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NEUROBEHAVIOURAL OUTCOME IN TRAUMATIC BRAIN INJURY IN  
RELATION TO NEUROPSYCHOLOGICAL PERFORMANCE AND COMPUTED  
TOMOGRAPHY DATA

by  
Shelley Ylioja

A Dissertation Submitted to the Faculty of Graduate Studies  
through Psychology  
in Partial Fulfillment of the Requirements for  
the Degree of Doctor of Philosophy at the  
University of Windsor

Windsor, Ontario, Canada

2012

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Neurobehavioural Outcome in Traumatic Brain Injury in Relation to  
Neuropsychological Performance and Computed Tomography Data

by

Shelley Ylioja

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## **AUTHOR'S DECLARATION OF ORIGINALITY**

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## **ABSTRACT**

The present study sought to determine whether information attained from computed tomography (CT) imaging and neuropsychological evaluation can predict degree of apathy, disinhibition, and executive cognitive dysfunction at one to five years following mild complicated, moderate, or severe traumatic brain injury (TBI). Furthermore, it examined the level of concordance between reports made by individuals with TBI and informants regarding these domains of neurobehavioural disturbance in daily life. Results showed that CT data collected in the acute post-injury stage was not predictive of the degree of neurobehavioural disturbance reported by either TBI survivors or informants one to five years later. While concurrent performance on neuropsychological testing was not predictive of self-reported difficulties in daily life in any of the three domains of interest, performance was predictive of informant-reported executive cognitive dysfunction. Finally, informants reported higher levels of disturbance than did the survivors themselves, with the greatest discrepancy present for level of executive cognitive dysfunction.

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## I INTRODUCTION

Moderate and severe traumatic brain injury (TBI) is frequently accompanied by neurobehavioural disturbances, and may involve a combination of disinhibited behaviour, apathy, and executive cognitive dysfunction (Gouick & Gentleman, 2004; McAllister, 2008). Despite the reported frequency of occurrence in TBI, research on these disturbances in the everyday lives of TBI survivors is limited. Such behavioural changes have a negative impact on many aspects of an individual's life (Gouick & Gentleman, 2004; Levin & Kraus, 1994), as well as on their family (Anderson, Parmenter, & Mok, 2002). Further research is necessary to elucidate whether certain evaluations (e.g., neuroimaging and neuropsychological testing) can inform how likely an individual is to experience such disturbances post TBI, to understand the reason for such changes from a neuroanatomical perspective, and to determine what cognitive deficits may underlie these behaviours.

Whereas the predictive utility of early injury information has been examined in relation to several aspects of outcome in TBI, very little research has examined predictive utility of such data in relation to TBI-related neurobehavioural disturbances. Thus, one goal of the current study was to examine the predictive utility of acute computed tomography (CT) data in relation to disinhibition, apathy, and executive cognitive dysfunction one to five years after injury. Additionally, the relationship between reports of neurobehavioural disturbance and neuropsychological test performance was examined to facilitate understanding of the underlying constructs of disinhibition, apathy, and executive cognitive dysfunction in TBI, and to provide information about how we should use neuropsychological test data to make predictions about neurobehavioural

disturbances in daily life. The final goal was to evaluate how closely the reports of survivors and their loved ones agreed with respect to these behavioural difficulties and whether level of agreement was consistent across these three domains of neurobehavioural disturbance. Before describing the expectations of the current study, the literature on neurobehavioural disturbances in TBI is reviewed.

### **A Review of the Literature on Neurobehavioural Disturbance after TBI**

The mechanism of injury in moderate to severe TBI will be outlined briefly to provide a basis for the discussion of expected neuroanatomical correlates of neurobehavioural disturbances. Next, the three areas of post-TBI neurobehavioural disturbance that are the focus of the current study will be reviewed. Specifically, each disturbance will be described, the literature on neuroanatomical correlates will be reviewed, and the relationship between daily life manifestations of each neurobehavioural disturbance and neuropsychological test performance will be summarized. Finally, research examining concordance between self and other reports of neurobehavioural disturbances in daily life will be described.

**Mechanism of injury in TBI.** The main mechanism of injury in TBI is diffuse axonal injury (DAI), particularly in non-penetrating TBI (Adams, Graham, Murray, & Scott, 1982). DAI is caused by axonal stretching and tearing during acceleration, deceleration, and rotational forces on brain matter (Gaetz, 2004). These forces initiate a series of events within axons including axoplasmic transport disruption, swelling, and disconnection leading to white matter damage, myelin loss, and gliosis (Povlishock, 1992; Povlishock, 2000). These forces also damage small blood vessels resulting in hemorrhages throughout white matter (Levine, Katz, Dade, & Black, 2002). DAI is

multi-focal and occurs mainly in cortical gray-white matter junctions, subcortical white matter, the corpus callosum, and the brainstem (Adams, Mitchell, Graham, & Doyle, 1977; Gaetz, 2004).

DAI in moderate to severe TBI is often accompanied by contusion, hematoma, and hemorrhage as a result of the brain coming into contact with the skull at high velocities (Adams, Graham, & Scott, 1980; Graham, Adams, & Gennarelli, 1988; Smith, Meaney, & Shull, 2003). Frontotemporal regions are the most common areas of focal damage in TBI, particularly the poles and ventral surface of these lobes, because of the anatomy of the skull (Adams et al., 1980; Bigler, 2007; Graham et al., 1988; McLellan, 1990). Contusions are generally on the cortical surface of the brain, but in severe cases they can extend to the subcortical white matter (Auerbach, 1986).

Aside from these primary mechanisms of injury, secondary injury mechanisms have a role in moderate and severe TBI. Possible secondary mechanisms of damage include herniation, increased intracranial pressure, edema, hypoxia, excitotoxicity, microvascular injury, and hypometabolism (Gennarelli, 1993; Graham et al., 1988; Povlishock & Katz, 2005). Primary damage to cortical gray matter can cause secondary atrophy to downstream white matter fibre tracts (Farkas & Povlishock, 2007; Povlishock, 1992; Povlishock & Katz, 2005). Alternately, primary damage to white matter tracts via DAI causes secondary degeneration of the gray matter to which these tracts provide input through the process of Wallerian degeneration (Farkas & Povlishock, 2007; Povlishock, 1992; Povlishock & Katz, 2005).

**TBI and neurobehavioural disturbance.** Despite frequent good physical recovery, such as healing of physical injuries and recovery of ability to conduct basic

activities of daily living independently, survivors of moderate to severe TBI (initial Glasgow Coma Scale < 13) often experience lasting changes in cognitive function (Draper & Ponsford, 2008), personality, and impulse control (Kim, 2002). These changes may be manifested as post-TBI behavioural disturbances which may include affective instability, irritability, agitation, aggression, immature behaviour, inappropriateness, lack of tact, rigidity, decreased motivation, asponaneity, decreased social perception, perseveration, and poor planning (Gouick & Gentleman, 2004; Levin & Kraus, 1994; McAllister, 2008; Prigatano, 1992; Ylvisaker et al., 2007). These behavioural disturbances can lead to a variety of problems in everyday life including diminished quality of life, inability to work, relationship difficulties, decreased self-esteem, trouble with the law, and substance use (Gouick & Gentleman, 2004; Levin & Kraus, 1994). Additionally, behavioural disturbance has been implicated as the most significant contributor to severity of stress experienced by family members of TBI survivors (Anderson et al., 2002; Brooks, Campsie, & Symington, 1986). Many of the behavioural disturbances frequently observed following TBI can be categorized into characteristic clusters of behaviour including disinhibition, apathy, and executive cognitive dysfunction.

***Disinhibited behaviour in TBI.*** Disinhibited behaviour or loss of the ability to regulate one's behaviour is relatively common in survivors of moderate or severe TBI (Dyer, Bell, McCann, & Rauch, 2006; Prigatano, 1992). In milder forms it may involve irritability, verbal hostility, shallowness, and inappropriate jocularity and can sometimes appear to be a magnification of premorbid negative personality traits. In more severe forms, it may present as a drastic change in personality, such as the emergence of

physical aggression, sexually disinhibited remarks and behaviour, poor impulse control, disregard of consequences, emotional lability, social inappropriateness, and self-destructive behaviour (Bezeau, Bogod, & Mateer, 2004; Levin & Kraus, 1994; Malloy, Bihle, Duffy, & Cimino, 1993; Namiki et al., 2008; Prigatano, 1992; Weddell & Leggett, 2006). Such behaviour frequently disrupts relationships with family and friends and creates conflict with colleagues and other work-related difficulties (Levin & Kraus, 1994). Disinhibition has been reported as being nine times more common in TBI than in stroke (Starkstein & Kremer, 2001). A single study by Ciurli, Formisano, Bivona, Cantagallo, and Angelelli (2011) reported a frequency of 28% after severe TBI in a group of 120 survivors one month to six years post injury. The cut-off for disinhibition was set at the 95<sup>th</sup> percentile of healthy control subjects' scores on the Neuropsychiatric Inventory.

*Neuroanatomical correlates of disinhibition.* Disinhibited behaviour or loss of the ability to regulate one's behaviour has typically been linked to frontal lobe damage in various populations (Burgess & Shallice, 1996; Drewe, 1975; Malloy, Webster, & Russell, 1985; Miller & Milner, 1985; Miller, 1992; Toczek, 1960). More specifically, such behaviour has been linked to the orbitofrontal region of the frontal cortex as far back as the 1800s, an association originally made by Leonore Welt (Starkstein & Kremer, 2001). The case of Phineas Gage in 1848 is a classic example of the behavioural changes that can occur following damage to the orbitofrontal cortex (Cato, Delis, Abildskov, & Bigler, 2004). In this famous case, a tamping iron that measured 3.5 feet long and weighed 13 pounds blasted through Gage's left cheek and out the top of his head, with areas of damage thought to have involved the bilateral orbitofrontal cortices, among other



frontal and subcortical white matter regions. His behaviour and personality are reported to have undergone marked change from that of a responsible and efficient foreman to someone who was disinhibited and socially inappropriate (Cato et al., 2004). Research since that time has continued to support a link between disinhibition and the orbitofrontal or ventromedial region (Blumer & Benson, 1975; Eslinger & Damasio, 1985; Grafman et al., 1996; Hecaen, 1964; Kim, 2002; Luria, 1969; Luria, 1973; Meyers, Berman, Scheibel, & Hayman, 1992; Starkstein & Robinson, 1997; Tranel, Bechara, & Denburg, 2002; Vanderploeg & Haley, 1990). Lesions or disruption of the orbitofrontal frontal-subcortical circuit, comprised of the orbitofrontal cortex and specific regions of the basal ganglia and thalamus, also have been linked to disinhibited behaviour in disorders such as frontotemporal dementia and Huntington's disease (Bonelli & Cummings, 2007; Cummings, 1993; Cummings, 1995; Masterman & Cummings, 1997; Starkstein & Kremer, 2001).

Disinhibited behaviour in TBI populations has been postulated to be a result of frontal lobe injury (Mattson & Levin, 1990; Oder et al., 1992). While the research literature does not contain many studies attempting to further isolate frontal neuroanatomical correlates of disinhibition in TBI, some evidence from research investigations (Rolls, Hornak, Wade, & McGrath, 1994; Weddell & Leggett, 2006) and case studies (Cicerone & Tanenbaum, 1997; Malloy et al., 1993; Namiki et al., 2008) exists to suggest that orbitofrontal cortex damage may be linked, as in other etiologies, to disinhibited behaviour in TBI. It is also possible that damage to subcortical white matter might contribute to this behaviour. Although these studies did not examine DAI, this is

the main mechanism of injury in non-penetrating moderate to severe TBI (Adams et al., 1982) and damage to subcortical white matter might be expected.

*Neuropsychological correlates of disinhibition.* The majority of studies across etiologies agree that individuals showing behavioural problems of disinhibition tend to have unaffected cognition in neuropsychological testing (Cato et al., 2004; Dimitrov, Phipps, Zahn, & Grafman, 1999; Eslinger & Damasio, 1985; Meyers et al., 1992). For example, Dimitriv et al. (1999) presented the case of a person who experienced marked behavioural changes following a penetrating head injury affecting the ventromedial regions of the frontal lobe. These changes were characterized by extreme social difficulties, lack of inhibition in conversation, impulsive relationship decisions, lack of responsibility, and an inability to hold a job. Yet his performance on a comprehensive neuropsychological test battery was intact.

With respect to TBI, three research studies were found that examined cognitive performance alongside reports of behavioural disinhibition in everyday life. A recent study using the Frontal Systems Behavior Scale (FrSBe), the measure used in the current study, involved 56 participants at three to nine weeks post injury who had sustained a mild (two-thirds of sample) or moderate TBI (Schiehser et al., 2011). Once effort was controlled for, self-reported disinhibition on the FrSBe was significantly correlated with an attention and processing speed composite and an executive functioning composite, but not with a memory composite. When entered into a regression model, however, degree of disinhibition was not predictive of any of the cognitive composites.

Another study examined motor and verbal aspects of impulsivity through behavioural observations in an inpatient rehabilitation setting amongst a group of 40

survivors of moderate to severe TBI (Votruba et al., 2008). Their verbal impulsivity construct is more similar to disinhibition as it is defined in the current study than is motor impulsivity. Of several neuropsychological tests administered, only Trails B performance was significantly related to verbal impulsivity. However, whereas the correlation was significant, Trails B performance was not found to be a significant predictor of verbal impulsivity.

Tate's (1999) study involved a group of 30 severe TBI survivors at six months post injury. Rule breaks on three cognitive tests were examined in relation to relatives' reports of disinhibited behaviour, measured with the Current Behaviour Scale. This scale includes a subscale measuring impulsivity, aggression, and restlessness, which has some overlap with the conceptualization of disinhibition in the current study. The number of rule breaks on word and design fluency tasks was significantly related to relatives' reports of disinhibited behaviour, whereas the number of rule breaks on a maze task was not.

Two TBI case studies involve reports of disinhibited and socially inappropriate behaviour in everyday life. A person with severe TBI assessed at three months post injury demonstrated severe perseveration on the Wisconsin Card Sorting Test, inability to inhibit responses on a go/no-go task, a large number of intrusions on a verbal generativity task, impaired memory for both verbal and visual information, and impaired complex visual perception (Malloy et al., 1993). On the other hand, a report of similarly disinhibited behaviour was presented by Namiki and colleagues (2008). At one year following his severe TBI this individual's performance was intact on neuropsychological

tests of problem solving, organizing, planning, decision making, perseveration, memory, and intelligence.

While research in other etiologies involving disinhibited behaviour in daily life tends to show intact neuropsychological performance, studies specific to TBI show some mixed results. Disinhibition has been found to be related to, but not predictive of, attention/processing speed and executive functioning (Schiehser et al., 2011), related to but not predicted by Trails B performance (Votruba et al., 2008), and related to rule breaks on verbal and nonverbal generativity tasks (Tate, 1999). One case study presents impaired performance on executive functioning and memory tasks (Malloy et al., 1993), while another presents intact cognitive skills (Namiki et al., 2008). Although there is evidence of a relationship between disinhibition in daily life to executive functioning and attention/processing speed on neuropsychological testing, the two studies that examined predictive ability in addition to correlation revealed that the relationship was relatively weak.

Moderate to severe TBI frequently involves widespread damage as a result of DAI, and locations of focal damage differ across cases. This variability may account for the differences in neuropsychological test performance across individuals who demonstrate disinhibited behaviour in daily life. Thus, disinhibition in daily life and poor neuropsychological test performance in a given area may not result from damage to the same brain region.

***Apathy in TBI.*** Diminished motivation, characterized by apathy, is quite common among TBI survivors. Estimates of frequency range from 45% (Ciurli et al., 2011) to 66% (Andersson, Gundersen, & Finset, 1999) of severe TBI cases and 71% of

mild to severe TBI cases (Kant, Duffy, & Pivovarnik, 1998). Apathy, the least severe and most common form of diminished motivation, involves a decrease in goal-directed behaviour (decreased initiative, productivity, socialization, and pursuit of interests), goal-directed thought (lack of plans, interests, curiosity, and perceived importance of daily/social activities), and emotional response to goal-related events (flat and indifferent affect [Marin, Biedrzycki, & Firinciogullari, 1991; Marin & Wilkosz, 2005]). Abulia is a more severe form of diminished motivation, involving diminished spontaneity, speech, and movement in addition to apathy (Lichter & Cummings, 2001). The most severe form of motivational change is akinetic mutism, characterized by absence of spontaneous movement, initiative, verbalization, and response to questions and commands, as well as indifference to pain, thirst, and hunger (Mega & Cohenour, 1997).

Apathy frequently is mistaken for depression or even laziness in TBI populations (Kant & Smith-Seemiller, 2002), but it is a distinct syndrome that can be present with or without depression (Kant et al., 1998). The most notable differences are the lack of emotional distress and somatic complaints in apathy as opposed to depression (Andersson & Bergedalen, 2002). Apathy in TBI survivors is a source of great burden for their families (Marsh, Kersel, Havill, & Sleigh, 1998) and reportedly is a particularly large barrier to independence at home and return to work (Cattelani, Roberti, & Lombardi, 2008; Prigatano, 1992).

*Neuroanatomical correlates of apathy.* It has been recognized for several decades that apathy may follow injury to the brain, particularly in cases of frontal lobe damage (e.g., Lishman, 1968; Luria, 1963, cited in Prigatano, 1992). Luria (1963, cited in Prigatano, 1992) wrote about asponaneity or loss of “mental tension” following large

bilateral frontal lesions. Blumer and Benson (1975) observed a “pseudodepressive syndrome” following frontal injury involving decreased speech, initiation, and libido, as well as apathy and indifference. Apathy has been further specified to be more commonly associated with right hemispheric as opposed to left hemispheric frontal lesions (Andersson et al., 1999; Finset & Andersson, 2000). Damage to the anterior cingulate cortex has been linked to apathy (Devinsky, Morrell, & Vogt, 1995; Fesenmeier, Kuzniecky, & Garcia, 1990; Gugliotta, Silvestri, De Domenico, Galatioto, & Di Perri, 1989; Nemeth, Hegedus, & Molnar, 1988; Saint-Cyr, Bronstein, & Cummings, 2002), as have lesions to subcortical regions, such as the caudate nucleus (Bhatia & Marsden, 1994), globus pallidus (Helgason, Wilbur, Weiss, Redmond, & Kingsbury, 1988; Laplane, Baulac, Widlocher, & Dubois, 1984; Starkstein, Fedoroff, Price, Leiguarda, & Robinson, 1993; Strub, 1989), and thalamus (Bogousslavsky, Regli, & Assal, 1986; Sandson, Daffner, Carvalho, & Mesulam, 1991; Stuss, Guberman, Nelson, & Larochelle, 1988). Disruption of the anterior cingulate frontal-subcortical circuit, comprised of the anterior cingulate region of the cortex and specific regions of the basal ganglia and thalamus, has been implicated as responsible for apathy in several conditions including Alzheimer’s disease, progressive supranuclear palsy, Parkinson’s disease, multiple sclerosis, and obstructive hydrocephalus (Bonelli & Cummings, 2007; Cummings, 1993).

Despite how frequently apathy is estimated to be present in TBI, research on the neuroanatomical correlates of apathy in this population is scant, and only two TBI studies on this topic were located. One study examined several cortical and subcortical regions and found evidence of a relationship between apathetic behaviours in 13 survivors of severe TBI at two months to one year post injury and hypometabolism in the left anterior

cingulate gyrus (Fontaine, Azouvi, Remy, Bussel, & Samson, 1999). Another study involved a mixed group of six TBI and ten stroke survivors and found apathy to be more common after lateral prefrontal cortex damage than after medial prefrontal injury at two weeks and at three months post injury (Paradiso, Chemerinski, Yazici, Tartaro, & Robinson, 1999). Caution must be taken in applying the findings of the latter study specifically to TBI given that it included a mixed sample with only three TBI subjects in each injury location group. There has been speculation about the role of frontal-subcortical circuit lesions in post-TBI apathy based on research in apathy in various disorders (Marin & Wilkosz, 2005), but no research specific to TBI has examined this hypothesis.

*Neuropsychological correlates of apathy.* Across etiologies such as Alzheimer's disease, Parkinson's disease, and HIV/AIDS, apathy has been related to various domains of neuropsychological performance. For example, apathy has been found to be related to working memory and response to interference aspects of executive function in HIV (Castellon, Hinkin, Wood, & Yarema, 1998; Castellon, Hinkin, & Myers, 2000). Problem solving and verbal generativity aspects of executive function, learning and memory, and naming ability have evidenced significant relation to apathy in Alzheimer's disease (Kuzis, Sabe, Tiberti, Dorrego, & Starkstein, 1999). In Parkinson's disease, diminished verbal generativity, mental flexibility, and memory have been found in individuals with apathy compared to those without (Starkstein et al., 1992). On the other hand, others have found no relationship between apathy and neuropsychological test performance (Rabkin et al., 2000).

Results are mixed regarding the relationship between neuropsychological test performance and apathy in TBI. One study examined cognition in relation to apathy in 53 severe TBI survivors at 2 to 36 months post injury (Andersson & Bergedalen, 2002). Higher apathy was significantly related to poorer learning and memory as well as executive functioning composite scores, but it was not significantly related to attention span, verbal skills, nonverbal skills, or motor speed composite scores. Apathy was found to be significantly related to psychomotor speed once dominant hand motor speed was controlled. Of the learning and memory, executive functioning, and psychomotor speed composites, only learning and memory predicted the apathy score.

Schiehser et al.'s (2011) study, previously mentioned with regards to disinhibition, involved 56 participants who had sustained a mild (two-thirds of sample) or moderate TBI three to nine weeks previously. Once effort was controlled for, self-reported apathy on the FrSBe was significantly correlated with an attention and processing speed composite but not with executive functioning or memory composites. When entered into a regression model, however, apathy was not predictive of attention and processing speed.

A study by Tate (1999), already mentioned in regards to disinhibition, examined apathy in a group of 30 severe TBI survivors six months post injury in relation to three cognitive tasks. Relatives' reports on the subscale of the Current Behaviour Scale that measures lack of energy, disinterest, and lack of initiative, were not significantly related to verbal and design generativity nor to perseverative errors.

Another study examined level of motivation, measured by degree of participation in inpatient rehabilitation therapy over one to eight sessions, in a mixed sample of 54



participants, of whom 67% had sustained a TBI and 33% a vascular injury (Al-Adawi, Powell, & Greenwood, 1998). Decreasing level of motivation was related to aspects of executive function tasks, including poorer verbal generativity, increased planning time, greater perseveration, and decreased chance of completing the Wisconsin Card Sorting Test, as well as to lower attention span and poorer performance on a selective reminding task. These authors found that level of motivation was not significantly related to psychomotor speed or general cognition.

Overall, the results are unclear regarding the relationship between neuropsychological test performance and apathy in TBI. Schiehser et al. (2011) found apathy to be related to, but not predictive of, attention/processing speed, whereas in Andersson and Bergedalen's (2002) study apathy was related to but not predicted by processing speed and was not related to attention. Andersson and Bergedalen found learning and memory to predict apathy, while Schiehser et al. failed to find a significant relationship. Executive functioning tests were related to, but not predictive of, apathy scores in Andersson and Bergedalen's study. Executive functioning was not related to apathy in two other studies (Schiehser et al., 2011; Tate, 1999). Al-Adawi et al.'s (1998) mixed sample study (67% TBI) showed a significant relationship between executive functioning measures and a measure of motivation that has some overlap with the concept of apathy.

***Executive cognitive dysfunction and TBI.*** Problems with executive cognitive functions are common among TBI survivors (Busch, McBride, Curtiss, & Vanderploeg, 2005; Fork et al., 2005; Scheid, Walther, Guthke, Preul, & Von Cramon, 2006; Serino et al., 2006), and involve difficulties in areas such as organization, planning, problem

solving, flexible thinking, monitoring, and distractibility (Levin & Kraus, 1994; McDonald, Flashman, & Saykin, 2002). Not surprisingly, such difficulties can be quite disabling to one's ability to function successfully on a day-to-day basis (McDonald et al., 2002).

Executive function is a term for which the definition is currently unresolved in the literature (Banich, 2009; Busch et al., 2005; Funahashi, 2001; Stuss & Alexander, 2007). Early theories and research on executive function focused only on the cognitive aspects of this domain (Happaney, Zelazo, & Stuss, 2004). Currently, however, many would argue that executive function involves more operations than these, and, in fact, includes behaviours such as initiation and inhibition (Anderson, 1998; Cicerone et al., 2006; Hanna-Pladdy, 2007), those reliant on the incorporation and modulation of emotions and instincts in directing behaviour (Ardila, 2008). Cicerone and colleagues conceptualize the cognitive aspects of executive function as one of several domains of executive function, referring to this domain as "executive cognitive function." Thus, for the current study the term "executive cognitive dysfunction" was borrowed from Cicerone and colleagues to more accurately reflect the aspect of executive function of interest.

Processes of executive cognitive dysfunction include working memory, planning, organization, and problem solving. The terms are defined as follows for the purpose of the current study. Working memory is defined as mental manipulation and monitoring of several pieces of information being simultaneously held in mind. Planning involves determining steps required to reach a goal. Organization involves ordering information in such a way as to make it meaningful and to allow the individual to reach a goal in a productive manner. Problem solving refers to generating hypotheses, choosing and

developing a strategy to reach a goal, incorporating external feedback, and monitoring one's progress to guide and change behaviour (cognitive flexibility) in complex or novel situations.

*Neuroanatomical correlates of executive cognitive dysfunction.* As with both disinhibition and apathy, executive cognitive dysfunction has typically been attributed to frontal lobe damage across various etiologies (Cicerone, Lazar, & Shapiro, 1983; Robinson, Heaton, Lehman, & Stilson, 1980; Royall, 2001; Slachevsky, Peña, Pérez, Bravo, & Alegría, 2006). Examination of specific frontal regions often implicates the dorsolateral area of the prefrontal cortex (Benton, 1968; Cicerone et al., 2006; Milner, 1971; Royall et al., 2002; Sarazin et al., 1998). Lesions to subcortical regions such as the caudate (Cummings, 1995; Mendez, Adams, & Lewandowski, 1989) and thalamus (Stuss et al., 1988) also have been implicated. Executive cognitive dysfunction in various disorders, such as subcortical dementias and frontotemporal dementia, has been linked to disturbance of the dorsolateral frontal-subcortical circuit (Cummings, 1990; Cummings, 1995).

Results of studies specific to TBI have found a relation between frontal lobe damage and executive cognitive dysfunction (Bergeson et al., 2004; Fontaine et al., 1999; Fortin, Godbout, & Braun, 2003; Shallice & Burgess, 1991; Von Cramon & Mattes-von Cramon, 1994) resulting in speculation that such disturbances in TBI are due to damage of frontal systems, either through damage to areas of the frontal cortex, areas of the brain that have connections with frontal regions, or the white matter tracts connecting frontal regions to other brain areas (McDonald et al., 2002). Studies also have found a relationship between executive cognitive dysfunction in TBI and damage to the

dorsolateral prefrontal cortex (Cazalis et al., 2006), both dorsolateral prefrontal and subcortical regions (Lombardi et al., 1999; Ptak & Schnider, 2004), overall white matter (Cazalis et al., 2006; Gansler, Covall, McGrath, & Oscar-Berman, 1996; Kraus et al., 2007; Scheid et al., 2006), and thalamic fibres (Little et al., 2010).

*Neuropsychological correlates of executive cognitive dysfunction.* In contrast with disinhibition and apathy, the presence of executive cognitive dysfunction in TBI survivors is typically determined by performance on standardized neuropsychological tests rather than by reports from daily life. Performances measured by traditional tests of executive function are those having similarity to the conceptualization of executive cognitive function in the current paper. However, reports of executive cognitive dysfunction in the real world are of interest in the current study. Whereas numerous reports exist of poor performance on traditional neuropsychological tests of executive function in moderate to severe TBI (Busch et al., 2005; Fork et al., 2005; Scheid et al., 2006; Serino et al., 2006), others cite examples of relatively normal performance on these neuropsychological tests despite difficulties in daily functioning thought to result from executive cognitive dysfunction.

Two case studies were selected to exemplify this discrepancy. The first examined an individual three months after a severe TBI (Satish, Streufert, & Eslinger, 2008). In spite of normal performance on traditional neuropsychological tests, including tasks of executive functioning, this individual experienced extensive problems at work and home characterized largely by disorganization, inefficiency, and inability to complete tasks. This same discrepancy between everyday functioning and formal testing has also been documented several years following injury. The second case involves a woman who

several years earlier had sustained a severe TBI with a localized lesion in the dorsolateral prefrontal cortex extending into the subcortical white matter (Ptak & Schnider, 2004). This woman had highly disorganized behaviour in daily life characterized largely by perpetual lateness as a result of an inability to prioritize activities, a tendency to become side-tracked, and the inability to use compensatory devices in an organized manner. These difficulties caused her to be unable to hold a job and resulted in social isolation. Of note, the researchers reported that they saw no evidence of the disinhibited or apathetic behaviour frequently seen in frontal lobe injuries in the extended time period they worked with this individual during assessment and a rehabilitation program. Despite the marked difficulty in daily life that appeared to stem from executive cognitive dysfunction, her performance on traditional neuropsychological tests was not impaired, including tests of executive function. However, further testing on two non-traditional neuropsychological tests revealed difficulties consistent with those in her everyday functioning. One task was unstructured and required planning and action scheduling based on externally presented rules and the other task involved increasing working memory requirements in the presence of distracters.

Boelen, Spikman, Rietveld, and Fasotti (2009) demonstrated discrepancy between real world and test-based performance in executive cognitive function in a brain injury sample of mixed etiologies. Participants were selected based on reports of difficulties in daily life with planning, organization, and problem solving. In this sample, 42% of individuals had sustained a TBI. Although the group with brain damage performed significantly worse than a control group on a questionnaire measuring degree of such

difficulties in daily life as well as on neuropsychological tests of executive function, the relation between daily report and test performance was poor.

A recent study by Schiehser and colleagues (2011) involved 56 participants (following exclusion of those with suboptimal effort) who had sustained a mild (two-thirds of sample) or moderate TBI. Self-reported executive cognitive dysfunction, as measured by the FrSBe, had a significant relation to an attention/processing speed composite and a smaller but still significant relation to an executive function composite at three to nine weeks post injury. Relation to a memory composite was not significant. When entered into a regression model, self-reported executive cognitive dysfunction was predictive of the attention/processing speed composite.

While tests of executive functioning are often impaired following moderate or severe TBI, it remains unclear how well such performances relate to reports of executive cognitive dysfunction in daily life. One research study found reports of day-to-day executive cognitive dysfunction to be related to and predictive of attention/processing speed and related to but not predictive of tests of executive function (Schiehser et al., 2011). Another found a poor relation to traditional neuropsychological tests of executive function in a mixed sample involving some TBI survivors (Boelen et al., 2009). Case studies have been published showing executive cognitive dysfunction in daily life alongside of intact neuropsychological test performance (e.g., Ptak & Schnider, 2004; Satish, et al., 2008). Factors making it difficult to draw a conclusion may include the paucity of studies examining this question, mixed etiology, variations in regions of focal damage, as well as differences between studies with respect to what neuropsychological tests were used, means of recording reported difficulty in real world executive cognitive

function, and time since injury. These difficulties are not restricted to the domain of executive cognitive dysfunction but could be applied to disinhibition and apathy as well.

**Self versus informant report of functioning in TBI.** There is some discussion in TBI outcome research about whether to get information about daily life functioning from the survivor or from an informant, as several studies demonstrate discrepancy between self and informant report of problems following TBI (Hart et al., 2003; Hart, Seignourel, & Sherer, 2009; Sherer et al., 1998). These studies reveal that survivors tend to report fewer difficulties than informants. However, level of agreement appears to vary with the type of function being reported on, injury severity, and time since injury. Specifically, the level of agreement between survivor and informant report appears to be better for physical functioning and worse for cognitive, emotional, and behavioural functioning (Cusick, Gerhart, & Mellick, 2000; McKinlay & Brooks, 1984; Trahan, Pepin, & Hopps, 2006). Injury severity has been reported to influence agreement, with evidence of greater discrepancy present in more severe injuries (Sherer, Hart, Whyte, Nick, & Yablon, 2005), although this has been shown to be dependant upon what aspect of functioning is being measured (Hart et al., 2003). Agreement also appears to improve with increasing time since injury (Hart et al., 2009; Vanderploeg, Belanger, Duchnick, & Curtiss, 2007).

Discrepancy has often been viewed as evidence of lack of awareness or insight by the survivor, with informant report considered to be more accurate. This view has been supported by studies showing that report by the family or caregiver tends to be more consistent with that of rehabilitation therapists (Fordyce & Roueche, 1986; Sherer et al., 1998). Informant report, however, can be influenced by the informant's own emotional well-being and acceptance of the survivor's post-injury status (McKinlay & Brooks,

1984; Santos, Castro-Caldas, & De Sousa, 1998). Additionally, there is evidence that level of agreement depends upon the relationship type, with greater disparity between spouse and survivor report than parent and survivor report (Santos et al, 1998; but see Cusick et al., 2000).

A few studies may provide information about expected concordance between survivor and informant report for disinhibition, apathy, and executive cognitive dysfunction, the aspects of neurobehavioural dysfunction of interest in the current study (Hart et al., 2003; Marsh & Kersel, 2006; Rochat et al., 2010). No TBI study was found that examined concordance with the measure that was used in the current study, but some studies have used measures that overlap with the domains of neurobehavioural disturbance as they are conceptualized here. One study examined impulsivity in TBI and found informant reports of most aspects of impulsivity, measured with a short form of the UPPS Impulsive Behavior Scale, to be significantly higher than survivor reports (Rochat et al., 2010). Marsh and Kersel (2006) examined agreement between informants and severe TBI survivors on several aspects of behavioural disturbance using the Head Injury Behaviour Rating Scale. Difficulties with impulsivity, motivation, and initiative were endorsed by a significantly greater percentage of informants than survivors, suggesting a discrepancy in disinhibition and apathy reports. Hart et al. (2003) found that the aggression and memory/attention subscales of the Neurobehavioural Functioning Inventory (NFI; Kreutzer, Seel, & Marwitz, 1999) were two of the scales for which survivors reported fewer symptoms compared to their informant. Given that aggression can be a part of disinhibition, and the memory/attention scale may share some aspects of



executive cognitive function, this finding may suggest that survivors would report fewer difficulties than informants in these areas of neurobehavioural disturbance.

Different scales were used across studies and the domains evaluated in these studies are not identical to the neurobehavioural disturbance domains of the current study. Nonetheless, poor concordance between survivor and informant report has been found for scales having similarity to the areas of neurobehavioural disturbance of interest here. Specifically, informants have reported higher levels of disturbance than the survivor self-reports for all three domains.

**Summary.** While reports of apathy, disinhibition, and executive cognitive dysfunction in everyday life are common following TBI, research on these neurobehavioural disturbances is limited within this population. Across a number of conditions, these disturbances have been correlated with frontal and frontal-subcortical pathway pathology. Within TBI, disinhibition has been linked to frontal and possibly orbitofrontal pathology, apathy has been correlated with anterior cingulate and lateral prefrontal pathology, and executive cognitive dysfunction has been related to frontal, dorsolateral prefrontal, subcortical, and overall white matter pathology.

While research in other etiologies involving disinhibited behaviour in daily life tends to show intact neuropsychological performance, studies specific to TBI show some mixed results.

Research has found disinhibition in TBI to be related to executive functioning, attention/processing speed, and memory, but the relationships were not strong enough to be predictive. Apathy has been correlated with performance on learning and memory, attention/processing speed, and executive function tests, although learning and memory

was the only performance with a strong enough relationship to be predictive of apathy across these studies. Similar to disinhibition, research on executive cognitive dysfunction in daily life and neuropsychological performance is conflicting. While some research has shown a correlation with attention/processing speed and executive function tasks, other research has revealed completely intact neuropsychological performance.

Finally, poor agreement between survivors and their loved ones about the survivor's daily functioning is quite common. Although level of agreement has been found to vary with the type of function being reported on, behavioural and cognitive disturbances in TBI are among those symptoms having the greatest survivor-informant discrepancy. Research involving behaviours that have similarity to the three domains of neurobehavioural disturbance of interest in the current study has found that informants report a higher level of disturbance compared to the self-report of survivors across all three domains. Studies have not examined whether one or more of these neurobehavioural disturbances has better concordance than the others.

### **A Review of the Literature on Acute CT Data in Relation to TBI Outcome**

The use of acute CT imaging in TBI is reviewed here first. Secondly, I summarize the literature examining acute CT data in relation to behaviour disturbance. Thirdly, I will give an overview of previous research on acute CT data and other aspects of outcome after TBI.

**CT imaging in relation to TBI outcome.** CT is the imaging method typically used with TBI patients in acute care settings for a number of reasons (Kurth & Bigler, 2008; Provenzale, 2007). First, CT imaging is able to determine the presence of acute intracranial injury, thereby providing vital information for early clinical treatment.

Second, CT scanners are widely available and are compatible with life support and other external devices that TBI patients frequently require. Third, it is a relatively quick procedure, and thereby an optimal imaging method for moderate to severe TBI patients who may be agitated, confused, and unable to follow commands.

CT imaging utilizes x-ray technology and images are based upon variation in tissue densities (Kurth & Bigler, 2008). While CT imaging is known to be less sensitive compared to newer imaging techniques that utilize magnetic resonance imaging (MRI) in detecting extent of injury in TBI, particularly DAI and small focal lesions, CT is as good or better at detecting hemorrhage, mass effect, and edema (Aiken & Gean, 2010; Kurth & Bigler, 2008). CT imaging is more suitable than MRI for acute imaging (Aiken & Gean, 2010).

In clinical settings, CT data are typically read and classified according to the Marshall Classification system, a system introduced in 1991 for the purpose of determining risk of decline or death in TBI patients (Marshall et al., 1991). The Marshall system classifies patients based on several CT characteristics, including presence of intracranial pathology, cistern compression, degree of midline shift, presence of mass lesion (contusions and/or hemorrhage) over a certain size, and need for surgical evacuation. There are six Marshall classes, ranging from no visible pathology to presence of mass lesions over 25 cc in size (see Table 2). The authors of the Marshall system found it to be correlated with GCS. Good inter-rater reliability has also been shown (Chun et al., 2010). This system was not created to give information about aspects of long-term outcome, but has use in predicting mortality outcome in TBI (Zhu, Wang, & Liu, 2009). However, there is evidence that this system has greater utility when used in

combination with specific lesion parameters. In fact, it may have less utility in predicting mortality than these specific lesion parameters used alone (Maas, Hukkelhoven, Marshall, & Steyerberg, 2005).

The prognostic utility of acute head CT imaging information has been explored in relation to aspects of outcome in TBI other than mortality. The Marshall classification, as well as other means of coding damage, such as by the lobe(s) involved, has been used for this purpose.

**CT and behavioural dysfunction in TBI.** A few investigations have examined acute CT findings in relation to behavioural dysfunction following TBI. Three studies used the Neurobehavioural Rating Scale (NRS; Levin et al., 1987), a trained observer-rated measure evaluating attention, orientation, memory, awareness, language, behaviour regulation, post-concussion symptomatology, and emotional state (Fork et al., 2005; Levin et al., 1987; Wallesch et al., 2001). The NRS is completed by a clinician based on observations made during an assessment and/or interview and appears to have adequate validity and inter-rater reliability (Tate, 2010).

The first study examined the NRS in relation to frontal lesions (Levin et al., 1987). No difference was found between individuals with CT evidence of frontal lesions ( $n = 26$ ) and individuals without evidence of frontal lesions ( $n = 26$ ) on any of the four NRS scales in a sample of mild to severe TBI survivors. The variability in time of measurement post injury, however, may have obscured any effect.

Another study compared groups with focal frontal ( $n = 12$ ), focal temporal ( $n = 6$ ), and absence of focal lesions ( $n = 34$ ), as well as a separate comparison of individuals with DAI ( $n = 10$ ) versus absence of DAI ( $n = 45$ ), on total NRS score at five to ten

months following mild or moderate TBI (Wallesch et al., 2001). Imaging data were based on acute CT scans. Individuals with focal frontal lesions differed from those without any focal lesions, while those with temporal lesions did not differ from either group.

Individuals with and without evidence of DAI failed to differ on the NRS.

Groups with acute CT evidence of focal frontal damage without DAI ( $n = 11$ ), DAI without focal damage ( $n = 11$ ), and normal CT ( $n = 17$ ) were compared on total NRS score within one month following mild to severe TBI and again at five to eight months (Fork et al., 2005). The overall NRS score within one month was significantly higher in both the frontal and DAI groups compared to those with normal CT scans, although the frontal and DAI groups failed to differ from one another. At five to eight months post injury, however, difference in the overall NRS score did not quite reach statistical significance across the DAI, frontal, and normal CT groups.

The NFI is another behavioural scale that has been examined in relation to acute CT data in TBI. The NFI includes six scales assessing depression, somatic problems, memory/attention, communication, motor, and aggressive behaviour. While the scale has adequate construct validity, reliability is unknown (Tate, 2010). A study by Lehtonen et al. (2005) compared TBI survivors with damage involving the frontal lobes ( $n = 118$ ), fronto-temporal region ( $n = 102$ ), cortical regions outside of the frontal lobes ( $n = 100$ ), and no CT pathology ( $n = 75$ ). The NFI was completed by both the survivor and a family member at one year post injury. The motor scale per informant report was the only aspect of the NFI that differed among the groups, with a significant difference observed between the frontal and no pathology groups.

Taken together, these results provide some evidence to suggest that overall behavioural dysfunction, as measured by the NRS or NFI, may be significantly higher in TBI survivors with frontal lesions than those without frontal lesions or those having no pathology on acute CT. However, while the NRS and NFI share some features with the neurobehavioural disturbances of interest in this study, most of the scales on these two measures evaluate other aspects of daily functioning.

**CT data and other areas of outcome in TBI.** Other areas of outcome in TBI have been examined in relation to acute CT data including cognition, psychosocial functioning, degree of overall disability, and supervision requirements.

Mixed results have been reported for a relation between acute CT data and cognitive outcome. Presence of lesions versus no lesions (Vilkkii, Holst, Ohman, Servo, & Heiskanen, 1992), presence of DAI (Wallesch et al., 2001), presence of DAI versus focal frontal cortical damage (Fork et al., 2005), as well as presence of focal frontal damage versus no focal damage (Wallesch et al., 2001) all have been found to be related to aspects of neuropsychological performance within four to ten months post injury. On the other hand, Lehtonen et al. (2005) found no differences between those with frontal, frontal-temporal, non-frontal cortical, and no acute CT pathology on any aspects of neuropsychological test performance at one year post injury. Also, with respect to early cognitive outcome, acute CT data have failed to add predictive utility beyond injury severity and demographic factors in predicting composites of early neuropsychological test performance during inpatient rehabilitation (Sherer et al., 2006).

Overall level of psychosocial outcome has been examined in relation to acute CT data. A recent article reviewed several studies that examined gross level of recovery of

psychosocial functioning using the Glasgow Outcome Scale (GOS; Jennett & Bond, 1975) at six months following a moderate or severe TBI (Husson, Ribbers, Willemse-Van Son, Verhagen, & Stam, 2010). The Marshall classification was used for the majority of studies included in the review. The review concluded that midline shift and subdural hematoma on acute CT were related to worse GOS scores, whereas intraventricular hemorrhage was not related to the GOS score. The data showed no conclusive relationship between the GOS score and the total Marshall classification score, presence or absence of compressed/absent cisterns, subarachnoid hemorrhage, epidural hematoma, and intracranial hemorrhage.

Another study found that psychosocial and other aspects of outcome at one year post injury differed according to, but were not predicted by, presence and location of acute CT abnormalities following mild or moderate TBI ( $n = 55$ ; Van Der Naalt, Hew, Van Zomeren, Sluiter, & Minderhoud, 1999). Outcome variables included the GOS, Differential Outcome Scale (Van Der Naalt et al., 1999; assesses a range of outcomes including social, behavioural, cognitive, and physical domains), and return to work or study. In terms of presence of abnormality on CT, the total Differential Outcome Scale score was lower in the group that had lesions of any kind and/or edema. With respect to location of injury, all three outcome measures were lower in those with a frontal-temporal abnormality, but no difference in outcome was observed for those with a frontal or temporal abnormality alone. Predictive analyses were also conducted, and presence and location of abnormalities on acute CT failed to predict outcome variables once length of posttraumatic confusion (PTC) was added as a predictor variable. This study included a mild to moderate TBI sample, in which outcome would be expected to be near the upper

end of the spectrum, thereby limiting the generalizability of the findings to a sample including severe TBI.

Psychosocial outcome was examined in the previously mentioned study by Lehtonen et al. (2005) using the Community Integration Questionnaire (CIQ; Willer, Rosenthal, Krueger, Gordon, & Rempel, 1993) at one year post injury. This scale measures psychosocial functioning more extensively than the GOS by assessing aspects of home, social, and work/study integration. Frontal ( $n = 118$ ), frontal-temporal ( $n = 102$ ), non-frontal cortical ( $n = 100$ ), and no CT pathology ( $n = 75$ ) groups did not differ on the Community Integration Questionnaire total score for either the patient or family version.

Outcome variables of ambulation, independence in several activities of daily living, and need for supervision have been found to be related to acute CT variables (Englander, Cifu, Wright, & Black, 2003). All participants in this study had sustained a mild complicated, moderate, or severe TBI and required inpatient rehabilitation. At discharge from inpatient rehabilitation, degree of midline shift and presence of subcortical contusions on acute CT were related to all three outcome measures, and presence of frontal or temporal contusions was related to supervision. At one year, presence of subcortical contusions on acute CT remained significantly related to ambulation and degree of midline shift remained related to supervision, but the presence of frontal or temporal contusions was no longer related to any of the outcomes.

**Summary.** Overall, although results are mixed, there is evidence that acute CT data are related to aspects of cognitive and functional outcome in TBI. The differences in CT parameters used across studies make it difficult to draw any overall conclusion about



which CT indices in particular are related to outcome. Some utilized the Marshall classification, including information on intracranial compression and types of hemorrhage and hematoma (Husson et al., 2010), whereas others utilized information on lobe of injury (Lehtonen et al., 2005; Van Der Naalt et al., 1999), subcortical lesions (Englander et al., 2003), DAI ( Fork et al., 2005; Wallesch et al., 2001), and presence of injury (Van Der Naalt et al., 1999; Vilkki et al., 1992).

### **The Present Study**

Previous research indicates that survivors of TBI often experience disinhibition, apathy, and executive cognitive dysfunction in their daily lives following injury. Questions remain, however, about the relationship between survivor and informant report in these domains of functioning. Earlier research suggests that the relationship between neurobehavioural disturbance and neuropsychological test performance still needs clarification as well. Additionally, there is a need to understand further the value of acute CT data in predicting neurobehavioural disturbance. The present study was designed to advance the field by examining these issues.

The first aim of the study was to determine whether acute CT data has utility in predicting the degree of disinhibition, apathy, and executive cognitive dysfunction experienced by survivors of mild complicated to severe TBI within one to five years post injury. Based on a review of the neuroanatomical correlates of disinhibition, apathy, and executive cognitive dysfunction in TBI and a review of research on acute CT in relation to several aspects of TBI outcome, it was expected that acute CT data would be predictive of neurobehavioural disturbance. Furthermore, there was no reason to suspect

that any one of the domains of behavioural disturbance would be predicted by CT information more than the other domains.

The second aim of the study was to examine the relationship between concurrent neuropsychological test performance and the degree of disinhibition, apathy, and executive cognitive dysfunction experienced in daily life by survivors of mild complicated to severe TBI at one to five years post injury. Review of the literature examining neuropsychological test correlates of disinhibition, apathy, and executive cognitive dysfunction in TBI was inconclusive, and therefore only tentative hypotheses were made. First, it was expected that the degree of reported disinhibition would not likely be predicted by any of the neuropsychological test scores. Second, degree of apathy may be predicted by performance on learning and memory, attention/processing speed, and possibly executive function tests. Third, degree of executive cognitive dysfunction may be predicted by attention/processing speed and executive function tasks, although research in this domain is quite conflicting.

A third aim of the study was to determine the degree of concordance between reports of disinhibition, apathy, and executive cognitive dysfunction made by individuals with TBI and informants. No study has examined this three-part classification of neurobehavioural changes (behavioural disinhibition, apathy, and executive cognitive dysfunction) in TBI simultaneously in a single study, and this study aimed to add information about whether different types of neurobehavioural disturbances have better concordance than others. It was hypothesized that concordance between the survivor and informant would be poor overall for reports of neurobehavioural disturbance, and that informants would report higher levels of disturbance than the survivors for all three

domains. Not enough information was available in the literature to make a hypothesis about the degree of concordance of the domains in comparison to one another.

## **II. METHOD**

The current project was approved by the University of Windsor's Research Ethics Board and Wayne State University's Human Investigation Committee.

### **Participants**

All TBI participants were enrolled in the Southeastern Michigan Traumatic Brain Injury System (SEMTBIS) project, a longitudinal follow-up study which is part of a multicenter TBI Model System project. Criteria for the SEMTBIS project include medically documented TBI, treatment at a level I trauma center within 24 hours of injury, admission to inpatient rehabilitation within 72 hours of acute care discharge, an age of at least 16 years at injury, and provision of informed consent by the person with TBI or legal proxy. To be enrolled in the project, the TBI participant must have sustained a mild complicated, moderate, or severe TBI as evidenced by an emergency room GCS score of 12 or below, or by a GCS of 13-15 with intracranial bleed. If GCS information was unavailable, it was required that there be evidence from medical records of a loss of consciousness greater than 20 minutes or PTC greater than 24 hours. Length of PTC is defined as the amount of time until two consecutive scores of  $\geq 25$  within 72 hours are achieved on the Orientation Log (O-LOG; Novack, 2000), a measure that assesses the individual's orientation to person, place, time, and situation.

TBI participants were contacted about the current project in person while participating in 1, 2, or 5 year follow-up testing for the SEMTBIS project at the Rehabilitation Institute of Michigan, or by telephone. Participation in the SEMTBIS

project occurs within the following time frame at each follow-up year: 1 year post injury  $\pm$  2 months, 2 years  $\pm$  3 months, 5 years  $\pm$  6 months. Individuals in the SEMTBIS project who were 3 or 4 years post injury and not due for their year 5 follow-up assessment with SEMTBIS within the next six months were contacted by phone about the proposed study. Those who agreed to participate in the current project completed the FrSBe questionnaire and neuropsychological testing. Individuals who chose to complete their SEMTBIS follow-up by telephone or mail rather than in person were also given an opportunity to participate in the current project by completing the FrSBe questionnaire via mail or telephone. Individuals who chose this option thus have no neuropsychological data concurrent with the neurobehavioural data gathered in the present study. These participants were mailed a packet including the FrSBe questionnaire, informed consent, and a pre-stamped return envelope. Acute CT data for all participants was drawn from the SEMTBIS archival database. TBI participants agreed in the informed consent to the use of their acute CT data and, when applicable, their neuropsychological data from the SEMTBIS project.

TBI participants were asked to have an individual who knows them well complete an informant FrSBe questionnaire. Informants had the option to participate in person, by mail, or by telephone. For those participating by mail or telephone, a packet including a family version of the FrSBe questionnaire, informed consent, and pre-stamped return envelope were sent home with the TBI participant (or mailed to the TBI participant along with their own packet for those who did not participate in person) to give to an informant. A follow-up telephone call was made to the TBI participant within a week to determine if

an informant had agreed to complete the questionnaire. Attempts were made to have complete questionnaires, with follow-up by telephone for any missed questions.

Informed consent was obtained from all TBI and informant participants.

Participants were compensated for their time and inconvenience with cash (in-person participation) or a gift card (telephone or mail participation).

## **Measures**

**Computed tomography data.** Acute injury CT scan data, collected within seven days of injury, were rated by a physiatrist who had completed an inter-rater reliability coding course for raters within the Traumatic Brain Injury Model Systems. Ratings included (1) extent of intracranial compression (no visible intracranial compression; cisterns present with a midline shift of 1 - 5 mm; cisterns compressed/absent with a midline shift of 0 – 5 mm; midline shift > 5 mm), (2) presence of intracranial hemorrhage and/or contusions or extra-axial collections; (3) presence of punctate/petechial hemorrhages; (4) presence of subarachnoid hemorrhage; (5) presence of intraventricular hemorrhage; (6) lobe and laterality of focal cortical contusions or hemorrhage in cerebral cortex; (7) presence and laterality of focal non-cortical contusions or hemorrhage (“non-cortical” including basal ganglia, brain stem, centrum semiovale, cerebellum, corpus callosum, internal and external capsules, midbrain, pons, subcortical white matter, and thalamus); (8) presence and laterality of epidural hematoma; (9) presence and laterality of subdural hematoma; and (10) presence of intraparenchymal fragments.

The number of participants who had pathology present for each of the CT variables is presented in Table 3, along with information on CT pathology by ethnicity, age, and education demographics.

**Neuropsychological tests.** Participants were administered the standard SEMTBIS neuropsychological test battery, which included the Trail Making Test A & B (Trails A, Trails B; Reitan, 1992), Symbol Digit Modalities Test written and oral (SDMT; Smith, 1991), Word Generation (FAS; Benton & Hamsher, 1989), California Verbal Learning Test-II (CVLT-II; Delis, Kramer, Kaplan, & Ober, 2000), Digit Vigilance Test (DVT; Lewis & Rennick, 1979); Wisconsin Card Sorting Test-64 (WCST-64; Heaton, Chelune, Talley, Kay, & Curtis, 1993), and Wechsler Test of Adult Reading (WTAR; The Psychological Corporation, 2001). All of these measures have acceptable reliability and validity (Strauss, Sherman, & Spreen, 2006), and have been used within TBI populations (Bercaw, Hanks, Millis, & Gola, 2011; Hanks et al., 2008). Specific variables used in analyses included Trails A completion time, Trails B completion time, SDMT-oral total, SDMT-written total, CVLT-II trials 1-5 total, CVLT-II short delay free recall total [CVLT-II SD], CVLT-II long delay free recall total [CVLT-II LD], FAS total number of words, WCST-64 total errors, DVT total time, and DVT total errors. To account for factors such as age, education, gender, and ethnicity, demographically adjusted t-scores or standard scores for the neuropsychological variables were used in all analyses. Demographic adjustments were based on the Heaton norms (Heaton, Miller, Taylor, & Grant, 2004) for Trails A, Trails B, FAS, and DVT, and the norms available in the test manuals for the CVLT-II, SDMT, and WCST-64. Table 4 lists what these demographic corrections included.

**Neurobehavioural measure.** The Frontal Systems Behavior Scale (FrSBe; Grace & Malloy, 2001) provided measures of the three domains of post-TBI neurobehavioural disturbances of interest (disinhibition, apathy, and executive cognitive dysfunction), as

well as an overall measure of neurobehavioural disturbance. Family and patient versions of the FrSBe were administered.

The FrSBe, originally the Frontal Lobe Personality Scale (FLOPS), was developed to capture disinhibition, apathy, and executive dysfunction in a single measure. In developing the FrSBe, the authors initially determined through literature review that disinhibition, apathy, and executive dysfunction syndromes are the prominent neurobehavioural disturbances following frontal injury (Grace, Stout, & Malloy, 1999). The authors then had several colleagues, including those considered to be experts in frontal-subcortical circuitry and behavioural sequelae, review the items before creating the final version of the questionnaire. The FrSBe has good construct validity (Grace et al., 1999), within scale reliability (Grace et al., 1999), internal consistency (Grace & Malloy, 2001; Velligan, Ritch, Sui, DiCocco, & Huntzinger, 2002), ecological validity in relation to daily functioning (Boyle et al., 2003; Hamilton et al., 2003; Norton, Malloy, & Salloway, 2001; Reid-Arndt, Nehl, & Hinkebein, 2007; Stout, Wyman, Johnson, Peavy, & Salmon, 2003), and convergent validity (Norton et al., 2001) in various neurological populations. Factor analysis has supported the subscale structure (Stout, Ready, Grace, Malloy, & Paulsen, 2003). Subscales include disinhibition, apathy, and executive dysfunction. A total score is calculated by combining the three subscale scores. The inventory is available in family and patient forms and includes an option to compare behaviour between two time points, prior to injury and at the present time. Raw scores can be converted to t-scores based on age, education, and gender.

FrSBe variables in the present study included apathy self report (Apathy\_self), disinhibition self report (Disinhibition\_self), executive dysfunction self report

(Executive\_self), total self report (Total\_self), apathy informant report (Apathy\_informant), disinhibition informant report (Disinhibition\_informant), executive dysfunction informant report (Executive\_informant), and total informant report (Total\_informant). Possible raw score ranges are 14 – 70 for apathy, 15 – 75 for disinhibition, 17 – 85 for executive dysfunction, and 46 – 230 for the total score.

Normative data for t-scores and cut-off scores on the FrSBe have been developed mainly with well-educated Caucasian samples (Tate, 2010), and it is unknown if the demographically adjusted t-scores and cut-off scores developed for the FrSBe subscales are valid in ethnicities other than Caucasians and in individuals with a low education level. Because over 50 percent of the participants in the current study were African American and many participants had a low level of education, FrSBe raw scores were used in analyses rather than t-scores or presence/absence of the disturbance at a clinically significant level based on a cut score.

### **III. RESULTS**

#### **Participants**

Participants included 95 survivors of mild complicated, moderate, or severe TBI who were one to five years post injury and 87 informants. TBI participants included 75 males and 20 females (see Table 5). Self-reported ethnicity included 48 African American, 43 Caucasian, and 4 some other ethnic background. Mean age was 40.2 years ( $SD = 14.7$ ,  $Mdn = 40.0$ , range = 18 – 80) and mean education level was 12.4 years ( $SD = 2.4$ ,  $Mdn = 12.0$ , range = 8 – 20). Cause of injury included 22 motor vehicle accidents, 19 falls, 14 pedestrians, 14 assaults with blunt instrument, 12 gunshot wounds, 9 motorcycle



accidents, 2 all-terrain vehicle accidents, 1 bicycle, 1 winter sport, and 1 hit by falling object.

Injury severity measures included emergency room GCS ( $M = 8.4$ ,  $SD = 4.3$ ,  $Mdn = 7.0$ , range = 3 - 15, missing = 5) and PTC length ( $M = 22.0$  days,  $SD = 18.2$ ,  $Mdn = 20.0$ , range = 0 - 74, still in PTC at discharge = 8, missing = 3). Based on GCS only (< 9 = severe, 9 – 12 = moderate, 13 – 15 = mild), the following severity classifications would be made: 46 severe, 19 moderate, and 25 mild complicated. GCS was not measured in two participants because they were in a medically-induced coma, and GCS was not in the medical records of an additional three participants. Based on PTC length only (> 7 days = severe, 1 – 7 days = moderate, <1 day = mild), the following severity classifications were made: 68 severe, 14 moderate, and 10 mild complicated. Length of PTC was missing for three participants. Using a combination of GCS and PTC information, injury classifications included: 75 severe, 10 moderate, and 10 mild complicated TBI participants. With this method, participants were placed into the category of greater severity if the GCS and PTC resulted in differing classifications.

Number of years post injury included a total of 20 at year one, 25 at year two, 3 at year three, 6 at year four, and 41 at year five (Table 5). Two reasons account for the relatively few participants at three and four years post injury. First, follow-up in the longitudinal SEMTBIS project does not occur at these years, limiting access to potential participants in this time frame. Second, there were few potential year three and four participants in the SEMTBIS project because of a period of time when the longitudinal project was unfunded and therefore participants were not being actively recruited during inpatient rehabilitation immediately post injury. There are several possible reasons

contributing to the large number of year five compared to years one and two participants. Likely the largest reason is that year five has a longer time frame around the anniversary of the injury date in which data can be collected ( $\pm 6$  months) compared to year one ( $\pm 2$  months) and year two ( $\pm 3$  months), according to SEMTBIS guidelines. Other anecdotal reasons for greater participation at year five may be that brain injury survivors are often functioning poorly within the first two years compared to five years post injury. Therefore, they may be less willing to participate in research or may have family members who are less willing to divulge current contact information. Also, many participants have a relationship with the SEMTBIS research team by year five because of yearly contact by the study coordinator, mailed birthday and holiday greetings, and previous participation. Thus, these individuals tend to be more willing to participate in other projects about which the coordinator contacts them.

Of the 95 TBI participants, neuropsychological data were not collected for seven participants who completed the FrSBe through the mail/phone and one participant who as a result of examiner error did not undergo neuropsychological testing. Of the 87 with neuropsychological data, six had incomplete data for the following reasons: visual difficulty ( $n = 2$ ), fine motor difficulty ( $n = 2$ ), expressive language problems ( $n = 1$ ), and administration error ( $n = 1$ ). Four participants scored fewer than 15 out of 16 correct on the CVLT-II Forced Choice task, a score indicative of insufficient effort (Moore & Donders, 2004). Although not a highly sensitive measure of effort, a score at that level is infrequent and it can be assumed that participants with a score in that range were not putting forth adequate effort. Neuropsychological test scores for these participants were removed from analyses to avoid confounding test results with obvious insufficient effort.

Therefore, a total of 83 participants had complete or partial neuropsychological test data. All TBI participants had complete acute CT data.

All informants were individuals identified voluntarily by the TBI participants as people who knew them well. Of a possible 95 informants, 87 completed the FrSBe questionnaire. One informant who missed a substantial number of questions was unable to be contacted, resulting in a total of 86 informants. Informants consisted of 26 spouses/partners, 49 immediate family members, 1 non-immediate family member, 5 friends, 3 caregivers, and 2 “others.” Seventy-eight informants (91%) had known the TBI participant prior to injury. Fifty-one informants (59%) live with the TBI participant. Time spent weekly with the TBI participant ranged from 1 to 168 hours ( $M = 67.6$ ,  $SD = 57.8$ ,  $Mdn = 48$  hrs, missing = 2). When asked how well they knew the TBI participant on a scale of 1 to 10, sixty informants (70%) gave a rating of 10 ( $M = 9.5$ ,  $SD = 1.0$ ,  $Mdn = 10$ , range = 5 – 10).

Self- and informant-report FrSBe raw values are presented in Table 6. Mean standardized scores on the neuropsychological test measures, excluding participants with insufficient effort, are presented in Table 7. Percentage of participants performing within the impaired range are also presented, broken down by the percentage with mildly impaired scores or greater ( $> 1$  SD below the normative mean) and moderately impaired scores or greater ( $> 2$  SD below the normative mean).

### **Data Cleaning**

The Shapiro-Wilk test of normality was performed for the neuropsychological test variables, FrSBe variables, and demographic variables (age at follow-up, education level at follow-up, GCS, and PTC). The following variables violated normality:

Disinhibition\_self (positive skew), Executive\_self (kurtosis), Total\_self (positive skew), age (positive skew), education (positive skew), GCS (kurtosis), and PTC (positive skew).

Square root, LOG, and inverse transformations were conducted for the three FrSBe variables violating normality. Of the transformations, LOG transformations corrected for non-normality with the most success according to guidelines provided by Tabachnik and Fidell (2001). Multiple regression analyses were conducted with untransformed as well as with LOG transformed variables for Disinhibition\_self, Executive\_self, and Total\_self. Analyses using any of the non-normal variables were conducted with nonparametric variations whenever this option was available in SPSS.

Neuropsychological, FrSBe, and demographic variables were evaluated for univariate outliers. The Trails A t-score had three outliers at a z-value greater than 2.58, two more than the acceptable number of cases at this level given the sample size. None of the variables had any z-value greater than 3.29. Screening of multivariate outliers will be discussed within the results of each analysis.

### **Prediction of Neurobehavioural Disturbances with Acute CT Data**

Multiple regression analyses were conducted to determine whether acute CT data were predictive of FrSBe scores. It had been hypothesized that brain CT data collected acutely post injury would predict degree of reported apathy, disinhibition, and executive dysfunction. Power analysis calculations for multiple regression with parameters of a power level of 0.8, an alpha level of 0.05, and a medium effect size of 0.15 indicated a minimum sample size requirement of 84 with the use of 4 predictors and a sample size of 91 with the use of 5 predictors. Because all participants had self-report FrSBe data but some were missing informant-report FrSBe data, the self-report FrSBe and CT analyses

had a sample size of 95 and the informant-report FrSBe and CT analyses had a sample size of 86. Four predictor variables were chosen: presence/absence of frontal cortical damage, temporal cortical damage, non-cortical damage, and midline shift >5mm. CT variables were dummy coded as “pathology present” or “pathology absent.” All CT variables had a split more balanced than 90/10, thus satisfying the requirement for use of dichotomous variables outlined in Tabachnik and Fidell (2001).

Specific CT variables for the analyses were chosen based on previous research. The frontal cortical variable was chosen because of past research showing a relation between frontal damage and neurobehavioural disturbance in TBI (e.g., Fortin et al., 2003; Shallice & Burgess, 1991; Weddell & Leggett, 2006), and research showing a relation between frontal damage on acute CT and various aspects of outcome in TBI (Englander et al., 2003; Wallesch et al., 2001). The temporal cortical variable was chosen because of research that has found acute CT temporal damage to be related to aspects of TBI outcome (Englander et al., 2003), and because of its frequency of damage in TBI (Adams et al., 1980; Bigler, 2007). The noncortical variable was chosen as a means of capturing subcortical circuitry damage which has been implicated as a correlate of executive cognitive dysfunction in some TBI studies (Little et al., 2010; Lombardi et al., 1999; Ptak & Schnider, 2004). Midline shift greater than 5 mm was chosen based on research examining acute CT data coded according to Marshall classification in relation to other aspects of outcome post TBI, in which degree of midline shift has been found to have a strong relationship to global outcome (Husson et al., 2010) and to independence (Englander et al., 2003).

The dependent variable for each multiple regression analysis included the total raw scores on the following FrSBe scales: Apathy\_self, Apathy\_informant, Disinhibition\_self, Disinhibition\_informant, Executive Dysfunction\_self, Executive Dysfunction\_informant, Total\_self, and Total\_informant. Multiple regression analyses were also run for the LOG transformations of Disinhibition\_self, Executive\_self, and Total\_self variables to compare with the non-transformed variables. Measures of influence were examined (Mahalanobis Distance values  $> 15$ , Cook's statistic  $> 1$ , standardized residuals  $> 3$ ), revealing no influential cases. A high level of collinearity was not detected. None of the predictor variables had variance inflation factors exceeding 4, none of the condition indexes were greater than 20, and none of the associated variance decomposition proportions were greater than .50. Examination of Durbin-Watson values revealed that independence of errors could be assumed.

Test of the full model against a constant-only model was not statistically reliable for any of the multiple regression analyses, indicating that the full set of predictors (CT variables) did not reliably predict any of the self or informant measures of behavioural disturbance (Table 8). Results using LOG transformed variables were very similar to the non-transformed variables.

**Exploratory analyses.** Because several of the informant-report multiple regression models were marginally significant, the relationship between acute CT data and reports of neurobehavioural disturbance at one to five years post injury was explored further. Point-biserial correlational analysis was performed to explore whether there were any statistically significant relationships. Disinhibition\_self and all FrSBe informant variables had moderate correlations with temporal pathology that were statistically

significant at an alpha level of less than .05, uncorrected for multiple comparisons due to the exploratory nature of the analyses (Table 9). All relationships were in the direction of higher (less favorable) FrSBe scores related to absence of temporal pathology.

Further exploratory analysis was conducted using two-tailed Wilcoxin Rank-Sum analyses to examine whether there were significant differences in FrSBe subscale scores for those with and without damage on the four CT variables. Nonparametric analyses were conducted because of normality violations on several of the FrSBe self-report variables. At an alpha level of .05, uncorrected for multiple comparisons due to the exploratory nature of the analyses, participants with and without temporal pathology had statistically significant raw scores differences on Disinhibition\_self, Apathy\_informant, Disinhibition\_informant, Executive\_informant, and Total\_informant (Table 10). No statistically significant differences were present between those with and without frontal damage, noncortical damage, or a midline shift > 5mm. Thus, compared to participants with acute CT evidence of damage to the temporal lobe, participants without acute CT evidence of temporal damage rated themselves as having higher disinhibition and were rated by informants as having higher levels of apathy, disinhibition, executive dysfunction, and overall behavioural disturbance.

The relationship between the absence of temporal pathology and reports of higher levels of behavioural disturbance was unexpected, and further exploration was conducted. First, participants with and without temporal pathology were examined as separate groups to determine whether those without temporal pathology happened to have a high frequency of pathology in another brain region that was not included in the analyses, thereby accounting for the unexpected direction of the relationship. The following

variables were examined: subarachnoid hemorrhage, intraventricular hemorrhage, punctate/petechial hemorrhage, parietal damage, occipital damage, subdural hematoma, epidural hematoma, any compression or midline shift, and concurrent frontal and temporal damage. None of these CT variables had a high frequency in the group without temporal pathology in comparison to the frequency in the group with temporal pathology. Thus, pathology in another brain region does not appear to account for the unexpected result regarding temporal pathology and FrSBe scores.

Second, demographic variables were examined in relation to presence/absence of temporal pathology. Point-biserial correlational analyses were conducted, revealing temporal pathology to be significantly related to years of education ( $r = .249, p = .015$ ), but not to age ( $r = .157, ns$ ), GCS ( $r = .035, ns$ ), or PTC ( $r = .083, ns$ ). Chi-square analyses revealed that presence/absence of temporal pathology did not significantly differ on sex ( $X^2 = .264, ns$ ) or ethnicity ( $X^2 = 2.934, ns$ ). That is, presence of temporal pathology was related to a higher education level, but not to other demographic and injury severity variables. The other CT variables were examined in relation to education level using point-biserial correlations, revealing that education level was not related to frontal pathology ( $r = .105, ns$ ), noncortical pathology ( $r = -.101, ns$ ), or midline shift  $> 5\text{mm}$  ( $r = -.063, ns$ ). Given the relationship between education and temporal pathology alongside of no relationship between education and other CT variables, it was hypothesized that education level could be responsible for the unexpected relationship between absence of temporal pathology and reports of higher levels of behavioural disturbance. Thus, a possible relationship between education level and FrSBe scores was explored next.



Kendall's tau nonparametric correlational analysis was used, given the non-normal distributions for several of the self-report FrSBe variables. All FrSBe variables except for Disinhibiton\_self were significantly related to education level in the direction of higher FrSBe scores related to lower education level. FrSBe variables were not correlated with age or sex (Table 11).

Next, partial correlations between temporal pathology and FrSBe variables were conducted, controlling for education level. Total\_informant was the only FrSBe variable that remained significantly related to temporal pathology ( $r = -.215, p = .048$ ). Therefore, it appears that the relationship between absence of temporal pathology and reports of higher levels of behavioural disturbances was mediated by there being a lower level of education by chance among those without temporal pathology compared to those with temporal pathology.

### **Prediction of Neurobehavioural Disturbances with Neuropsychological Performance**

It was tentatively hypothesized that the degree of reported disinhibition would not be predicted by any of the neuropsychological test scores, that degree of apathy might be predicted by performance on learning and memory, attention/processing speed, and possibly executive function tests, and that reports of executive cognitive dysfunction might be predicted by attention/processing speed and executive function tasks.

Multiple regression analyses were conducted to determine whether performance on neuropsychological tests was predictive of self- and informant-reported FrSBe scores. Power analyses calculations with parameters of a power level of 0.8, an alpha level of 0.05, and a medium effect size of 0.15 gave an estimated minimum sample size requirement of 84 with 4 predictors and 76 with 3 predictors. Missing and incomplete

neuropsychological data resulted in sample sizes of 79 for self-report FrSBe and 70 for informant-report analyses. Nevertheless, it was decided that 4 predictor variables would be used for the analyses as the sample size to predictor ratio is still well within the suggested size. Predictor variables included SDMT-written, CVLT-II trials 1-5 total, Trails B, and WCST-64 total errors. Variables were chosen to represent the domains of processing speed/attention (SDMT-written), learning and memory (CVLT-II trials 1-5 total), and executive function (Trails B time and WCST-64 total errors). The choice of which measure(s) would be used to represent each domain was based on normality, collinearity, and previous research. The dependent variable for each separate regression analysis was the total raw score on the following FrSBe scales: Apathy\_self, Apathy\_informant, Disinhibition\_self, Disinhibition\_informant, Executive Dysfunction\_self, Executive Dysfunction\_informant, Total\_self, and Total\_informant.

Measures of influence and multivariate outliers were examined for all eight models (Mahalanobis Distance values  $> 15$ , Cook's statistic  $> 1$ , standardized residuals  $> 3$ ). Although a single case had a standardized residual greater than 3 in the Apathy\_informant analysis, further examination of the case revealed no other diagnostic statistics at a level that would be cause for concern and the regression results did not change by any appreciable degree when run with and without the case. Thus, the case remained in the analysis. A high level of collinearity was not detected. None of the predictor variables had variance inflation factors exceeding 4, none of the condition indexes were greater than 20, and none of the associated variance decomposition proportions were greater than .50. Examination of Durbin-Watson values revealed that

independence of errors could be assumed. Partial plots showed no violations of homogeneity of variance and linearity.

Test of the full model against a constant-only model was statistically reliable for Executive\_informant, indicating that the full set of predictors (neuropsychological test variables) reliably predicted the degree of executive cognitive dysfunction reported by an informant ( $F_{4,65} = 2.90$ ,  $R^2 = .15$ ,  $p = .029$ ). Thus, 15% of the variability on the informant's report of executive cognitive dysfunction was predicted by knowing the scores of these four neuropsychological test performances. The full set of predictors failed to reliably predict any of the other measures of behavioural disturbance (Table 12). Based on significance values of the standardized beta weights, informant report of executive cognitive dysfunction was reliably predicted by performance on SDMT-written and CLVT-II trials 1-5 total (Table 13). The regression analyses were repeated using transformed FrSBe variables for those that violated normality. There was no appreciable difference when using transformed variables (see Table 12).

To explore the relationship between FrSBe reports and additional neuropsychological test performances, nonparametric Kendall-tau two-tailed correlation coefficients were examined for FrSBe variables and neuropsychological test scores, including additional test scores that were not part of the regression analyses. Nonparametric correlational analyses were used because of the violations to normality with three of the self-report FrSBe variables. Results are presented in Table 14, and are not corrected for multiple analyses. Sample sizes for the self-report and informant-report correlations ranged from 73 to 82 and from 64 to 73, respectively, depending on the number of missing data for the various neuropsychological tests. SDMT, CVLT-II trials

1-5, and CVLT-II LD were related to Executive\_informant, SDMT and CVLT-II trials 1-5 were related to Total-informant, and SDMT was related to Executive\_self. All correlations were in the direction of poorer test performance related to reports of greater behavioural disturbance.

### **Self and Informant Concordance on the FrSBe**

The final aim of the study was to assess the concordance rate between self and informant reports of neurobehavioural disturbance. It was hypothesized that concordance rates for all three domains (apathy, disinhibition, and executive cognitive dysfunction) would be poor, with informants reporting higher levels of disturbance compared to individuals with TBI. No hypothesis was made about the degree of concordance of the domains in comparison to one another.

Discrepancy scores were calculated by subtracting the TBI participant's score from that of the informant's for each FrSBe scale. Medians, quartiles, and ranges are presented in Table 15. These scores show that informants tend to report higher degrees of disturbance than the TBI participants on all FrSBe scales.

To assess the degree of concordance between self- and informant-reports, Lin's concordance correlation coefficients were calculated for each FrSBe scale (Lin, 1989). If survivor versus informant scores were plotted on a scatterplot, perfect concordance between the two would result in a plotted line of 45 degrees. Lin's concordance correlation coefficient considers both precision (Pearson's correlation) and accuracy (how far the data deviates from 45 degrees) to determine the nearness of the data to the line of perfect concordance. Perfect concordance between the variables would result in a value of 1. Ratings of Lin's concordance values have been specified as follows: > 0.8

“almost perfect,” 0.61 – 0.80 “substantial,” 0.41 – 0.60 “moderate,” and 0.21 – 0.40 “fair.” Lin’s concordance correlation coefficient was 0.43 for apathy, 0.40 for the total score, 0.36 for disinhibition, and 0.27 for executive cognitive dysfunction. This suggests a moderate degree of concordance for apathy and a fair concordance for the other scales.

Finally, Wilcoxin Signed Rank analyses were conducted to determine if self and informant reports differed significantly. Results showed significant differences for all FrSBe scales, with the largest difference between self and informant report for executive cognitive dysfunction (Table 16).

#### **IV. DISCUSSION**

The current study sought to determine whether information attained from CT imaging and neuropsychological evaluation can predict the degree of apathy, disinhibition, and executive cognitive dysfunction reported at one to five years following severe, moderate, or mild complicated TBI. Furthermore, it examined the level of concordance between reports made by individuals with TBI and informants regarding these domains of neurobehavioural disturbance in daily life. Results showed that CT data collected in the acute post-injury stage was not predictive of the degree of neurobehavioural disturbance reported by either TBI survivors or informants one to five years later. Concurrent performance on neuropsychological testing was predictive of informant-reported executive cognitive dysfunction, but was not predictive of self-reported difficulties in daily life in any of the three domains of interest. Finally, informant reports showed higher levels of disturbance than the survivor reports, with the greatest discrepancy present for level of executive cognitive dysfunction.

#### **Computed Tomography and Neurobehavioural Outcome**

CT is the typical means of imaging used clinically in acute TBI due to its utility in providing acute injury information, its ease of access, and its compatibility with life support systems. Therefore, in the majority of cases, CT data collected in the acute phase post injury is the imaging information available to clinicians working with TBI patients. The present study examined whether such imaging has prognostic value regarding specific aspects of neurobehavioural outcome. Results indicate that the presence or absence of pathology in the frontal, temporal, and subcortical regions, as well as the degree of midline shift on CT scans within seven days of injury were not predictive of the degree of apathy, disinhibition, executive cognitive dysfunction, or overall level of neurobehavioural disturbance reported by survivors and informants.

The domains of neurobehavioural disturbance examined in the current study are different than those of previous studies, thereby extending research to a broader array of neurobehavioural dysfunction. Four previous studies examining neurobehavioural outcome and early CT data were found in the literature. These studies have generally revealed a weak relationship to outcome within the first year post injury. Three studies showed that degree of neurobehavioural disturbance did not differ for those with versus those without various types of pathology on brain CT (Fork et al., 2005; Lehtonen et al., 2005; Levin et al., 1987). The fourth found group differences based on presence/absence of frontal pathology on CT (Wallesch et al., 2001). Overall, the current results support the findings of the majority of prior research suggesting that early CT information does not have utility in providing information about neurobehavioural outcome in the months to years following TBI.

Several studies have focused on functional outcome, as opposed to neurobehavioural disturbance, in relation to acute CT. Research on early CT information in relation to functional outcome in daily life is mixed; some studies have found a relation (Englander et al., 2003; Husson et al, 2010) while others have not (Lehtonen et al., 2005). However, few studies have examined the predictive ability of acute CT regarding longer term functional outcome at one year or more post injury. Two research projects that have examined this question have found that CT data has failed to predict various aspects of functional outcome including life satisfaction, level of disability, and social functioning (Van Der Naalt et al., 1999; Williams, Rapport, Hanks, Millis, & Greene, 2012). The findings of these studies and the current study taken together strongly suggest that acute CT data fails to provide prognostic information regarding several aspects of neurobehavioural and functional outcome in daily life at one year or more post injury.

Studies have typically examined CT findings based on area or type of pathology within the brain. It is possible that other means of classifying CT data, such as by overall number of lesions or the size of lesions in certain regions, may have better utility in prognosis of daily functioning. Presence or absence of pathology in a certain region may not be sufficiently sensitive classification. Another possibility is that while CT is invaluable during the acute stage of TBI, perhaps other methods or combinations of methods of imaging attained early on have more utility in informing longer term prognosis with respect to daily functioning. While research exists that examines early neuroimaging findings using various magnetic resonance techniques in relation to outcome in moderate to severe TBI, such studies have typically focused on global aspects

of outcome. For example, level of disability within the first two years after TBI, as measured by the GOS, has been predicted by MRI findings attained during the acute post-injury phase utilizing T2-weighted imaging and fluid-attenuated inversion recovery imaging (Chastain et al., 2009), as well as depth of lesion analysis (Lagares et al., 2009; Skandsen et al., 2011). Research has also found MRI techniques to be superior to acute CT data in predicting global outcome on the GOS (Chastain et al., 2009). However, very little research has examined these more sophisticated imaging techniques during the acute TBI stage in relation to more specific aspects of long-term outcome such as behavioural and cognitive abilities. Most studies examining the relation to specific disturbances have utilized these imaging techniques in post-acute phases (e.g., Salmond et al., 2006; Warner et al., 2010), but it is possible that data attained using these techniques at the acute phase also would have prognostic value for these aspects of outcome.

### **Neuropsychological Function and Neurobehavioural Disturbance**

The second aim of the study was to examine the relationship between concurrent neuropsychological test performance and the degree of reported disinhibition, apathy, and executive cognitive dysfunction in the daily lives of survivors of mild complicated to severe TBI at one to five years post injury. Informant report of executive cognitive dysfunction was predicted by concurrent performance on a small group of standardized neuropsychological tests. Specific tests had unique predictive power, including the SDMT and CVLT-II total learning score. Thus, poorer performance on measures of attention/processing speed and learning predicted higher levels of informant-reported executive cognitive dysfunction. Self-reported neurobehavioural disturbance was not predicted by concurrent neuropsychological test performance.



The present findings suggest that the level of executive cognitive dysfunction in daily life can be predicted by select performances on concurrent standardized neuropsychological tests. However, as with a recent study using the FrSBe in a mild to moderate TBI sample within three months of injury (Schiehser et al., 2011), executive cognitive dysfunction in daily life was not predicted by neuropsychological tests that are traditionally thought to measure executive functions. Rather, similar to the present findings, Schiehser et al. found that an attention/processing speed composite was predicted by self-reported executive cognitive dysfunction on the FrSBe, whereas an executive functioning composite was not. Taken together, the results of the current study and Schiehser et al.'s study suggest that difficulties with attention and processing speed, among the most common deficits in TBI (Mathias & Wheaton, 2007), might underlie executive cognitive dysfunction in daily life. In fact, it has been hypothesized by some researchers that executive functioning deficits on testing following TBI are caused by deficiencies in more basic skills, such as attention and processing speed (Felmingham, Baguley, & Green, 2004). The current results also suggest that attention and processing speed not only are associated with difficulties in daily functioning during the immediate months post injury, as in Schiehser et al.'s study, but continue to be related to these problems up to five years later.

The present study also implicated learning ability as predictive of executive cognitive dysfunction in daily life. It is possible that learning was found to be important by virtue of the attention requirements involved in such a task. The association could also be a function of the semantic clustering component to the CVLT-II learning trials that can be utilized to facilitate learning. That is, the ability to spontaneously cluster a word list

according to underlying semantic structure is thought to reflect an aspect of executive functioning (Gershberg & Shimamura, 1995). Alternately, learning ability may be necessary for success in everyday situations involving executive cognitive functions.

Results add support to the importance of attention/processing speed and learning measures in predicting various aspects of outcome after TBI. Verbal list learning on the CVLT-II or the Rey Auditory Verbal Learning Test and performance on the SDMT were recently found to be the two measures from a battery of tests that predicted level of disability and functional independence at two years post injury in a study of moderate to severe TBI (Bercaw et al., 2011). The predictive nature of these same measures in the current study demonstrates the utility of these indices in predicting yet another aspect of outcome in TBI, executive cognitive dysfunction.

Neither disinhibition nor apathy was strongly related to neuropsychological test performance. Research examining these domains of disturbance in relation to neuropsychological testing in TBI is limited, and the current study adds information to this area of research.

Our results regarding disinhibition are in line with the two previous TBI studies that have also examined the predictive relationship between disinhibition and neuropsychological tests (Schiehser et al., 2011; Votruba et al., 2008). Research focused on other neurological disorders has typically found a similar result, with disinhibition present in daily life alongside of normal performance on neuropsychological testing (Cato et al., 2004; Dimitrov et al., 1999; Eslinger & Damasio, 1985; Meyers et al., 1992).

Past research on apathy and neuropsychological test performance provides differing results, and the current study supports those that have found apathy to not have

a strong relation with neuropsychological testing. Of the two research studies in the TBI literature that have examined the link between reported apathy and neuropsychological testing, Schiehser et al.'s (2011) study found similar results to those in the present study. Although they found a significant relation between the FrSBe Apathy scale and an attention/processing speed composite score, the Apathy scale was not predictive of any of the neuropsychological composite scores. The other study found apathy to be predicted by learning and memory (Andersson & Bergedalen, 2002). The current study suggests that clinicians may require questionnaire data from a significant other to determine the presence of disinhibition and apathy in an individual's daily life following TBI, as such difficulties may not be isolated by neuropsychological testing.

The current study found significant correlations between a few neuropsychological tests and informant reports of the FrSBe executive cognitive dysfunction and FrSBe total scores. However, there were no significant correlations or predictors for the FrSBe apathy and disinhibition scales. Thus, the lack of relationship between most FrSBe scales and neuropsychological test scores found in the current study might suggest that the FrSBe adds non-redundant information to assessment data within a TBI population.

Previous research has found the FrSBe to be related to neuropsychological test performances in various etiologies and healthy samples. Most previous studies have employed informants to complete the FrSBe questionnaire, but some studies have focused on self-report. In a dementia sample, all informant-reported FrSBe scales were predicted by one or more neuropsychological tests (Paulson et al., 1996). Velligan et al. (2002) found that all clinician-rated FrSBe scales were related to two executive

functioning measures in a schizophrenia sample. A study examining individuals with amyotrophic lateral sclerosis found that informant reports of the apathy and executive cognitive dysfunction scales were related to several of the neuropsychological tests administered, while the disinhibition scale was not (Witgert et al., 2010). Total FrSBe score, based on self report by individuals with multiple sclerosis, was found to be predicted by several of the neuropsychological measures within a battery of tests (Basso et al., 2008).

The ecological validity of neuropsychological testing has become increasingly important, such that neuropsychologists are often required to comment on implications for everyday functioning from objective test findings. There is currently controversy in the literature with regards to how well neuropsychological tests that are thought to measure executive functions are able to predict executive functioning in the real world (Burgess et al., 2006). Some researchers have found a relationship between neuropsychological tests of executive functioning and reports of such abilities in daily life (Gargia-Molina et al., 2012, Malloy et al., 1993), while others have not (Boelen et al., 2009; Dimitriv et al., 1999; Namiki et al., 2008; Satish et al., 2008).

Our finding that executive functioning tests did not predict self or informant reports of executive cognitive dysfunction in everyday life is in line with previous studies demonstrating discrepancy between these means of measuring executive function abilities. This adds support to the argument for the importance of questionnaire data in assessing the broad domain of executive functioning, at least within the TBI population. However, it is important to note that only two neuropsychological tests of executive functioning were examined in our regression analyses, so it is possible that different

results would have been found using additional tests from the executive functioning domain. On the other hand, the current results also could suggest that questionnaire data is inaccurate, as it is not in line with neuropsychological testing. For instance, it is known that many factors can influence informant report, such as emotional state, personality, degree of acceptance or denial of injury consequences, amount of time spent together, type of relationship, perceived significance of various post injury difficulties, social environment, and level of burden experienced by the informant (Lanham et al., 2000; McKinlay & Brooks, 1984; Santos et al., 1998). Thus, it is difficult to determine how accurate these reports may be in representing true abilities of the individual with TBI. Clearly, more research and the development of a standard by which to determine the ecological validity of questionnaire and objective test data are required. Given the current state of research, it is perhaps prudent for the neuropsychologist to collect questionnaire information in addition to neuropsychological testing and consider both types of data in order to reach accurate conclusions regarding executive functioning abilities.

Furthermore, although the ability of executive functioning tests to give information about real world executive functioning has been questioned, these tests have been found to be predictive of many other aspects of functioning in daily life (e.g., Hanks et al., 1999).

This indicates the utility of such measures within clinical assessments.

### **Concordance Level of Self and Informant Report**

The third aim of the current study was to examine the level of concordance between self and informant reports regarding disinhibition, apathy, and executive cognitive dysfunction in daily life. Results showed that informants reported higher levels of all three aspects of neurobehavioural disturbance than did the survivors themselves.

This is in line with previous research examining similar areas of functioning, as well as research examining several other aspects of cognitive and behavioural difficulties, in which informants tend to report higher levels of disturbance than TBI survivors (Hart et al., 2003; Hart et al., 2009; Marsh & Kersel, 2006; Rochat et al., 2010; Sherer et al., 1998). Of the three domains examined in this study, level of executive cognitive dysfunction exhibited the greatest discrepancy between self and informant report.

The concordance levels of self and informant report in the current study were lower than those of Hart et al.'s (2003) study, which utilized the same method of calculating concordance. The six NFI scales in that study had Lin's concordance levels ranging from 0.63 – 0.69, compared to levels ranging from 0.27 – 0.43 on the FrSBe in the present study. The lower concordance level in the present study relative to Hart et al.'s study may indicate greater level of discrepancy for the domains of neurobehavioural disturbance we examined relative to the domains covered by the NFI (depression, somatic, memory/attention, communication, aggression, motor), although there is overlap between some areas of functioning addressed by the NFI and FrSBe. Our lower level of concordance also could be influenced by factors such as smaller sample size and demographic differences. It was not possible to compare directly the level of concordance in the present study to the other TBI studies examining similar areas of functioning due to differences in methods of analyzing the agreement between patient and informant reports.

Previous research has found that concordance between self and informant reports improves with increasing time since injury (Hart et al., 2009; Vanderploeg, et al., 2007). While Hart et al.'s (2003) results are in line with that finding, with an increase in concordance over the first year, level of agreement for several areas of functioning was

still quite low at one year post injury. The current study did not examine change in concordance over time, but results suggest that the concordance level between self and informant report remains quite low up to five years post injury.

In so far as is known, this is the first study to examine the concordance levels of apathy, disinhibition, and executive cognitive dysfunction domains relative to one another. Previous research has found that certain aspects of outcome in TBI, such as cognitive, emotional, and behavioural functioning, have poorer self and informant concordance levels compared to physical functioning (Cusick et al., 2000; Hart et al., 2003; McKinlay & Brooks, 1984; Trahan et al., 2006). This study adds more detailed information by comparing the level of discrepancy for specific aspects of neurobehavioural disturbances. Results suggest that self and informant agreement is lower with regards to executive cognitive dysfunction than it is for disinhibition and apathy.

Discrepancy between self and informant reports is frequently used as a measure of the level of anosognosia, or lack of awareness of deficits among individuals with TBI. This practice is based on the assumption that informant reports are more accurate than that of TBI survivors. However, the concordance level results of the current study are not intended as measures of awareness of deficit. As outlined above, several factors have been raised as potential influences on both self and informant questionnaires, such as response style, item interpretation, emotional state, personality, degree of acceptance or denial of injury consequences, amount of time spent together, type of relationship, perceived significance of various post injury difficulties, and level of burden experienced by informant (Lanham et al., 2000; McKinlay & Brooks, 1984; Santos et al., 1998). Thus,

it is not assumed that the informant's report is necessarily more accurate. However, the finding that the TBI participant's neuropsychological test performance was associated with informant but not self report of executive cognitive dysfunction suggests that the informant report is more accurate than that of the individual with TBI for this particular domain of disturbance. The data do not allow conclusions about whether the survivor or informant report is more accurate regarding level of disinhibition or apathy.

### **The FrSBe Measure**

Only a limited number of published TBI studies have utilized the FrSBe. These studies were examined to compare how similar the FrSBe values attained in the current study are to those of previous studies. Of the five TBI studies located that used the entire FrSBe or portions of the measure and also reported the average FrSBe values, two studies utilized raw score values as in the present study. These two studies reported raw score means that were quite similar to those measured within the current sample (see Table 17) for both self-ratings (Larson & Perlstein, 2009) and informant ratings (Larson & Perlstein, 2009; Stout et al., 2003). The other three studies reported mean FrSBe values as t-scores. Although we did not use FrSBe t-score values in our analyses due to the demographic differences in our sample relative to the normative sample, t-score values were calculated for the purpose of comparison to previous research. Self-reported scores in Schiehser et al.'s (2011) study of mild and moderate TBI were relatively similar to our self-report t-score means. On the other hand, self-reported mean t-scores attained by Reid-Arndt et al (2007) were higher than ours. Also, a study using only the apathy scale of the FrSBe found a mean informant-reported apathy t-score that is substantially higher than our informant-reported apathy t-score (Lane-Brown et al., 2009).



Overall, comparison of our FrSBe values to previous TBI studies revealed that the raw scores of the present study are in line with those of previous studies, but there are conflicting data with regards to t-scores. Differences relative to Reid-Arndt et al.'s (2007) study could be due to the nature of the sample, as that study used a neuropsychology clinic sample. Those referred for neuropsychological assessment might represent a subset of TBI survivors who experience more post-injury difficulties, which could include a higher level of neurobehavioural disturbance. In contrast, our sample included individuals who were consecutively recruited during inpatient rehabilitation relatively soon after the injury into a longitudinal TBI project, and may conceivably demonstrate a wider range of outcome in the years post injury. It is feasible that higher apathy informant t-scores in Lane-Brown et al.'s (2009) study could be due to their use of a severe TBI sample. However, when the informant FrSBe t-scores for the severe TBI cases in the current study were examined as a separate group, there was no appreciable difference relative to the entire sample or relative to those with mild complicated or moderate TBI. There is no mention of ethnicity in any of the three studies using demographically corrected t-scores. As this variable was the greatest difference between the current sample and the normative FrSBe sample, differences in t-scores between the current and prior studies due to ethnicity differences can not be ruled out. Overall, the comparison of our findings to previous FrSBe values suggests that caution should continue to be taken in using the FrSBe t-score conversions with individuals who are dissimilar to the normative sample.

The study conducted by Schiehser et al. (2011) included mostly mild TBI survivors while the current study included more severe TBI survivors. Nevertheless, the FrSBe self-report t-scores were similar. As neurobehavioural difficulties are known to be

more common with injuries of greater severity (Levin et al., 1987), one would expect the self-reported FrSBe levels to be higher in the present study. Thus, the similarity in self-reported scores across the two studies may provide support for presence of diminished awareness of difficulties among survivors of more severe TBI.

With the exception of self-reported disinhibition, all FrSBe raw scores were related to education. Age and gender were not related to any FrSBe scores. This is in contrast to the healthy normative sample in which these demographic variables were all found to be important, with age, education, and gender accounting for 18% of the variance in informant reports and 11% of the variance in self reports. Previous TBI studies have not examined demographic variables in relation to FrSBe scores. Two studies using the FrSBe in other patient groups did so. Grace et al (1999), examining a neurological sample of a variety of etiologies, found higher total informant-reported FrSBe scores to be related to males and to lower education level, but not to age. In a schizophrenia sample, neither gender nor ethnicity was found to be significantly related to clinician-rated total FrSBe score (Velligan et al., 2002). Neither of these studies examined self-reported FrSBe scores. The current study adds to the FrSBe literature regarding the importance of education level in FrSBe scores.

### **Study Limitations**

There are limitations to the current findings that must be recognized, including aspects of the TBI sample. First, the sample included individuals who had sustained a TBI of a severity requiring inpatient rehabilitation. Thus, the sample did not include individuals whose injury was too mild to require inpatient rehabilitation or too severe to allow participation in a rehabilitation program. Additionally, some patients with severe

TBI who received inpatient rehabilitation may have been functioning at too low of a level to be able to participate in follow-up research. Thus, the findings are not representative of the TBI population as a whole. Second, the current study included a time range of one to five years post injury, and it is possible that a more narrow time range may have resulted in different findings. For example, perhaps the areas of neurobehavioural disturbance under study are at a higher level at one and two years post injury compared to five years as recovery occurs and compensation strategies are implemented, and thus perhaps neurobehavioural disturbance at these time points would be differentially predicted by acute CT data. Third, the mixed TBI etiologies might be viewed as a limitation, as various etiologies have differences in injury mechanism that might influence cognitive and neurobehavioural outcome. However, research has generally failed to find large differences in outcome across TBI etiologies (Ylloja, Hanks, Baird, & Millis, 2010; Zafonte et al., 1997). Alternately, the mixed sample of TBI etiologies could also be viewed as a strength, as it is more representative of the broad array of TBI cases that are seen by clinicians. Therefore, the results can be generalized to a wider range of individuals with TBI.

It is possible that having participants choose an informant rather than requiring informant reports to be completed by an individual with a particular relationship to the participant may have been a confounding factor in the informant-reported FrSBe scales. However, Cusick et al. (2000) used criteria similar to the current study in their analysis of self versus informant reports of post-TBI outcome and found that the nature of the TBI survivor-informant relationship did not influence the results.

Our study examined current neurobehavioural functioning as opposed to a change in functioning from before injury. Thus, we were unable to account for the possibility that some patients may have already been at a high level on some of the FrSBe items prior to injury, due to personality style, for example. This may be particularly the case with disinhibited behaviour, as it could be elevated by a pre-morbid risk-taking personality style (Kim, 2002). This is a potential confound for the analyses examining the predictive ability of cognitive deficits and CT pathology on FrSBe scores. However, given the known tendency to over-rate premorbid functioning after experiencing a negative event such as TBI (Gunstad & Suhr, 2001; Hilsabeck, Gouvier, & Bolter, 1998), we decided not to have participants complete the pre-injury portion of the FrSBe questionnaire.

## **Conclusion**

The present findings provide evidence that standardized neuropsychological test scores can predict degree of concurrent executive cognitive dysfunction in daily life. However, rather than traditional executive function tests providing such information, the findings suggest that more basic cognitive functions, such as attention, processing speed, and learning, contribute to executive cognitive functioning in daily life. Results support the utility of questionnaire information in delineating the degree of disinhibition and apathy, as well as executive cognitive function, post TBI. The current findings also add support to the growing evidence that acute CT data has limited utility in predicting long term outcome in TBI. In line with previous research, informant and self report information can be quite discrepant, with higher levels of neurobehavioural disturbance reported by informants. Results add unique information suggesting that certain aspects of neurobehavioural disturbances have poorer self versus informant concordance relative to

others. Finally, comparison of FrSBe scores attained in the current study to those in previous TBI studies supports the use of caution in converting FrSBe raw scores to demographically corrected t-scores with individuals who are demographically dissimilar to the normative sample. This is the first study to begin to compile FrSBe data for a TBI sample that has a majority of African American participants and a lower education level compared to previous studies that have used this measure in TBI. Further research in such samples will be valuable for expanding the use of the FrSBe.

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## TABLES

Table 1

*Acronyms Used Throughout Body of Document*

Acronym	Definition
Apathy_self	Apathy self report on the FrSBe
Apathy_informant	Apathy informant report on the FrSBe
CT	computed tomography
CVLT-II 1-5	California Verbal Learning Test –II trials 1-5 total
CVLT-II SD	California Verbal Learning Test –II short delay recall total
CVLT-II LD	California Verbal Learning Test –II long delay recall total
DAI	diffuse axonal injury
Disinhibition_self	Disinhibition self report on the FrSBe
Disinhibition_informant	Disinhibition informant report on the FrSBe
Executive_self	Executive dysfunction self report on the FrSBe
Executive_informant	Executive dysfunction informant report on the FrSBe
FAS	word generation
FrSBe	Frontal Systems Behavior Scale
GCS	Glasgow Coma Scale
GOS	Glasgow Outcome Scale
MRI	magnetic resonance imaging
NFI	Neurobehavioural Functioning Inventory
NRS	Neurobehavioural Rating Scale
SEMTBIS	Southeaster Michigan Traumatic Brain Injury System

PTC	posttraumatic confusion
SDMT	Symbol Digit Modalities Test
TBI	traumatic brain injury
Total_self	FrSBe self report total score
Total_informant	FrSBe informant report total score
Trails A	Trail Making Test A
Trails B	Trail Making Test B
WCST-64	Wisconsin Card Sorting Test – 64 card version
WTAR	Wechsler Test of Adult Reading

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Table 2

*Marshall Classification System for Brain CT*

Marshall	Descriptor	CT characteristics
Class I	Diffuse Injury I	No visible pathology
Class II	Diffuse Injury II	Cisterns present with midline shift 0-5mm, &/or lesions present, no lesion >25cc
Class III	Diffuse Injury III (swelling)	Cisterns compressed or absent with midline shift 0-5mm, no lesion >25cc
Class IV	Diffuse Injury IV	Midline shift >5mm, no lesion >25cc
Class V	Evacuated mass lesion	Any lesion surgically evacuated
Class VI	Non-evacuated mass	Lesion > 25cc not surgically evacuated

Table 3

*Presence of Pathology on CT and Demographics of Groups With and Without Pathology*

	Pathology present ( <i>N</i> = 95)		Pathology / no pathology	
	<i>n</i>	Ethnicity ( <i>n</i> ) C/AA/other	Age ( <i>M</i> )	Edu ( <i>M</i> )
Punctuate/petechial hemorrhage	50	21 / 27 / 2	41.7 / 38.6	12.6 / 12.2
Subarachnoid hemorrhage	51	28 / 20 / 3	43.0 / 37.0	12.8 / 11.9
Intraventricular hemorrhage	15	8 / 7 / 0	39.7 / 40.4	12.7 / 12.4
Frontal	63	28 / 31 / 4	40.1 / 40.1	12.6 / 12.1
Temporal	38	21 / 15 / 2	43.1 / 38.4	13.1 / 12.0
Parietal	32	15 / 15 / 2	40.9 / 40.0	12.4 / 12.4
Occipital	8	3 / 5 / 0	41.4 / 40.1	13.5 / 12.3
Subcortical	20	6 / 12 / 2	33.0 / 42.0	12.0 / 12.5
Epidural hematoma	11	7 / 3 / 1	36.2 / 40.8	12.7 / 12.4
Subdural hematoma	42	23 / 18 / 1	42.6 / 38.3	12.2 / 12.6
Midline shift (any)	34	18 / 14 / 2	43.4 / 38.5	12.3 / 12.5
Midline shift (> 5mm)	15	7 / 6 / 2	42.5 / 39.8	12.1 / 12.5

C = Caucasian, AA = African American, other = some other ethnicity, Edu = education

Table 4

*Demographic Corrections Applied to Neuropsychological Test Scores*

	Age	Education	Ethnicity	Sex
Trails A & B	x	x	x	x
DVT	x	x	x	x
FAS	x	x	x	x
CVLT-II	x			x
SDMT	x	x		
WCST-64	x	x		

Trails A = Trail Making Test A, Trails B = Trail Making Test B, DVT = Digit Vigilance Test, FAS = word generation, CVLT-II = California Verbal Learning Test-II, SDMT = Symbol Digit Modalities Test, WCST-64 = Wisconsin Card Sorting Test – 64 card version



Table 5

*Demographics of the TBI Sample*

		<i>n</i>	%
Gender	Male	75	78.9
	Female	20	21.1
Ethnicity	Caucasian	43	45.3
	African American	48	50.5
	Other	4	4.2
Years post TBI	1	20	21.0
	2	25	26.3
	3	3	3.2
	4	6	6.3
	5	41	43.2
		<i>M (SD)</i>	Range
Age		40.2 (14.7)	18 - 80
Education		12.4 (2.4)	8 - 20
GCS		8.4 (4.3)	3-15
PTC		22.0 (18.2)	0 - 74

GCS = Glasgow Coma Scale, PTC = posttraumatic confusion (days)

Table 6

*Self- and Informant-reported FrSBe Raw Scores*

FrSBe Variable	<i>M (SD)</i>	<i>Mdn</i>	<i>Range</i>
Self report ( <i>n</i> = 95)			
Apathy	29.1 (8.7)	29.0	14-55
Disinhibition	29.7 (9.7)	27.0	15-54
Executive	36.6 (10.7)	36.0	17-57
Total	95.4 (26.3)	91.0	46-154
Informant report ( <i>n</i> = 86)			
Apathy	32.5 (10.5)	32.0	14-59
Disinhibition	31.6 (10.0)	30.0	15-58
Executive	43.4 (11.9)	43.5	17-69
Total	107.5 (29.2)	107.5	46-180

*Mdn* = median

Table 7

*Neuropsychological Test Scores: T-Scores and Percentage with Impaired Scores*

	Mean t-score	% impaired > 1 SD	% impaired > 2 SD
Trails A	45.5	32.1	8.6
Trails B	43.9	32.1	13.6
SDMT-written	38.8	49.4	26.6
SDMT-oral	39.9	48.8	22.5
DVT time	41.7	43.6	17.9
DVT errors	49.7	13.7	4.1
CVLT-II 1-5	43.8	39.0	17.1
CVLT-II SD	43.8	42.7	18.3
CVLT-II LD	42.3	46.3	22.0
FAS	42.6	36.6	9.8
WCST-64 errors	40.5	52.5	15.0

Trails A = Trail Making Test A, Trails B = Trail Making Test B, SDMT = Symbol Digit Modalities Test, DVT = Digit Vigilance Test, CVLT-II 1-5 = California Verbal Learning Test-II trials 1-5 total, CVLT-II SD = California Verbal Learning Test-II short delay recall total, CVLT-II LD = California Verbal Learning Test-II long delay recall total, FAS = word generation, WCST-64 errors = Wisconsin Card Sorting Test – 64 card version total errors

Table 8

*Summary of Multiple Regression Analyses for Acute CT Variables Predicting FrSBe**Scores*

Dependent Variable	$R^2$	$F$	$p$
Self report ( $n = 95$ )			
Apathy	.07	1.70	.158
Disinhibition	.06	1.47	.217
Executive	.06	1.47	.218
Total	.07	1.72	.153
Disinhibition_LOG	.07	1.69	.160
Executive_LOG	.06	1.49	.211
Total_LOG	.08	1.95	.110
Informant report ( $n = 86$ )			
Apathy	.09	1.98	.105
Disinhibition	.10	2.12	.086
Executive	.10	2.21	.076
Total	.10	2.35	.061

LOG = LOG transformed variables

Table 9

*Point Biserial Correlations between FrSBe Variables and Acute CT Variables*

FrSBe Variable	Frontal	Temporal	Noncortical	> 5mm shift
Self report ( <i>n</i> = 95)				
Apathy	.099	-.157	-.157	-.050
Disinhibition	-.024	-.204*	-.146	-.003
Executive	-.007	-.172	-.149	.066
Total	.021	-.197	-.166	.009
Informant report ( <i>n</i> = 86)				
Apathy	-.013	-.259*	-.014	-.156
Disinhibition	.034	-.217*	.135	-.118
Executive	.024	-.258*	.098	.003
Total	.017	-.272*	.080	-.095

\**p* < .05, two-tailed

Table 10

*Wilcoxin Rank-Sum Results for Presence versus Absence of Temporal Pathology on Acute CT*

FrSBe Variable	<i>Mdn</i>		<i>T</i>	Effect size
	Pathology present	Pathology absent		
Self report ( <i>n</i> = 95)				
Apathy	29.0	28.0	1682.00	-.11
Disinhibition	25.0	29.0	1556.00*	-.21
Executive	33.5	39.0	1601.50	-.17
Total	90.0	96.0	1587.50	-.18
Informant report ( <i>n</i> = 86)				
Apathy	29.5	34.5	1212.50*	-.25
Disinhibition	26.5	32.0	1228.00*	-.24
Executive	38.0	45.0	1229.50*	-.24
Total	97.5	111.0	1218.50*	-.25

\**p* < .05, two-tailed, *Mdn* = median, *T* = Wilcoxin Rank-Sum statistic

Table 11

*Correlations between FrSBe Variables and Demographics*

FrSBe Variable	Education <sup>a</sup>	Age <sup>a</sup>	Sex <sup>b</sup>
Self report ( <i>n</i> = 95)			
Apathy	-.159*	-.064	.014
Disinhibition	-.135	-.085	.127
Executive	-.175*	-.042	.006
Total	-.170*	-.067	.054
Informant report ( <i>n</i> = 86)			
Apathy	-.219**	-.031	-.022
Disinhibition	-.174*	-.125	-.112
Executive	-.250**	-.096	-.085
Total	-.246**	-.084	-.081

\* $p < .05$ , \*\* $p < .01$ ; two-tailed; not corrected for multiple comparisons; <sup>a</sup> Kendall-tau correlations; <sup>b</sup> point-biserial correlations

Table 12

*Summary of Multiple Regression Analyses for Neuropsychological Performance**Predicting FrSBe Scores*

Dependent Variable	$R^2$	$F$	$p$
Self report ( $n = 79$ )			
Apathy	.05	0.93	.450
Disinhibition	.03	0.53	.716
Executive	.09	1.71	.156
Total	.05	1.06	.385
Disinhibition_LOG	.03	0.48	.749
Executive_LOG	.09	1.78	.143
Total_LOG	.05	1.05	.386
Informant report ( $n = 70$ )			
Apathy	.10	1.83	.134
Disinhibition	.08	1.47	.221
Executive	.15	2.90	.029*
Total	.13	2.42	.057

\* $p < .05$ , LOG = LOG transformed variables



Table 13

*Multiple Regression Results Predicting Informant Reports of Executive Dysfunction*

Variable	<i>B (SE)</i>	$\beta$	<i>p</i>	<i>sr</i> <sup>2</sup>
Constant	40.67 (9.02)		.000	
SDMT-written	-2.59 (1.22)	-.30	.037*	.06
CVLT-II trials 1-5	-0.28 (0.12)	-.32	.023*	.07
Trails B	0.26 (0.17)	.24	.127	.03
WCST-64 errors	0.01 (0.13)	.01	.913	.00

\**p* < .05, *B* = beta weight, *SE* = standard error,  $\beta$  = standardized beta, *sr*<sup>2</sup> = semipartial squared, Trails B = Trail Making Test B, SDMT = Symbol Digit Modalities Test, CVLT-II 1-5 = California Verbal Learning Test-II trials 1-5 total, WCST-64 errors = Wisconsin Card Sorting Test – 64 card version total errors

Table 14

*Correlations between Neuropsychological Test Scores and FrSBe Variables*

	Self				Informant			
	A	D	E	Tot	A	D	E	Tot
Trails A	-.094	-.027	-.091	-.078	-.047	-.073	-.119	-.086
Trails B	-.052	-.044	-.144	-.106	.026	.028	-.031	.005
SDMT-written	-.144	-.064	-.159*	-.125	-.160	-.101	-.191*	-.172*
SDMT-oral	-.136	-.082	-.170*	-.138	-.087	-.097	-.230**	-.150
DVT time	.047	.062	.022	.046	.105	.070	.086	.104
DVT errors	-.026	.000	-.117	-.057	.046	.128	-.005	.087
CVLT-II 1-5	-.083	-.023	-.086	-.064	-.073	-.103	-.226**	-.169*
CVLT-II SD	-.041	.022	-.064	-.024	.011	-.061	-.160	-.075
CVLT-II LD	-.069	-.006	-.087	-.059	-.052	-.078	-.219**	-.135
FAS	-.084	.049	-.047	-.028	.014	.059	.040	.040
WCST-64 errors	-.014	.030	-.032	-.006	.022	.067	-.042	.005

\* $p < .05$ , \*\* $p < .01$ , two-tailed, not corrected for multiple comparisons, Self  $n = 73 - 81$ ,

Informant  $n = 64 - 73$ , A = Apathy, D = Disinhibition, E = Executive, Tot = Total, Trails

A = Trail Making Test A, Trails B = Trail Making Test B, SDMT = Symbol Digit

Modalities Test, DVT = Digit Vigilance Test, CVLT-II 1-5 = California Verbal Learning

Test-II trials 1-5 total, CVLT-II SD = California Verbal Learning Test-II short delay

recall total, CVLT-II LD = California Verbal Learning Test-II long delay recall total,

FAS = word generation, WCST-64 errors = Wisconsin Card Sorting Test – 64 card

version total errors

Table 15

*Difference Scores: Informant-Report Minus Self-Report*

FrSBe Variable	Median Difference	25 <sup>th</sup> percentile	75 <sup>th</sup> percentile	Range
Apathy	3.00	-5.00	10.25	-20 - 30
Disinhibition	4.00	-4.25	9.00	-23 - 31
Executive	9.00	-3.00	16.00	-27 - 37
Total	15.50	-10.25	31.75	-59 - 94

*n* = 86

Table 16

*Wilcoxin Signed Rank Test Comparing Informant versus Self Report on FrSBe Scales*

FrSBe Variable	<i>Mdn</i> (quartiles)		<i>T</i>	Effect size
	Self	Informant		
Apathy	27.0 (22.75, 35.25)	32.0 (25.25, 39.0)	-2.840**	.217
Disinhibition	26.5 (22.0, 36.0)	30.0 (24.0, 38.25)	-2.185*	.167
Executive	36.0 (26.0, 46.25)	43.5 (36.0, 52.0)	-4.567***	.348
Total	90.5 (74.25, 116.0)	107.5 (84.0, 128.25)	-3.874***	.295

\* $p < .05$ , \*\* $p < .01$ , \*\*\* $p < .001$ ,  $n = 86$ , *Mdn* = median, *T* = Wilcoxin Signed Rank Test value

Table 17

*Comparison of FrSBe scores to Prior TBI Studies Using the FrSBe*

FrSBe scale	Raw score				
	Current study		Larson & Perlstein (2009) <i>n</i> = 16		Stout et al (2003) <i>n</i> = 29
	Self	Informant	Self	Informant	Informant
Apathy	29.1	32.5	30.13	31.19	32.3
Disinhibition	29.7	31.6	32.19	32.88	29.5
Executive	36.6	43.4	39.44	44.25	41.3
Total	95.4	107.5	101.75	108.32	103.1
	t-score				
	Current study		Reid-Arndt (2007) <i>n</i> = 76	Schiehser et al (2011) <i>n</i> = 71	Lane-Brown et al (2009) <i>n</i> = 34
	Self	Informant	Self	Self	Informant
Apathy	56.8	68.3	71.08	59.5	75.0
Disinhibition	55.4	62.0	62.72	52.4	
Executive	59.2	64.8	72.18	60.9	
Total	59.2	67.1	76.29		

Scores are presented as mean values

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