F4	45	Moderate-Severe	MVA	Bilateral frontal lobe, medial temporal lobes minimal subarachnoid hemorrhage noted	93.75
F5	40	Moderate-Severe	Fall	Subarachnoid hemorrhage layers within the right sylvian fissure and right frontal sulci. Hyper attenuating foci within the right occipital lobe, anterior rectus gyri, and left temporal lobe	87.5
F6	32	Moderate-Severe	MVA	Punctate areas of increased attenuation are noted within the frontal lobes bilaterally, right greater than left, as well as the anterior right temporal lobe, consistent with hemorrhagic contusions	100
F7	43	Moderate-Severe	MVA	Small right frontal subcortical hemorrhages and possible hemorrhages within the right internal capsule	93.75
F8	25	Moderate-Severe	MVA	Subtle subarachnoid hemorrhage is present at the vertex at the posterior frontal lobes, both parietal lobes	93.75
F9	31	Moderate-Severe	Fall	Severe encephalopathy	62.5
F10	43	Moderate/moderate-severe	Other	Subarachnoid hemorrhage and occipital skull fracture	100
F11	54	Mild/moderate-severe	Fall	Bifrontal hemorrhagic contusion and occipital fracture	100
F12	49	Severe/moderate-severe	Fall	Subarachnoid hemorrhage and intracerebral hemorrhage	81.25
F13	41	moderate-severe	Fall	Subarachnoid hemorrhage	87.5
F14	61	Mild/Moderate-severe	Other	Subarachnoid hemorrhage along the left precentral sulcus and worsening left occipital scalp hematoma	93.75
F15	24	Severe	MVA	Bilateral frontal and occipital lobes, right temporal lobe, right thalamus and midbrain, right cerebellar vermis	81.25

F16	47	Severe	MVA	Bilateral frontal, temporal, and parietal lobes	62.50
F17	20	Severe	Thalamic arteriovenous malformation	Massive intraventricular hemorrhage in all ventricles; left frontal ventriculostomy	81.25
F18	48	Severe	MVA	Bilateral frontal lobes, caudate nucleus	100.00
F19	36	Severe	MVA	Right frontal and temporal lobes	93.75
F20	22	Severe	MVA	Bilateral frontal and temporal lobes	81.25
F21	49	Mild-Moderate	MVA	Normal	93.75
F22	42	Severe	Fall	Left Frontotemporal parietal lobe, subdural and intradural hematomas	81.25
F23	26	Severe	MVA	Left orbital floor fracture, left scapula fracture, small right temporal subarachnoid hemorrhage	87.5