Inhibitory Control and Reward Processes in Children and Adolescents with Traumatic Brain Injury and Secondary Attention-Deficit/Hyperactivity Disorder

by

Katia Joanne Sinopoli

A thesis submitted in conformity with the requirements for the degree of Doctor of Philosophy
Department of Psychology
University of Toronto

© Copyright by Katia Joanne Sinopoli (2010)
Inhibitory Control and Reward Processes in Children and Adolescents with Traumatic Brain Injury and Secondary Attention-Deficit/Hyperactivity Disorder

Katia Joanne Sinopoli

Doctor of Philosophy

Department of Psychology
University of Toronto

2010

Abstract

Children with traumatic brain injury (TBI) often experience difficulties with inhibitory control (IC), manifest in both neurocognitive function (poor performance on the stop signal task, SST) and behavior (emergence of de novo attention-deficit/hyperactivity disorder, or secondary ADHD, S-ADHD). IC allows for the regulation of thought and action, and interacts with reward to modify behaviour adaptively as environments change. Children with developmental or primary ADHD (P-ADHD) exhibit poor IC and abnormalities when responding to rewards, yet the extent to which S-ADHD is similar to and different from P-ADHD in terms of these behaviours is not well-characterized. The cancellation and restraint versions of the SST were used to examine the effects of rewards on 2 distinct forms of IC in children and adolescents divided into 4 groups (control, TBI, S-ADHD, and P-ADHD). The SST requires participants to respond to a “go signal” and inhibit their responses when encountering a “stop signal”. Rewards improved performance similarly across groups, ages, and cancellation and restraint IC tasks. Adolescents exhibited better IC and faster and less variable response execution relative to children. Significant IC deficits were found in both tasks in the P-ADHD group, with participants with S-ADHD exhibiting intermediate cancellation performance relative to the other groups.
Participants with TBI without S-ADHD were not impaired on either task. The relationship between neurocognitive and behavioral IC was examined by comparing multi-informant ratings of IC across groups, and examining the relationship between ratings and IC performance on the SST. Participants in the control and TBI groups were rated within the typical range, and exhibited fewer problems than either of the ADHD groups, who differed from each other (the P-ADHD group was rated as more inattentive than the S-ADHD group). Moderate to high concordance was found between parent and teacher reports, each of which was poorly concordant with self-reports. The P-ADHD and S-ADHD groups were unaware of their own deficits. Poorer IC predicted parent and teacher classification of participants into ADHD subtypes, although IC did not predict rating concordance. Despite similar clinical presentations, S-ADHD and P-ADHD differ in the phenotypic expression of behaviour and manifestation of IC across contexts.
Acknowledgments

I would like to thank Dr. Maureen Dennis for her extraordinary mentorship throughout my PhD. She has taught me valuable skills that will undoubtedly further my career, including how to think critically, how to ask the important questions, and how to write to deadlines. Importantly, Dr. Dennis has shown me that having a passion for science is what drives a successful research career rather than a desire for fame or glory. She took a chance on a “rat girl”, and helped me realize my potential by allowing me to discover what drives me to learn, succeed, and advance within the discipline of psychology. I will be forever grateful to Dr. Dennis for what I have learned over the last five years, and I hope to continue learning from her and benefitting from her expertise as I enter the next phase of my education.

I would also like to thank my dissertation committee members; Drs. Russell Schachar, Mary Lou Smith, and Jay Pratt. Dr. Schachar graciously shared his stop signal tasks with me, and his helpful comments and interpretations have been invaluable throughout this entire process. Dr. Smith’s concerns and suggestions throughout my PhD were essential in the streamlining of my experiments and in the interpretation of the results, and I am grateful for her clinical supervision and expertise throughout my first clinical practicum.

A special thanks to Dr. Talar Hopyan for her support, guidance, and friendship. She has lent an empathetic ear during more than one challenging period of my PhD, and has been quick to acknowledge my accomplishments and celebrate my successes.

I would also like to thank my friends and family for their unwavering support and love. While it is not always easy dealing with a frustrated student, they have endured my ups and downs, and have always been present when I needed them. My parents and sister have always given me their unconditional love and support, and this has made me strive to be the best I can be. My girlfriends, my sisters, their love, friendship, support, humor, and “real talk” has been instrumental throughout the dissertation, and I look forward to celebrating future achievements with them. I’d like to thank my grandparents for their patience and for always letting me know that they are there for me, regardless of our disagreements and different outlooks on life. Last but certainly not least, I’d like to thank my fiancé Jeremy. Words cannot express how grateful I am to have him in my life. He has calmed my fears, eased my self-doubts, and has been the greatest
cheerleader anyone could have. Not once has he ever doubted my abilities, and through him I found the strength to get through the most challenging and difficult times of this degree. He showed me how never to give up, how to look at the glass half full, and how to keep my head up even when I wanted to bury it in the sand. I couldn’t have asked for a better partner in life.

I am also indebted for the technical assistance I have received from research assistants both in Dr. Dennis’ and Dr. Schachar’s labs, including Alexandra Basile, Renee Ferrell, Arianna Stefanatos, Tara Goodale, and Shirley Chen.

Lastly, I would like to acknowledge the various granting agencies that have provided me with funding throughout my PhD: the Hospital for Sick Children (Restracomp Award), the Government of Ontario (Ontario Graduate Scholarship), and the Ontario Neurotrauma Foundation (ONF PhD Award).
# Table of Contents

Acknowledgments ......................................................................................................................... iv

Table of Contents .......................................................................................................................... vi

List of Figures ................................................................................................................................. xi

List of Appendices .......................................................................................................................... xiii

Chapter 1 Introduction .................................................................................................................. 1

Chapter 2 Reward Improves Cancellation and Restraint Inhibition Across Childhood and Adolescence ......................................................................................................................... 11

1 Method ........................................................................................................................................ 15

1.1 Participants ............................................................................................................................... 15

1.2 Stop Signal Tasks ........................................................................................................................ 16

1.3 Statistical Analyses .................................................................................................................... 18

2 Results ........................................................................................................................................ 20

2.1 Participant Characteristics ......................................................................................................... 20

2.2 Cancellation ............................................................................................................................... 20

2.2.1 Reward Effects ..................................................................................................................... 20

2.2.2 Age Effects ........................................................................................................................... 21

2.2.3 Order Effects ........................................................................................................................ 21

2.3 Restraint .................................................................................................................................... 21

2.3.1 Reward Effects ..................................................................................................................... 21

2.3.2 Age Effects ........................................................................................................................... 22

2.3.3 Order Effects ........................................................................................................................ 22

2.4 Task Comparisons .................................................................................................................... 23

3 Discussion ................................................................................................................................... 23

3.1 Reward Effects .......................................................................................................................... 24
3.2 Age Effects ................................................................................................................. 26
3.3 Task Effects .................................................................................................................. 29
3.4 Conclusions .................................................................................................................. 30

Chapter 3 Traumatic Brain Injury and Secondary Attention-Deficit/Hyperactivity Disorder in
Children and Adolescents: The Effect of Reinforcement on Inhibitory Control ............... 43

4 Method .......................................................................................................................... 49

4.1 Participants ................................................................................................................... 49

4.2 Rating Scales: Inclusion and exclusion criteria ............................................................ 51

4.3 Stop Signal Tasks .......................................................................................................... 52

4.4 Statistical Analyses ...................................................................................................... 55

5 Results ............................................................................................................................. 56

5.1 Participant Characteristics ........................................................................................... 56

5.2 Cancellation ................................................................................................................... 56

5.2.1 Group and Reward Effects ...................................................................................... 57

5.2.2 Order Effects ........................................................................................................... 57

5.3 Restraint ....................................................................................................................... 58

5.3.1 Group and Reward Effects ...................................................................................... 58

5.3.2 Order Effects ........................................................................................................... 58

5.4 Injury Variables ............................................................................................................. 59

5.4.1 Cancellation ............................................................................................................. 59

5.4.2 Restraint ................................................................................................................... 59

6 Discussion ....................................................................................................................... 60

6.1 Group Effects .............................................................................................................. 60

6.2 Reward effects ............................................................................................................ 63

6.3 Conclusions .................................................................................................................. 65
Chapter 4 The Relationship between Multi-Informant Behavioural Ratings and Inhibitory Control Performance on Cancellation and Restraint Tasks in Children with Traumatic Brain Injury ................................................................. 78

7 Method ................................................................................................................. 80

  7.1 Participants ................................................................................................. 80

  7.2 Questionnaires: Conners 3rd Edition ......................................................... 82

  7.3 Neurocognitive testing: Stop Signal Tasks .................................................... 84

  7.4 Statistical Analyses ...................................................................................... 85

8 Results ............................................................................................................... 86

  8.1 Participant Characteristics ........................................................................... 86

  8.2 Validity of Ratings ....................................................................................... 87

  8.3 Group Differences across Raters ................................................................. 87

  8.4 Conners-P: Group Differences ..................................................................... 87

  8.5 Conners-T: Group Differences ..................................................................... 88

  8.6 Conners-SR: Group Differences ................................................................... 88

  8.7 Concordance between the Conners-P and Conners-T ............................... 89

  8.8 Concordance between Conners-P and Conners-SR .................................... 90

  8.9 Concordance between Conners-T and Conners-SR .................................... 91

  8.10 IC Performance: Cancellation and Restraint .......................................... 92

    8.10.1 Cancellation ......................................................................................... 92

    8.10.2 Restraint ............................................................................................. 92

  8.11 Relationship between SST Performance and Conners 3 Ratings .............. 92

  8.12 Relationship between the number of ADHD Symptoms and IC Performance ... 93

    8.12.1 Cancellation ......................................................................................... 93

    8.12.2 Restraint ............................................................................................. 93

  8.13 Is IC performance related to ADHD status? ............................................. 93

    8.13.1 Cancellation ......................................................................................... 94
List of Tables

Table 1. Participant Characteristics (Chapter 2)

Table 2. Accuracy on Go Trials: Mean Percent Correct (standard deviation)

Table 3. Participant Characteristics (Chapter 3)

Table 4. Accuracy and Variability of Go Responses (Means and standard deviations)

Table 5. Regression Table: Significant Predictor: Age at Injury (all p’s <0.05)

Table 6. Participant Characteristics (Chapter 4)

Table 7. Summary of Group Differences across the Conners-P, Conners-T, and Conners-SR

Table 8. Parent-Teacher Discrepancy Ratings (Means and standard deviations)

Table 9. Parent-Self-Reports Discrepancy Ratings (Means and standard deviations)

Table 10. Teacher-Self-Reports Discrepancy Ratings (Means and standard deviations)

Table 11. Summary of Discrepancy Ratings

Table 12. Correlation Coefficients (r) between SST Performance and Ratings

Table 13. Regression Results
List of Figures

Figure 1. Cancellation and Restraint Models of the Stop Signal Task (with and without rewards)

Figure 2. Mean (standard error, SE) SSRT in the Cancellation Version of the SST

Figure 3. Mean (SE) Percent Inhibition in the Cancellation Version of the SST

Figure 4. Mean (SE) MRT in the Cancellation Version of the SST

Figure 5. Mean (SE) SDRT in the Cancellation Version of the SST

Figure 6. Mean (SE) Percent Inhibition in the Restraint Version of the SST

Figure 7. Mean (SE) SSRT in the Restraint Version of the SST

Figure 8. Mean (SE) MRT in the Restraint Version of the SST

Figure 9. Mean (SE) SDRT in the Restraint Version of the SST

Figure 10. Mean (SE) Percent Inhibition across Groups and Reward Conditions, Cancellation

Figure 11. Mean (SE) SSRT across Groups and Reward Conditions, Cancellation

Figure 12. Mean (SE) MRT across Groups and Reward Conditions, Cancellation

Figure 13. Mean (SE) Percent Inhibition across Groups and Reward Conditions, Restraint

Figure 14. Mean (SE) SSRT across Groups and Reward Conditions, Restraint

Figure 15. Mean (SE) MRT across Groups and Reward Conditions, Restraint

Figure 16. Cancellation and Restraint Models of the SST
Figure 17. Conners-P Ratings across Groups

Figure 18. Conners-T Ratings across Groups

Figure 19. Conners-SR Ratings across Groups
List of Appendices

Appendix 1. TBI severity coding scale. Severity was coded utilizing this novel scale that incorporated GCS scores and injury information available on all pre-surgical CT reports.

Appendix 2. A) Injury severity characteristics, B) TBI and S-ADHD Group Characteristics
Chapter 1
Introduction

Inhibitory control (IC) is a key component of executive functioning involved in the self-regulation of behaviour, and it interacts with other executive-cognitive processes such as working memory to guide adaptive interactions with the environment (Fuster, 2002; Logan, 1994). The IC construct itself is not unitary, but involves distinct processes such as cancellation and restraint. Cancellation refers to inhibiting or stopping an already initiated or ongoing action; for example, stopping the swing of a baseball bat as the pitch leaves the strike zone. Restraint refers to withholding or preventing a prepotent response before it is initiated. Typical “first-person shooter” video games often involve this type of IC, requiring gamers to shoot at one type of target (the bad guy), but restrain from shooting at another (innocent bystanders).

Deficits in IC are reflected not only in performance on neurocognitive tests of cancellation and restraint IC, but also in behaviours such as inattention, impulsivity, and hyperactivity. In children, these types of behaviours are observed by parents in the context of family and home, and by teachers in the context of peers, playground, and classroom. Self-report ratings of inattention, impulsivity, and hyperactivity reveal how a child perceives his/her IC (dis)abilities, and any discrepancies between child and informant ratings provide some information about the child’s deficit awareness.

Acts of IC do not occur within a motivational vacuum. Slamming on the brakes in response to a red light is done to avoid a car accident or a ticket. For a child, acting in a controlled manner may generate a reward in the form of praise or a tangible reward such as a cookie. Indeed, behavior is often performed in order to avoid a punishment or to gain a reward. But how does reinforcement affect IC? At a developmental level, IC and reward systems are both immature in children (e.g.,
Geir & Luna, 2009; Rubia, Smith, & Taylor, 2007). At a behavioral level, reinforcement can both facilitate and hinder IC, depending on the strength and direction of the reinforcer. At a neural level, rewards may directly influence the interaction between IC and motivational centers in the brain, or may alter the activity in other brain centers that integrate inhibition and motivation (Padmala & Pessoa, 2010). Because cancellation and restraint have different measurement parameters, developmental trajectories, and neurological underpinnings (see below; Chevrier, Noseworthy, & Schachar, 2007; Konishi, Nakajima, Uchida, Sekihara, & Miyashita, 1998; Konishi et al., 1999; Johnstone et al., 2007; Williams, Ponesse, Schachar, Logan, & Tannock, 1999), different forms of IC may be differently modifiable by reward across development.

Poor IC has been documented across a wide range of neurodevelopmental and acquired disorders of childhood, but a recent literature review suggests that IC may differ in degree and in kind across disorders (see Dennis, Sinopoli, Fletcher, & Schachar, 2008). Because the literature review compared disorders in different studies using different IC paradigms and measures, important questions remain to be investigated: Do childhood disorders with IC problems differ in the magnitude of IC difficulties or in the type of deficit? Is the reason for similar IC problems in two groups superficial, or does it arise from different basic mechanisms?

The objective of this dissertation was to examine the broader questions about IC posed above in children and adolescents with traumatic brain injury (TBI) who have developed attention-deficit/hyperactivity disorder (ADHD) subsequent to the injury (secondary ADHD, S-ADHD). Although 10-19 % of children with TBI exhibit a pre-injury diagnosis of ADHD (Gerring et al., 1998; Max et al., 2004; Max et al., 1998; Slomine et al., 2005), approximately 15-20% of survivors develop de novo symptoms of ADHD (Gerring et al., 1998; Gerring et al., 2000;
Herskovits et al., 1999; Max et al., 2005a; Max et al., 2005b; Slomine et al., 2005; Yeates et al., 2005). Brown and colleagues (1981) published the first account of S-ADHD, describing a hyperkinetic syndrome accompanied by a disinhibited state and impulsiveness in a subset of severely-injured pediatric patients 2 years post-TBI. Subsequent studies have revealed that S-ADHD is the most common psychiatric disorder in children with TBI (Max et al., 1998), manifesting as early as 6 months post-injury and persisting into the chronic phase of recovery (Levin et al., 2007; Max et al., 2005a, 2005b).

Inattentive and hyperactive/impulsive symptoms of S-ADHD peak at 6 months post-injury, with greater and more frequent changes in hyperactive/impulsive symptoms over time, resulting in the inattentive subtype being most prominent in this population (Levin et al., 2007). A number of pre-injury variables have been found to be significantly associated with the emergence of S-ADHD, including lower socioeconomic status, greater psychosocial adversity and adaptive functioning, poorer family functioning, and poorer socialization and communication skills (Gerring et al., 1998; Levin et al., 2007; Max et al., 2004; Max et al., 2005a, 2005b). Children who develop S-ADHD also tend to develop new-onset, persistent personality changes, exhibit greater affective lability and aggression, and experience the emergence of de novo oppositional defiant/conduct/disruptive behaviour disorders (Gerring et al., 1998; Levin et al., 2007; Max et al., 2004; Max et al., 2005a, 2005b). On the other hand, diagnosis of S-ADHD is not related to age at assessment, age at injury, severity of injury, sex, number of lesions, lesion area and/or volume (Gerring et al., 2000; Herskovits et al., 1999; Levin et al., 2007; Max et al., 1998; Max et al., 2004; Max et al., 2005a, 2005b). There is some evidence of a relationship between lesion location and diagnosis in the acute phase of injury, specifically damage to the orbitofrontal gyrus (Max et al., 2005a), basal ganglia (especially the putamen), and thalamus (Herskovits et al., 1999; Gerring et al., 2000), yet other studies have failed to show a relationship between lesion
location and S-ADHD diagnosis, especially in the chronic phase of recovery (Max et al., 2004; Max et al., 2005b).

Previous research has mainly focused on elucidating the factors that predict the onset of S-ADHD; however the meaning of an S-ADHD diagnosis remains unclear. One important area of study is whether S-ADHD is an acquired condition that reflects abnormalities much like those present in children with developmental or primary ADHD (P-ADHD). P-ADHD is associated with IC deficits that range across a number of tasks, including cancellation and restraint (e.g., Schachar, Logan, Robaey, Chen, Ichowicz, & Barr, 2007; Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005). Poor IC is a well-studied deficit in P-ADHD thought to reflect frontostriatal dysfunction (e.g. Aron & Poldrack, 2005), and is a candidate endophenotype for the disorder (Crosbie, Perusse, Bar, & Schachar, 2008). If children with S-ADHD present with IC difficulties, are they similar to the prototypical IC deficits of children with P-ADHD, and are deficits apparent in both cancellation and restraint paradigms? If so, does this suggest similarity in underlying processes/mechanisms between S-ADHD and P-ADHD? Alternatively, do children with S-ADHD exhibit a “pastel” version of P-ADHD or a fundamentally distinct IC profile?

The question of IC abilities in youths with S-ADHD is both urgent and problematic. Deficits in this group are poorly characterized. Compared to children with TBI without ADHD, children with S-ADHD exhibit greater impairments in attention (Slomine, Salorio, Grados, Vasa, Christensen, & Gerring, 2005) but similar cancellation IC indicating an impairment only relative to healthy controls (Konrad et al., 2000a; Konrad et al., 2000b). On the other hand, poorer cancellation IC has been documented in children with both a severe TBI and S-ADHD diagnosis relative to children with TBI only and healthy controls (Schachar et al., 2004), suggesting that those with greater injury severity and a de novo diagnosis of ADHD are more susceptible to
disinhibition than those with less severe injuries. To date, no study has examined restraint IC in children with S-ADHD. Because difficulties with IC tend to resolve by 2 years post-TBI (Leblanc et al., 2005), a major problem with the Konrad et al. (2000a, 2000b) studies is that they included children in the in the acute and chronic phases of recovery. Thus further studies are warranted to examine the long-term influences of TBI and S-ADHD on both cancellation and restraint IC, and how reward may impact each of these processes.

To address the issues outlined above, IC on neurocognitive tests of rewarded and unrewarded cancellation and restraint tasks were examined in a S-ADHD group and in three other carefully selected groups. Typically developing children and adolescents formed a healthy control group that was used, first, to chart previously unstudied age-related changes in cancellation and restraint under conditions of reward, and, second, to provide benchmarks of typical development for the clinical comparison groups. Children with TBI without a diagnosed S-ADHD (TBI group) allowed the study of the effects of childhood TBI on IC processes, independent of clinical ADHD status. While not all children with TBI develop S-ADHD, it remains unclear whether children with S-ADHD exhibit a similar neurocognitive phenotype to children with TBI without a diagnosis of ADHD, despite the expression of behaviorally significant attention problems. If children with TBI are shown to exhibit similar IC deficits as those with S-ADHD, then the link between IC dysfunction and specific psychiatric syndromes like ADHD may need to be re-examined. The P-ADHD group included children and adolescents with the primary, developmental form of the attention disorder. Carefully parsing similarities and differences in both neurocognitive and clinical features of S-ADHD and P-ADHD examines the question of whether deficits in IC are qualitatively and quantitatively different, as well as whether or not these deficits arise from similar mechanisms.
In addition to exhibiting IC deficits, children with P-ADHD also respond abnormally to rewards (e.g., Haenlein & Caul, 1987; Sonuga-Barke, 2002). How rewards affect IC in this population is not yet clear, with methodological confounds complicating the interpretation within and across studies. Very little is known about how rewards affect cognition and behavior (specifically IC) in children with S-ADHD. There is some evidence of a delay aversion in children with S-ADHD (Konrad et al., 2000a); a deficit thought to be related to abnormalities in the mesolimbic reward system (see Sonuga-Barke, 2002). Only one study has examined the effects of reward on cancellation IC in this population, revealing that rewards improve the latency to inhibit responses despite persisting impairments relative to controls (Konrad et al., 2000b). However, as mentioned previously, the Konrad et al. (2000a, 2000b) studies included children in both the acute and chronic phase of injury, tempering the interpretation of these results. To date, no study has articulated similarities and differences in how S-ADHD and P-ADHD groups respond to rewards. Comparisons between groups on rewarded IC tasks would further delineate S-ADHD from P-ADHD, and would show whether reward effects are independent or enmeshed with disorder-specific IC deficits. If there is indeed an abnormality in reward processing in ADHD, interventions that utilize reward as a motivational strategy for the adjustment of behaviour may need to be modified in order to account for these difficulties.

With the general objective of understanding S-ADHD in mind, the dissertation proceeded to execute a series of steps. The first two steps involved solving a pair of methodological problems: the comparability of different IC tasks and the issue of how to reward inhibition but not response execution (“going”). While there is consensus that the stop signal task (SST) and the go/no-go task (GNG) both measure IC (the former measuring cancellation, the latter, restraint), attempts to ascribe these to different underlying processes are confounded by differences in methodology. The SST mixes sensory modalities, with a visual go signal (to respond to) and an auditory stop
signal (signaling cancellation), while the GNG task involves a visual go signal and a visual no-go signal for restraint. Thus, IC in the GNG task may be confounded by the demands that the task places on selective attention rather than on IC (Aron & Poldrack, 2005; Rubia, Smith, Brammer, & Taylor, 2003). Schachar and colleagues (2007) addressed this problem by creating a restraint version of the SST to address cancellation and restraint in a common methodology with a common metric of inhibition (stop signal reaction time, SSRT). STEP 1 involved the adaptation of this methodology for the dissertation studies.

One difficulty in studying IC and reward is that many previous studies rewarded both response execution and IC, or used both reward and punishers within the same paradigm, effectively confounding the motivational manipulation. As a result, it is not possible to identify which operation are the targets of reinforcement. Further, the addition of both rewards and punishers in a single paradigm has limited the comprehension of the effect of reward on IC. STEP 2 involved creating a paradigm where only successful cancellation and restraint were rewarded, and where response execution and failed inhibition trials had no overt motivational consequences.

STEP 3 involved collecting benchmark data for how IC and reward interact in typically developing children and adolescents. Chapter 2 examined the effect of increasing reward magnitude (no reward, low reward, high reward) on restraint and cancellation in healthy participants aged 7-17 years old. The specific aims of the study were to show how reward improved IC cancellation and IC restraint in typically developing children and adolescents, and given the immaturity of both reward and inhibition systems, to chart age-related differences in how rewards affect IC from childhood through adolescence.

Having demonstrated the appropriateness of the new IC reward paradigms for typically developing children and adolescents, the dissertation progressed onto STEP 4, which involved
the administration of the restraint and cancellation versions of the SST (reward and non-reward conditions) to the four carefully selected groups described above (controls, TBI, S-ADHD, and P-ADHD). The results of those comparisons are described in Chapter 3. The first specific aim was to delineate TBI from S-ADHD. Approximately 10-20% of children with TBI were predicted to exhibit symptoms consistent with a S-ADHD diagnosis, and these participants were expected to exhibit poorer IC on the SST measures of cancellation and restraint relative to those with TBI only or controls. Participants in the P-ADHD group were expected to exhibit poorer IC relative to controls, with rewards potentially improving this performance. In a direct comparison of the ADHD groups, similar IC performance may reflect similarities in underlying mechanisms of dysfunction, and would show that children with TBI without S-ADHD are behaviorally distinct from TBI without S-ADHD. These findings would have implications for the assessment and prediction of deficits following TBI, and may indicate the need for a similar treatment approach for children with S-ADHD as is established for children P-ADHD. However, stimulant medication that is effective in treating the developmental form of the disorder is less effective in controlling S-ADHD (Jin & Schachar, 2004), suggesting potential differences between the disorders that may be apparent at the behavioral level as well. Differences in IC between the ADHD groups would suggest that S-ADHD is not merely an acquired form P-ADHD despite overlap in clinical expression, and would suggest the need for further delineation of deficits in the S-ADHD group and interventions targeted to their specific dysfunction.

STEP 5 involved the ecology of behavioral IC (inattention, impulsivity, and hyperactivity) at home and at school and its relation to IC on the cancellation and restraint tasks. Children and adolescents are surrounded by people who form constant impressions of their IC and attentional abilities. Parents of children with IC deficits can report on home and leisure behavior in the family, while teachers see these children with peers in the classroom and playground.
Considerable debate exists in the literature about self-knowledge of deficits in typically developing children and in those with TBI, mainly due to the dearth of information on this topic. After TBI, adults exhibit a lack of awareness of the consequences of their injury, with incongruence between self and other ratings of behavioral and affective functioning (e.g., Bivona et al., 2008; Hart, Seignourel, & Sherer, 2009; Prigatano, 1996). Similarities and differences between the ways in which parents and teachers rate the IC behaviour of children with S-ADHD relative to children with P-ADHD remains to be explored, and no study to date has assessed how children with S-ADHD rate their own behaviours.

Chapter 4 addressed three specific aims related to the issues presented above: 1) how do parents, teachers, and the children themselves rate inattention, hyperactivity/impulsivity, and DSM-IV-TR ADHD symptoms? 2) What are the levels of rater concordance and to what extent are the three raters endorsing the same symptoms? 3) How are behavioral ratings related to neurocognitive measures of restraint and cancellation IC? These questions are intrinsically interesting and provide missing information about how children with S-ADHD behave in the real world and about whether children with TBI have insight into their level of inattention, impulsivity, and hyperactivity. Overall, the study in Chapter 4 is a natural extension of the previous studies, as it provides information on other aspects of behaviour in children with S-ADHD and also describes the ecological congruence between the IC behaviors and neurocognitive measures of IC.

For all study groups, ratings of behavioural IC were defined as behaviours that reflected poor inhibition on the Conners 3rd Edition (Conners 3; Conners, 2008) multi-informant rating scales. Subscales of interest were those that measured inattention, hyperactivity/impulsivity, and DSM-IV-TR ADHD symptom criteria. The Conners 3 was chosen as an appropriate tool to assess IC
behaviors reported by parents, teachers, and the participants themselves. It assesses ADHD behaviours such as inattention, hyperactivity, and impulsivity, as well as associated behaviours such as oppositionality and academic difficulties. Importantly, it includes items that correspond to the DSM-IV-TR ADHD subtypes of hyperactivity/impulsivity and inattention, so that ADHD symptoms can be measured both quantitatively and categorically. All scales are easy to administer and score and the results can be easily profiled for each participant. The normative sample that the scale is based on is large, with ratings taken from over 8000 individuals in over 200 rural and urban sites in Canada and the US, including individuals from different social classes, ethnicities, ages and gender. Moreover, the scale yields moderate to high validity and reliability coefficients (Conners, 2008).

STEP 6 involved reflecting on some of the more general questions arising from the three studies. The general discussion of these questions is in Chapter 5, and includes the following issues: the developmental course of IC and reward processes; how IC problems manifest across a range of childhood disorders and the interpretation of IC behavioral phenotypes and IC neurocognitive phenotypes; and the ecological validity of IC tasks. Chapter 5 ends with the suggestion of some avenues for future research, limitations of the dissertation studies, and a return to the question driving the dissertation: what, if anything is unique about IC in S-ADHD and how does it differ from P-ADHD?
Chapter 2
Reward Improves Cancellation and Restraint Inhibition Across Childhood and Adolescence

Inhibitory control (IC) is a regulatory mechanism that facilitates adaptive interactions with the environment by aligning current thought and action with priorities of changing goals and stimuli (Logan, 1994). IC involves rapid, voluntary, internally generated acts that oppose excitatory (“go”) signals to respond, and interacts with other adaptive processes such as performance monitoring and error adjustment (Logan, 1994; Verbruggen & Logan, 2008). Motor inhibition functions include (but are not limited to) withholding or restraining a response before it is initiated, and canceling or stopping a prepotent, ongoing response. Reinforcement of these processes may promote favourable outcomes (successful inhibition) or prevent negative outcomes (failed inhibition). In the present study, the effects of reward on the IC functions of cancellation and restraint were examined in typically developing children and adolescents.

Like other regulatory mechanisms such as working memory or performance monitoring, IC improves with development. The latency to cancel a response becomes faster throughout childhood and adolescence, with only limited slowing in older adults (Williams, Ponesse, Schachar, Logan, & Tannock, 1999). Restraint inhibition, in contrast, peaks around age 12 years (Levin, Culhane, Hartmann, Evankovich, & Mattson, 1991). Age-related improvements in both types of IC are thought to reflect maturation of frontostriatal circuitry (Liston et al., 2006; Rubia, Smith, & Taylor, 2007) which includes non-linear decreases in cortical gray matter accompanied by linear increases in myelination (Giedd et al., 1999; Gogtay et al., 2004; Sowell, Thompson, Holmes, Jernigan, & Toga, 1999).
Acts of IC occur within a motivational context of reward, non-reward, and punishment. As with substrates of the IC system, the neural substrates of the reward system, including dopaminergic networks, are also immature in children and adolescents (Geir & Luna, 2009; Meng, Ozawa, Itoh, & Takashima, 1999). What is not understood is how reward modulates different forms of IC throughout development. In typically developing children, the effect of reinforcers on cancellation and restraint have been variously reported as facilitatory (Desman, Petermann, & Hampel, 2008; Huang-Pollock, Mikami, Pfiffner, & Burnett, 2007; Kohls, Peltzer, Herpertz-Dahlmann, & Konrad, 2009; Scheres, Oosterlaan, & Sergeant, 2001), impairing (Wodka et al., 2007), or as having no effect on either process (Iaboni, Douglas, & Baker, 1995; Oosterlaan & Sergeant, 1998; Slusarek, Velling, Bunk, & Eggers, 2001). It may be that typically developing children perform at optimal levels with very minimal levels of reinforcement (Slusarek et al., 2001), such that any further incentives may have null effects or result in slowing response execution to ensure successful inhibition.

Although centrally located neural substrates such as the ventrolateral prefrontal cortex or basal ganglia may be important for both cancellation and restraint (Dillon & Pizzagalli, 2007; Leung & Cai, 2007; Xue, Aron, & Poldrack, 2008), evidence supports the idea of distinct pathways mediating each form of inhibition. Specifically, cancellation may engage a predominately bottom-up, rapid control system involved in the detection of salient sensory stimuli (i.e., the stop signal; e.g., Chevrier, Noseworthy, & Schachar, 2007; see Downar, Crawley, Mikulís, & Davis, 2002), while restraint may be mainly dependent on a top-down system driven by regulatory centers in the dorsal aspects of the prefrontal cortex (e.g., Kelly et al., 2004). Given that restraint and cancellation differ in their measurement (see below), developmental trajectory, and neurological underpinnings, then the way each is modifiable by reward might be dissociable as well.
Understanding the developmental effects of reward on inhibition has been clouded by a set of methodological problems. Some studies lack a neutral reward condition (Huang-Pollock et al., 2007; Iaboni et al., 1995; Oosterlaan & Sergeant, 1998; Slusarek et al., 2001), or confound the influence of both rewards and punishments on response execution and IC processes (Shanahan, Pennington, & Willcutt, 2008; Slusarek et al., 2001). One study showed that rewards and punishments ameliorated IC as well as feedback about the “correctness” of the response (Desman et al., 2008), and another showed that reinforcement decreased the latency to cancel a response by only 5-13 milliseconds (Scheres et al., 2001). The Kohls et al. (2009) study of rewarded restraint involved children, leaving developmental questions about adolescence unexplored.

To date, no study has compared how rewards affect restraint and cancellation inhibition in the same study and with methodologically comparable paradigms. Cancellation inhibition is often measured with the stop signal task (SST; Logan & Cowan, 1984; Logan, 1994). The SST consists of a primary visual choice reaction time task (responding quickly to one of 2 “go signals”), and a secondary task where participants are instructed to stop responding to go signals when the auditory “stop signal” occurs (Logan & Cowan, 1984; Logan, 1994). The stop signal is presented at various delays following the onset of the go signal such that the response is cancelled rather than withheld. The latency of inhibitory control (i.e., the stop signal reaction time, SSRT) is estimated as a measure of the efficiency of inhibitory control (Logan, 1994).

Restraint inhibition is typically measured with the go/no-go (GNG) task in which participants respond as quickly as possible to a go stimulus and inhibit their responses to a no-go stimulus, each occurring on separate trials. Responses to the no-go stimulus (commission errors) index failed inhibitory control.
The present study compared cancellation and restraint inhibition in comparable experimental paradigms in typically developing children and adolescents, and analyzed whether these forms of IC were modifiable by reward. In addressing the methodological criticisms of previous studies, only successful IC trials were rewarded, and these effects were compared to performance during a neutral, non-reward condition. To make task procedures comparable over different inhibition operations, we employed the cancellation and restraint versions of the SST (Schachar et al., 2007). Critics of the GNG task argue that because a similar modality is required to discriminate between go and no-go stimuli (i.e., both are visual cues occurring on separate trials), the act of inhibition may be confounded with the process of selective attention, so that the demands on IC may be weaker in the GNG task than in the SST (Aron & Poldrack, 2005; Rubia, Smith, Brammer, & Taylor, 2003). To make the SST and GNG tasks methodologically comparable, Schachar and colleagues (2007) developed a restraint (i.e., GNG) version of the SST where the delay between the onset of the go and stop signal is zero. Thus, the concurrent presentation of the go and stop signals interrupts the preparation of a response rather than interrupting an ongoing response (Schachar et al., 2007). In this manner, prepotent responding to the go signal is withheld, similar to the GNG task. Importantly, the no-go signal in the restraint version of the SST is an auditory tone, which minimizes the task demands on selective attention.

We predicted that rewards, which promote approach and consumption (Schultz, 2006), would improve IC across tasks. Given the immaturity of both the reward and inhibition systems, we hypothesized that there would be age-related differences in the way in which rewards affect inhibition processes, with greater reward-induced facilitation of IC apparent in the adolescent than in the child group.
1 Method

1.1 Participants

We recruited 66 healthy children and adolescents aged 7 to 17 years old through flyers and community advertisements. Brief telephone interviews were conducted at recruitment with each participant’s parent to exclude participants with neurological or psychiatric disorders, mental retardation, learning disabilities, or sensory or motor impairments. Nine participants cancelled or missed their appointments. To confirm that our participants were typically developing children and adolescents with no significant behavioural impairments, parent ratings of each participant’s behaviour were assessed with the Conners 3rd Edition Rating Scales (Conners 3; Conners, 2008). The Conners 3 assess behaviours and symptoms of attention-deficit/hyperactivity disorder (ADHD) as well as other difficulties related to inattention and/or hyperactivity such as executive dysfunction and oppositionality. Scales of interest on the Conners 3 included the Diagnostic and Statistical Manual of Mental Disorders, 4th edition text revision (DSM-IV-TR; American Psychological Association, 2000) Scales, which assess behaviours related to ADHD, conduct disorder, and oppositional defiant disorder, and DSM-IV-TR Symptom Counts which reflect the criteria needed to make a diagnosis of either of these disorders. Participant data were excluded from further analyses if parent ratings revealed significant elevations (T-score of 65 or greater) on the DSM-IV-TR Scales and met criteria for any disorder on the DSM-IV-TR Symptom Counts. Based on these criteria, 13 participants were excluded. The remaining 44 participants (22 female, 22 male; mean age, 12.44 years) were divided into two age groups: a TEEN group (N=22, aged 13 to 17 years), and a CHILD group (N=22, aged 7 to 12 years).

All participants were administered the Vocabulary and Matrix Reasoning subscales of the Wechsler Abbreviated Scale of Intelligence (WASI), and overall score was used to exclude
participants with IQ scores under 75. Demographic information was recorded at recruitment, including household income, parental occupation, and parental education. The socioeconomic status (SES) of each participant was computed using the Hollingshead Four-Factor Index (Hollingshead, 1975), which includes parental occupation and education. Family Hollingshead scores were calculated for each participant by averaging the SES scores of both parents. Family SES data was based on data from one parent when this was the only information available.

Prior to testing, informed consent was obtained from each parent, and assent was obtained from each participant. This experiment was conducted with approval of the Research Ethics Boards at the Hospital for Sick Children and the University of Toronto.

1.2 Stop Signal Tasks

The SST is based on a formal model that conceptualizes performance as a race between go processes (triggered by the go signal) and stop processes (triggered by the stop signal; Logan & Cowan, 1984; Logan, 1994; Verbruggen & Logan, 2008). As go and stop processes “race” against each other, the process that “wins” the race determines the outcome (Logan & Cowan, 1984; Logan, 1994). Because inhibition is unobservable, the race model allows for the measurement of the latency of IC (i.e., the SSRT) and the factors that affect the probability and latency of stopping the ongoing response (Logan, 1994).

Two versions of the SST were used to measure canceling and restraining a prepotent response (see Figure 1; Logan, 1994; Schachar et al., 2007). In both versions, the primary task involved the computerized presentation of one of two possible go signals (an X or an O) on each trial. Participants were instructed to respond to these stimuli as quickly as possible by making the appropriate button press on a handheld controller. The auditory stop signal (a 1000 Hz tone emitted from computer speakers) occurred randomly on 25% of trials, and participants were
instructed to inhibit their responses to the go signal when they heard this tone. Logan (1994) reasoned that presenting the stop signal on only 25% of trials ensures that enough data on IC can be collected while minimizing expectation for the stop signal, which can result in slower go reaction time on the go trials as a strategy to increase the probability of inhibition.

In the restraint (GNG) version of the task, the stop signal was presented at the same time as the go signal. Because the delay between the onset of the go and stop signal is zero, the response is inhibited during the preparation of the response and before being executed (Schachar et al., 2007). In the cancellation version, the stop signal was presented at various delays following the go signal to allow for the interruption of an ongoing response. The initial delay period between the presentation of the go and stop signal was set at 250 milliseconds and was adjusted dynamically based on the participants’ performance (Logan, 1994). Using this dynamic tracking of performance, the probability of inhibition on stop signal trials should converge on approximately 50%, regardless of whether or not participants slowed their go signal reaction time as a strategy to increase successful inhibition (Logan & Cowan, 1984; Logan, 1994).

The initial presentation of either version of the SST was a neutral or non-reward (NO) condition, where participants received no specific feedback about performance. Rather, at the end of each block, the words “Good work! Press a button to keep going” appeared in the middle of the screen. Following the NO condition, the participants were told that they would perform the task for a second time where they could receive 2 points each time they successfully inhibited their responses (low reward condition, LOW). They were also told that they would be performing the task for a third time, where they could win 10 points for each successful inhibition trial (high reward condition, HIGH), and if they could acquire 400 points by the end of the testing session, they would receive a prize (a $10 gift certificate for the movies). Bonus points were offered for
pushing the buttons as quickly as they could when they saw the go stimuli. Although no bonus points were actually rewarded, this instruction was introduced to reduce the tendency for participants to slow their go RT to ensure successful inhibition (and thus win more points).

Points earned in the LOW and HIGH conditions were immediately represented on the screen in a visual analog scale (the scale was left empty in the NO condition). At the end of each block, a message appeared in the middle of the screen updating participants of how many points they had just won in that specific block (e.g., “You won 10 points.”). Points earned were tallied by the examiner, and total scores (and the prize) were revealed at the end of the testing session. The reward conditions were always presented in the same ascending order of magnitude (NO, LOW, HIGH).

All participants completed both the cancellation and restraint (GNG) versions of the SST three times in order to examine performance under three different reward conditions (NO, LOW, HIGH). Each reward condition consisted of 120 trials divided into 5 blocks of 24 trials each, with the stop signal randomly occurring on 30 trials. The first block in each task was a practice block, data from which were not utilized in subsequent analyses. The order of administration of each version was counterbalanced, with a break between, during which other tasks were administered.

1.3 Statistical Analyses

Age group differences in WASI and SES scores were examined with an analysis of variance (ANOVA), and chi-squared tests compared group differences in sex and handedness.

Consistent with previous studies (Band, van der Molen, & Logan, 2003; Schachar, Levin, Max, Purvis, & Chen, 2004; Shuster & Toplack, 2009), participants were excluded from the data analyses if the following conditions were met: less than 66% accuracy on go trials, mean go
reaction time (MRT) less than 100 milliseconds, and for the cancellation version only, percent inhibition (reflecting the amount of responses that were inhibited) less than 12.5% or greater than 87%. Based on these criteria, one participant was excluded from subsequent analyses of the cancellation and restraint data.

Dependent variables of interest in both versions of the SST (and across reward conditions) were related to response execution and IC. Response execution measures included MRT, standard deviation of go reaction time (SDRT), and accuracy on go trials (percent correct). IC measures included SSRT and percent inhibition. SSRT was estimated via the integration procedure (Logan, 1994). First, the go reaction times for trials in which there were no stop signals presented were collapsed and rank ordered. Then, the go reaction time that corresponded to the probability of inhibition was determined, and the SSRT was estimated by subtracting the mean delay from this new “integrated go reaction time”. For instance, if a participant inhibited 55% of their go responses when the stop signal was presented, then the 55th slowest go reaction time was used as the integrated go reaction time measure. This method can be used to estimate SSRT for both cancellation and restraint versions of the SST (Schachar et al., 2007).

Performance on each task was compared separately for each dependent variable utilizing repeated measures ANOVA, with reward condition as the within-subjects factor (NO, LOW, HIGH), and group (CHILD, TEEN) and order (cancellation administered first, restraint administered first) as the between-subjects factors. Repeated measures ANOVAs were also utilized to compare MRT and SSRT between the restraint and cancellation tasks separately for each reward condition. The only significant finding from analyses of sex differences was that females exhibited more variable performance than males on the cancellation task (data not shown), so we did not include sex in any further analyses.
2 Results

2.1 Participant Characteristics

Table 1 describes the participant characteristics. No participants were excluded based on WASI scores below 75. Although there was a significant difference in IQ between groups (F(1, 42)=6.08, p=0.018), mean IQ scores were within the normal range. Family SES scores and handedness were similar between groups, as was the gender distribution.

2.2 Cancellation

Approximately 50% of inhibition trials were successfully inhibited across reward conditions, and there was no significant effect of age group on percent inhibition, confirming that the tracking algorithm was successful at limiting the probability of inhibition to approximately 0.5 across reward conditions and across participants.

2.2.1 Reward Effects

Repeated measures ANOVAs revealed a significant main effect of reward on SSRT (linear effect, F(2, 78)=3.770, p=0.027; see Figure 2) and percent inhibition (linear effect, F(2, 78)=6.116, p=0.003; see Figure 3). Conversely, reward did not alter MRT (see Figure 4), SDRT (see Figure 5), or the accuracy of responses on go trials (see Table 2). Therefore, as reward magnitude increased, the latency to cancel a response decreased, but the probability of inhibition also decreased. The speed and variability of response execution and primary task accuracy were not altered by reward. Across reward conditions, there were no significant interactions between any of the dependent variables and age, suggesting that reward did not alter performance differently across age groups.
2.2.2 Age Effects

There were significant main effects of age group on the percentage of accurate responses on go trials (F(1, 39)=12.569, p=0.0011), MRT (F(1, 39)=11.102, p=0.002), SDRT (F(1, 39)=11.000, p=0.002), and SSRT (F(1, 39)=7.698, p=0.008). Participants in the TEEN group exhibited faster and less variable go responses, were more accurate when responding to go stimuli, and exhibited faster latencies to cancel a response when encountering a stop signal.

2.2.3 Order Effects

There were no main effects of task order on go task accuracy, MRT, SDRT, or SSRT, nor were there any significant interactions between these variables and order across reward conditions. There was, however, a main effect of order on percent inhibition (F(1, 39)=8.896, p=0.005) and an interaction between this variable and inhibition task order (F(2, 78)=5.005, p=0.009), revealing that participants cancelled responses to a greater degree when the cancellation version was administered first, especially in the no reward condition. There were no significant interactions between any of the other dependent variables, task order, and age group across any of the reward conditions.

2.3 Restraint

2.3.1 Reward Effects

There was a main effect of reward on the percentage of responses inhibited (linear effect, F(2, 78)=4.386, p=0.016; see Figure 6), indicating fewer errors of commission as rewards increased. Reward also decreased the latency of SSRT (linear effect, F(2, 78)=9.378, p<0.001; see Figure 7), decreased the percentage of correct go responses (linear effect, F(2, 78)=3.368, p=0.04; see Table 2), and decreased MRT (linear effect, F(2, 78)=5.559, p=0.005; see Figure 8). Reward did not affect SDRT (see Figure 9). Thus, increasing reward magnitude helped restraint IC by
increasing the percentage of inhibited responses and decreasing inhibition speed. Reward also
decreased the latency to execute a response while also decreasing the accuracy to respond to the
go signal, suggesting a speed-accuracy tradeoff that did not influence the variability of
responses. There were no significant interactions between any of the dependent variables and age
across reward conditions, suggesting similar effects of reward across age groups.

2.3.2 Age Effects

There were significant main effects of age group on all response execution measures: accuracy of
go responses (F(1, 39)=13.453, p=0.001), MRT (F(1, 39)=18.062, p<0.001), and SDRT (F(1,
39)=11.544, p=0.002). Compared to children, adolescents exhibited faster, less variable and
more accurate go responses. There was no significant main effect of age group on percent
inhibition, but adolescents were faster at inhibiting their responses relative to children (SSRT;
F(1, 39)=19.246, p<0.001).

2.3.3 Order Effects

Order of task administration did not influence MRT, SDRT, or SSRT across reward conditions.
There was an interaction effect between order and percent inhibition (F(2, 78)=3.518, p=0.034)
revealing that fewer responses were restrained in the NO condition and more responses were
restrained in the HIGH condition if the cancellation version was administered first. There was
also a main effect of order on go task accuracy (F(1, 39)=4.800, p=0.035), showing better
accuracy on the go task if the restraint version was administered first. There were no significant
interactions between any of the dependent variables, order, and age group across any of the
reward conditions.
2.4 Task Comparisons

MRT was faster in the restraint version across reward conditions (linear effects; NO, $F(1, 39)=4.803$, $p=0.034$; LOW, $F(1, 39)=25.658$, $p<0.001$; HIGH, $F(1, 39)=19.958$, $p<0.001$). However, this effect in the NO condition may have been driven by the order of task administration: MRT was faster in the restraint version only if the cancellation task was administered first, but was slower when the restraint version was administered first (interaction effect; $F(1, 39)=14.564$, $p<0.001$). Conversely, SSRT was faster in the cancellation version of the SST across reward conditions (linear effects; NO, $F(1, 39)=117.336$, $p<0.001$; LOW, $F(1, 39)=226.802$, $p<0.001$; HIGH, $F(1, 39)=137.360$, $p<0.001$). There was a significant interaction between age group and SSRT in the NO condition ($F(1, 39)=6.768$, $p=0.013$), suggesting that in the absence of reward, the finding of faster SSRT in the cancellation relative to restraint version was greater only in the CHILD group. Participants in the TEEN group exhibited shorter SSRT and MRT compared to participants in the CHILD group (data not shown).

3 Discussion

The present study explored the effect of reward magnitude on two different forms of IC (cancellation and restraint) in typically developing children and adolescents. Increasing the magnitude of reward earned for successful inhibition improved both cancellation and restraint IC. The lack of interaction between age group and reward suggests that reward facilitated inhibition to a similar degree across ages. On both versions of the SST, adolescents were faster at inhibiting and executing responses, and were less variable and more accurate in their go responses relative to younger children. Inhibition was faster in the cancellation version and response execution was faster in the restraint version, although both findings may be mediated
by the order of task administration in the neutral condition. These results bear on the effects of reward, age, and inhibition task.

### 3.1 Reward Effects

Reward operated similarly on cancellation and restraint to decrease the latency to inhibit responses (i.e., SSRT). There were fewer commission errors in the restraint task following administration of reward (i.e., percent inhibition increased), especially in the adolescent group. In the cancellation task, reward decreased the percentage of responses that were inhibited, but it seems that this effect was mainly due to the order of task administration. Regardless, neither reward nor order effects changed the frequency of cancellation IC (approximately 0.5). The effect of reward on go task accuracy in the restraint version was also mediated by task order. The data are consistent with the general idea that reward effects are sensitive to context (e.g., Guitart-Masip, Bunzeck, Stephan, Dolan, & Duzel, 2010; Luo, Ainslie, Giragosian, & Monterosso, 2009).

Reward did not differentially alter restraint or cancellation as shown by the lack of a significant interaction between the dependent variables and task version. In the cancellation version, rewards did not merely increase general information processing or approach behaviours because there were no significant influences of reward on the speed of response execution as measured by MRT. These data support the idea that “going” and “stopping” processes in the cancellation task are dissociable (e.g., Aron, Fletcher, Bullmore, Sahakian, & Robbins, 2004; Chambers et al., 2007), and rejects the claim that the speed of response execution is directly tied to the speed of cancellation SSRT (see Alderson, Rapport, & Kofler, 2007). In the restraint version, increasing reward magnitude decreased MRT and decreased go task accuracy in addition to its effects on IC. Given that the stop and go signals are presented concurrently in restraint, the processes of
“going” and “restraining” may be more closely related than in the cancellation version of the SST, which may indicate a potential shared mechanism for response execution and IC in restraint that is not apparent in cancellation.

Incentive learning involves the detection and estimation of the valence of appetitive stimuli (rewards), followed by signals about the actual magnitude of the incentive and prediction errors that allow for the adjustment of behaviour (Geir & Luna, 2009). Our results may allow us to speculate about the brain bases that may underlie the facilitation of IC processes by reward. To influence IC processes, rewards may directly influence the interaction between cognitive control and motivational centers in the brain, or may be altering the activity in other areas that are responsible for the integration of inhibition and motivation (Padmala & Pessoa, 2010). In the present study, rewards may operate on overlapping neural substrates that mediate each form of inhibitory control to effect the preparation of the inhibition function via stimulation of the reward pathway.

We propose that stop signals that signify increased rewards for successful inhibition are more salient than non-rewarding stop signals, enhancing the preparation of inhibition via stimulation of bottom-up, inferior frontal gyrus (IFG)-mediated pathways, which in turn may have facilitated the cancellation or restraint of a response. While the active suppression of motor responses is largely undertaken by activity in the basal ganglia (Mink, 1996), successful restraint and cancellation also involve activation of the IFG (e.g., Chevrier et al., 2007; Konishi, Nakajima, Uchida, Sekihara, & Miyashita, 1998; Konishi et al., 1999). The IFG may be part of a network that arouses attention when salient information, such as a stop signal, is detected in the environment (Downar et al., 2002). The IFG may also signal when inhibitory control demands increase or when previously learned information needs to be inhibited as task demands change.
Thus, the role of the IFG in cancellation may be to direct attention toward the stop signal to improve the efficiency of inhibition while decreasing the prepotent drive on go responses. Because restraint places a high cognitive demand on response preparation and selective attention prior to the presentation of the no-go stimulus (Johnstone et al., 2007; Kelly et al., 2004), successful restraint may rely predominantly on a top-down control system driven by regulatory structures such as the dorsolateral (Garavan, Ross, Murphy, Roche, & Stein, 2002; Kelly et al., 2004; Menon, Adleman, White, Glover, & Reiss, 2001), mid frontal, and dorsal premotor prefrontal cortices (Kelly et al., 2004; Watanabe et al., 2002). Thus, the bottom-up “saliency detection” and “behavioural updating” system associated with the bilateral IFG may interact with a top-down control system to result in successful restraint inhibition.

Alternatively (or concurrently), reward signals may facilitate IC at the level of the basal ganglia by similarly altering the preparation of the motor response. When the environment changes and salient stimuli are detected, nigrostriatal and mesolimbic dopamine neurons are activated and the subsequent dopamine release converges with glutamatergic output from the orbitofrontal cortex and amygdala on dendritic spines in the dorsal and ventral striatum (Horvitz, 2002). Dopamine acts to “gate” basal ganglia processing of the glutamatergic sensorimotor and incentive-related information in the striatum by enhancing strong signals and dampening weak signals (see Horovitz, 2002). Here, rewards may facilitate preparation of the inhibition response by enhancing the gating mechanism of dopamine in the striatum.

### 3.2 Age Effects

Consistent with previous research (Hale, 1990; Johnstone et al., 2007; Williams et al., 1999), we found that adolescents exhibited faster and more accurate IC and response execution than
younger children. For appropriate preparation, initiation, and on-line control of behaviour, a balance between inhibition and response execution processes needs to be established (Rubia et al., 2001). This balance seems to improve with development, with age-related changes in SSRT distinct from age-related changes in go RT (Williams et al., 1999), suggesting distinct neural mechanisms subserving the maturation of speeded information processing. Improvements in IC may also be related to age-dependent improvements in other regulatory processes, such as working memory, decision-making, and performance monitoring (e.g., Roncadin, Pascual-Leone, Rich, & Dennis, 2007; Velanova, Wheeler, & Luna, 2009).

The neural circuits subserving inhibition mature into adulthood, and these changes correlate with more efficient and controlled responses (Rubia et al., 2007). For instance, activity of the IFG is greater in adults than in adolescents during successful inhibition, with linear progressive changes occurring in response to successful stopping from ages 10-42 years in the bilateral inferior prefrontal cortex, thalamus, caudate, and cerebellum (Rubia et al., 2007). Group differences in SSRT may be related to increased recruitment of the IFG with age, which would increase the saliency of the stop signal, thereby improving cancellation (Chikazoe et al., 2009). Restraint inhibition matures somewhat earlier in development relative to cancellation, with adult levels in performance reached by age 12 years (Levin et al., 1991). Increased maturation of the frontostriatal system is related to improvements in restraint, with linear progressive changes observed in the striatum and inferior and mesial prefrontal cortices correlated with successful no-go trials (Liston et al., 2006; Rubia et al., 2006). Therefore, group differences in restraint performance, both in terms of the latency to inhibit a response and percent inhibition, may reflect age-related changes in the frontostriatal circuitry. In particular, the maturation of cognitive control centers in the prefrontal cortex may promote developmental changes in restraint (Kelly et al., 2004).
Like the inhibition system, reward circuitry, including the dopamine system, also matures with age (Meng et al., 1999; Segawa, 2000; Spear, 2000). Adolescents recruit the same neural circuitry as adults when encountering rewards (e.g., Bjork et al., 2004; Ernst et al., 2005; Galvan et al., 2006), but relative to adults, exhibit decreased activation of the ventral striatum when anticipating rewards (Bjork et al., 2004), but hyperactivation that is sustained and more diffuse in both the ventral striatum and orbitofrontal cortex with reward consumption (Ernst et al., 2005; Galvan et al., 2006; May et al., 2004). Hyperactivity in reward-related centers of the adolescent brain parallel the exaggerated dopaminergic response to rewards that is apparent during adolescence (Laviola, Macri, Morley-Fletcher, & Adriani, 2003); despite relatively low basal levels of dopaminergic output (Andersen & Gazzara, 1993). Moreover, adolescents show increased activity in the ventral striatum in anticipation of a high reward, but decreased activity in the same region in anticipation of a low reward (Galvan et al., 2006).

Immaturities in the reward system may bias the underdeveloped adolescent inhibition system towards actions that result in immediate rewards as a result of greater reward-seeking (Galvan, 2010; Geir & Luna, 2009). This can be adaptive if the decision is appropriate but maladaptive if the behaviour is based on receipt of immediate rewards (Geir & Luna, 2009). On the other hand, the hypoactive nature of anticipatory signals may drive high sensation seeking, which when paired with an immature IC system and hyperactive consummatory signals, may bias adolescents towards poor decisions marked by impulsivity and a lack of inhibition driven toward obtaining high-risk, short-term goals (Ernst, Pine, & Hardin, 2006; Fareri, Martin, & Delgado, 2008; Geir & Luna, 2009). Thus, one might expect that the adolescent group would have had an exaggerated response to rewards given the apparent hyperactivity in their reward circuitry, perhaps leading to faster SSRT during the high reward condition. While the slope of the reward effects on inhibition appears greater in the adolescent group in both tasks, there were no significant interactions.
between inhibition measures during reward trials and age group on either task, suggesting that reward improves inhibition similarly across the developmental span studied here. The data do not decide between a range of possibilities that may account for the apparent discrepancy between the results and predictions based on the reward literature, which include: a lack of statistical power; an underdeveloped IC system in the child group, biasing them toward high rewards, thereby equating the response to rewards between age groups; and the fact that reward systems in children may develop in some form earlier than expected. A direct comparison to adult participants group may have shown the exaggerated response to reward hypothesized to be present in adolescents.

### 3.3 Task Effects

The behavioural literature suggests that cancellation and restraint are different forms of inhibition, and this is supported by developmental studies and research on neural function (e.g., Johnstone et al., 2007; Schachar et al., 2007). The present data provide further support for the idea that IC is not a unitary construct by utilizing methodologically comparable inhibition tasks, and also adds new information about how reward acts on each type of inhibition process. The latency to inhibit a response was faster when a response needed to be cancelled, but the latency to execute a response was faster in the restraint version. However, without reward present, “go” responses in restraint were only faster in the NO condition when the cancellation version was presented first. Therefore, under conditions of reward, it is easier to execute a response if the demands on IC are to restrain a response. As argued by Schachar and colleagues (2007), because the restraint task has a delay period of zero between presentation of the go and stop signal, it allows an individual to delay responding to decide whether or not to respond, which might account for longer SSRT in the restraint task.
3.4 Conclusions

Rewards facilitated both restraint and cancellation IC in typically developing children and adolescents. Although cancellation IC was faster than restraint IC, both were similarly affected by rewards. Adolescents were faster and more accurate across tasks, and age did not interact with task version. These findings confirm that reward can positively alter inhibition processes throughout development. Ongoing studies examine whether or not rewards influence inhibition in children and adolescents with known inhibition deficits and reward-related sensitivities such as those with ADHD or acquired traumatic brain injuries.
### Table 1

**Participant Characteristics**

<table>
<thead>
<tr>
<th>Group</th>
<th>Age (Years)*</th>
<th>WASI Scores*</th>
<th>Family SES*</th>
<th>Handedness (Right : Left)</th>
<th>Sex (Females : Males)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHILD</td>
<td>9.52 (1.8)</td>
<td>116 (12.8)</td>
<td>54 (6.6)</td>
<td>19:3</td>
<td>13:9</td>
</tr>
<tr>
<td>TEEN</td>
<td>15.36 (1.3)</td>
<td>108 (7.3)</td>
<td>51 (5.5)</td>
<td>22:0</td>
<td>8:14</td>
</tr>
</tbody>
</table>

*Mean (standard deviation)
Table 2

Accuracy on Go Trials: Mean Percent Correct (standard deviation)

<table>
<thead>
<tr>
<th>GROUP</th>
<th>CANCELLATION</th>
<th>RESTRAINT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NO</td>
<td>LOW</td>
</tr>
<tr>
<td>CHILD</td>
<td>96.1 (5.0)</td>
<td>95.8 (4.6)</td>
</tr>
<tr>
<td>TEEN</td>
<td>99.1 (1.4)</td>
<td>98.2 (2.4)</td>
</tr>
</tbody>
</table>
Figure 1

Cancellation and Restraint Models of the Stop Signal Task (with and without rewards)

Trials 1 and 2 represent the primary task in both versions, where a go signal (X in Trial 1, O in Trial 2) is presented for 1000 milliseconds (ms) following a 500 ms fixation point. Participants were instructed to respond to these stimuli as quickly as possible by making the appropriate button press on a handheld controller. An inhibition trial is depicted in Trial 3. In the cancellation version (left panel), the initial auditory stop signal was presented 250 ms following onset of the go signal. If a participant was able to successfully inhibit his/her response, then the delay was increased by 50 ms on the subsequent stop trail to increase the level of difficulty. If the
participant was unable to inhibit his/her response, then the delay was decreased by 50 ms on the subsequent stop trial to make cancellation easier. In the restraint version (right panel), the stop signal was always presented at the same time as the go signal (the delay between the onset of the go and stop signal was zero). In both versions of the task, the feedback following the inhibition trials were identical. Failed inhibition (i.e., going instead of stopping or withholding) resulted in no feedback in the NO condition. In the LOW and HIGH conditions, failed inhibitions resulted in the failure to win points. Successful inhibition in the NO condition also resulted in no feedback. However, each successful inhibition in the LOW and HIGH conditions resulted in the receipt of 2 or 10 points, respectively.
Figure 2

Mean (standard error, SE) SSRT in the Cancellation Version of the SST

SSRT decreased with increasing reward magnitude, and participants in the TEEN group exhibited faster SSRT relative to participants in the CHILD group.
Percent inhibition decreased with reward, but there were no effects of age or an interaction between reward and age.
MRT was not altered by increasing reward magnitude, but was faster in the TEEN group relative to the CHILD group.
SDRT was not altered by increasing reward magnitude. Participants in the TEEN group exhibited less variable responses relative to participants in the CHILD group.
Percent inhibition increased with reward, but there were no effects of age or an interaction between age and reward.
SSRT decreased with increasing reward magnitude, and participants in the TEEN group exhibited faster SSRT relative to participants in the CHILD group.
MRT decreased with increasing reward, and was faster in the TEEN group relative to the CHILD group.
Mean (SE) SDRT in the Restraint Version of the SST

SDRT was not altered by increasing reward magnitude. Participants in the TEEN group exhibited less variable responses relative to participants in the CHILD group.
Chapter 3
Traumatic Brain Injury and Secondary Attention-Deficit/Hyperactivity Disorder in Children and Adolescents: The Effect of Reinforcement on Inhibitory Control

Traumatic brain injury (TBI) is common in children and adolescents, often resulting in significant long-term cognitive and behavioural consequences including inattention (Catroppa, Anderson, & Stargatt; Cicerone, 1996; Dennis, Wilkinson, Koski, & Humphreys, 1995) and poor inhibitory control (IC; Levin, Hanten, Zhang, Swank, Hunter, 2004; Levin et al., 1993; Konrad, Gauggel, Manz, & Scholl, 2000a, 2000b). Childhood TBI may also lead to persistent personality changes (Max et al., 2000; Max et al., 2005a, 2005c), increases in aggressive behaviour (Cole et al., 2008), and the emergence of new-onset psychiatric disorders such as attention-deficit/hyperactivity disorder (i.e., secondary ADHD (S-ADHD); Max et al., 1998; Max et al., 2005a, 2005b).

S-ADHD occurs in approximately 15-20% of TBI survivors without a previous history of ADHD (Gerring et al., 1998; Gerring et al., 2000; Herskovits et al., 1999; Max et al., 2005a, 2005b; Slomine et al., 2005; Yeates et al., 2005). This de novo diagnosis of ADHD manifests as early as 6 months post-TBI (Max et al., 2005a) and persists into the chronic stage of recovery (e.g., Max et al., 1998, 2005b). It is not clear whether S-ADHD is simply the acquired form of developmental or primary ADHD (P-ADHD), sharing commonalities in cognitive, behavioural and functional outcomes, or whether fundamental differences exist between these disorders despite similarities in overt behavioral expression. Differences between P-ADHD and S-ADHD have been shown in terms of the expression of behavioral symptoms as well as in the underlying pathology associated with each diagnosis. For example, children with P-ADHD exhibit structural and functional abnormalities throughout the cerebrum, particularly in frontostriatal networks.
(e.g., Casey et al., 1997; Castellanos et al., 1996), yet there is only limited evidence to suggest that damage to similar neural networks is correlated with diagnosis of S-ADHD (Gerring et al., 2000; Herskovits et al., 1999; Max et al., 2005b). While both groups of patients experience deficits with IC (e.g., Schachar, Levin, Max, Purvis, & Chen, 2004b; Schachar, Logan, Robaey, Chen, Ickowicz, & Barr, 2007), the nature and magnitude of IC difficulties in children with S-ADHD have not been well-studied, and it is currently unknown whether both groups exhibit similar deficits across all IC tasks or whether their responses to reinforcement are similar.

The behavioral phenotype of attention-inhibition deficits in P-ADHD has been parsed in a number of different ways. A key distinction is that between canceling or stopping an ongoing prepotent response and restraining or withholding an action. Children with P-ADHD exhibit deficits in both cancellation and restraint (e.g., Schachar, et al., 2004a; Schachar et al., 2007). Cancellation may be measured with the stop signal task (SST; Logan & Cowan, 1984; Logan, 1994), in which participants are instructed to respond as quickly as possible to one of 2 visual “go” signals and stop responding when they hear the auditory stop signal (which is presented after varying delays following the go signal). Poor or inefficient inhibition is manifested as longer latencies to respond to the stop signal, or slower stop signal reaction time (SSRT). Restraint is commonly measured with the go/no-go (GNG) task which requires participants to respond as quickly as possible to a visual go stimulus, but to withhold their responses when they encounter a visual “no-go” stimulus. Poor restraint is indexed by the number of responses made to no-go stimuli (commission errors).

In addition to difficulties with IC, children with P-ADHD respond abnormally to rewards and exhibit failures in reinforcement learning in general, with some theorists speculating that these children have a preference for immediate reward (Sonuga-Barke, 2002) and/or an insensitivity to
reward such that greater amounts of reinforcement are required to motivate behaviour (e.g. Haenlein and Caul, 1987). Douglas (1985) argues that children with P-ADHD focus on rewards and on the prospect of attaining rewards, and this increased vigilance may help to reduce impulsive responses, which in turn should facilitate IC.

To date, results of studies of IC and reward in children with P-ADHD are equivocal, with reports of reward facilitation (Desman, Petermann & Hampel, 2008; Huang-Pollock, Mikami, Pfiffner, & McBurnett, 2007; Konrad et al., 2000b; Scheres, Oosterlaan, & Sergeant, 2001; Stevens, Quittner, Zuckerman, & Moore, 2002; Tamm & Carlson, 2007), reward impairment (Gomez, 2003; Shanahan, Pennington, & Willcutt, 2008; Wodka et al. 2007), or null effects (Crone, Jennings, & van der Molen, 2003; Iaboni, Douglas, & Baker, 1995; Oosterlaan & Sergeant, 1998). Methodological problems that complicate interpretation within and across these studies include: lack of a control group (Tamm & Carlson, 2007); no non-reward condition to compare reinforcement effects to (Huang-Pollock et al., 2007; Iaboni et al., 1995; Oosterlaan & Sergeant, 1998); confounding of rewards and punishments (Crone et al., 2003; Gomez, 2003; Shanahan et al., 2008; Wodka et al., 2007); rewarding both response execution and inhibition (Huang-Pollock et al., 2007; Shanahan et al., 2008; Stevens et al., 2002); the finding that feedback alone produces similar improvements to rewards (Desman et al., 2008); and the existence of normal inhibition in P-ADHD groups (Crone et al., 2003; Scheres et al., 2001), which makes it difficult to ascertain if rewards facilitated or impaired performance. Current behavioural therapies for P-ADHD utilize rewards and response costs to modify behaviour (Oosterlaan & Sergeant, 1998), so clarification of the relationship between IC and reward in children with P-ADHD has important therapeutic applications. For instance, if rewards can act to “normalize” IC, then the focus of behavioural therapy should be on training children with P-ADHD to achieve and maintain an adequate
motivational state to help reduce impulsivity, thus strengthening IC and other regulatory processes (Luman, Oosterlaan, & Sergeant, 2005).

Relative to typically developing children, children with S-ADHD exhibit poor response execution and cancellation IC on the SST, but similar performance to children with TBI without a S-ADHD diagnosis (Konrad et al., 2000a, 2000b). An inhibition deficit has been documented relative to children with TBI in those with both a severe TBI and S-ADHD diagnosis (Schachar et al., 2004b), suggesting that those with greater injury severity and a de novo diagnosis of ADHD are more susceptible to disinhibition than those with less severe injuries. Because most studies include children in both chronic and acute phases of recovery, the interpretation of data on inhibition in TBI and S-ADHD populations is not clear. For instance, children with TBI exhibit an initial deficit in SSRT that resolves by two years post-injury (Leblanc et al., 2005). Further, commission errors on the GNG task decrease with time since injury, with greater injury severity resulting in poorer improvement over time (Wassenberg, Max, Lindgren, & Schatz, 2004). To date, only two studies have assessed both P-ADHD and S-ADHD groups on the SST (Konrad et al., 2000a, 2000b), but because the performance was not directly compared between groups, it is currently unknown whether or not these patients cancel their responses in a similar manner. No study has compared the performance of children with P- and S-ADHD on other forms of IC, such as restraint.

Little is known about reinforcement learning in children with S-ADHD or specifically how reward variables influences inhibition in this population. Konrad and colleagues (2000b) rewarded successful inhibition on the SST, which improved cancellation performance in children with TBI and S-ADHD, although not to the point of comparability to controls. At the same time, reward facilitated inhibition in children with P-ADHD such that their performance was similar to
controls. However, the ADHD groups were not directly compared in this study (Konrad et al., 2000b), so it is unknown whether or not they responded similarly to reward.

While comparisons to non-injured controls are helpful in determining whether and how children with S-ADHD differ from typically functioning children in terms of IC and responses to reward, and comparisons to children with TBI without S-ADHD indicate the specific deficits S-ADHD confers beyond the consequences of TBI, a direct comparison to children with P-ADHD may reveal the degree and intensity of deficits in S-ADHD. This later comparison would also clarify whether both forms of ADHD reflect a similar disinhibition syndrome despite differences in etiology. Although childhood TBI can affect a number of cognitive processes, poor IC on the SST (longer SSRT) has been proposed as a candidate endophenotype for P-ADHD (Crosbie, Perusse, Bar, & Schachar, 2008). If children with TBI exhibit similar IC deficits as those with ADHD, then the link between IC dysfunction and specific psychiatric syndromes like ADHD may need to be re-examined. If children with S-ADHD exhibit similar deficits in cancellation and restraint to children with P-ADHD, then S-ADHD may be thought of as an acquired disorder that mimics the P-ADHD endophenotype, which would inform not only the brain bases of IC deficits in P-ADHD, but also the neural bases of IC in general. If the two groups differ across measures or exhibit a dissimilar pattern of results, then there is evidence that S-ADHD is a separate disorder from P-ADHD, in terms of both underlying mechanisms and associated behavioural deficits. If both groups of children respond similarly to reward despite differences in IC, then it may be concluded that rewards operate similarly on IC across groups suggesting a powerful effect of motivational variables in spite of differences in brain abnormalities. In sum, each different pattern of results would have specific and direct implications for the assessment and treatment of S-ADHD.
The objective of the present study was to understand how reward modulates cancellation and restraint inhibition in developmental (P-ADHD) and acquired (S-ADHD) forms of ADHD. We compared the 2 forms of inhibition in 4 groups of participants (typically developing children, children with P-ADHD, children with TBI in the chronic stage of recovery, and children with TBI in the chronic stage of recovery with a research diagnosis of S-ADHD). We used two versions of the SST to measure cancellation and restraint that differed only in the presentation of the stop signal (Schachar et al., 2007). Because the no-go signal in the restraint version of the SST is an auditory tone, task demands are equated thus minimizing reliance on selective attention that are associated with the traditional GNG task (Aron & Poldrack, 2005; Rubia, Smith, Brammer, & Taylor, 2003). Following the administration of the standard IC tasks, we then investigated the relation between reward and IC by rewarding successful cancellation and restraint.

Predictions concerned both group and reward effects, and were aligned with the literature reviewed earlier. We predicted that approximately 15-20% of children with TBI would exhibit symptoms consistent with a S-ADHD diagnosis, and these participants were expected to exhibit poorer IC on the SST measures of cancellation and restraint relative to those with TBI only or to healthy controls. Given that time since injury ameliorates cancellation deficits in children with TBI (Leblanc et al., 2005), and that participants in the TBI group in the present study were also in the chronic phase of recovery, we predicted that children with TBI without S-ADHD would exhibit IC like that of normal controls under all reward conditions. Participants in the P-ADHD group were expected to have poorer IC relative to controls, with rewards possibly improving IC performance. If rewards can improve IC deficits in the P-ADHD group to levels exhibited by typically developing children, it may suggest that children with P-ADHD also suffer from an inability to self-motivate their own behaviour.
4 Method

4.1 Participants

Children and adolescents aged 7 to 17 years old were recruited into three groups. Participants in the initial TBI group (n=63) were recruited through trauma registries at the Hospital for Sick Children in Toronto. Inclusion criteria included the presence of a non-inflicted, non-penetrating TBI at least 1 year but no more than 6 years prior to testing, hospitalization for at least one night for the TBI, the absence of multiple head injuries, and no pre-injury neurological disorders. Ten participants cancelled or missed their appointments, and 4 participants were excluded due to the presence of a pre-injury P-ADHD diagnosis. Forty-nine participants formed the final TBI group (21 female, 28 male; mean age, 11.89 years; mean age of injury, 8.07 years). Severity of injury was defined by categories outlined by the method of Teasdale and Jennet (1974), separating participants into those with mild (n=28), moderate (n=6), and severe (n=16) injuries based on initial post-resuscitation Glasgow Coma Scale (GCS) scores. For patients that did require resuscitation, the lowest GCS score on record was used. Severity was also classified utilizing a new scale that generated a total severity score out of 20, including both a scaled GCS and the presence of specific brain abnormalities on pre-surgical, inpatient computed tomography (CT) scans (see Appendix 1).

Twenty children from the community were recruited into the initial P-ADHD group. Inclusion criteria included the diagnosis of ADHD from a health care professional and a negative history for TBI. Two participants were excluded from further analyses due to the lack of significant parent and teacher endorsement of clinically significant ADHD symptoms required for an ADHD diagnosis on Conners 3rd Edition Rating Scales (Conners 3; Conners, 1998). One participant initially recruited for the control group was included in the P-ADHD group based on
significant endorsement of diagnostic criteria for ADHD on the same scale (see below). The final P-ADHD group (n=19; 2 female, 17 male; mean age, 10.70 years) included 12 participants who were either drug naïve or were not currently taking any psychotropic medication for their ADHD. The remaining participants were currently undergoing pharmacological treatment (with 2 participants taking multiple medications); these participants were asked to discontinue treatment for 24 hours prior to testing.

Sixty-six typically developing children were recruited into an initial control group (CON group) through flyers and community advertisements. Nine participants cancelled or missed their appointments and 13 participants were excluded based on clinically significant elevations on the Conners 3 rating scales (see below). The final CON group consisted of 44 participants (21 female, 23 male; mean age, 12.44 years).

Telephone questionnaires were conducted with each participant’s parent during recruitment to screen for eligibility for participation. Exclusion criteria for TBI and P-ADHD groups included the presence of mental retardation, severe psychiatric disorder (e.g. psychosis), and sensory or motor impairments. Exclusion criteria for the CON group included a history of TBI, P-ADHD, neurological or psychiatric disorders, mental retardation, learning disabilities, and sensory or motor impairments.

All participants were administered the Vocabulary and Matrix Reasoning subscales of the Wechsler Abbreviated Scale of Intelligence (WASI); participants with Full Scale IQ scores under 75 were excluded. Informed consent was obtained prior to testing from each participant’s parent, and assent was obtained from the participants themselves. This experiment was conducted with approval of the Research Ethics Boards at the Hospital for Sick Children and the University of Toronto.
4.2 Rating Scales: Inclusion and exclusion criteria

The Full Form of the Conners 3 was administered to each participant’s parent and teacher. The Conners 3 assesses behaviours related to ADHD symptoms and possible comorbid conditions, as well as other variables such as cognitive difficulties (Conners, 2008). For the purpose of the present study, we examined whether or not participants were rated as exhibiting elevated T-scores (i.e., over 65) on the Diagnostic and Statistical Manual of Mental Disorders, 4th edition text revision (DSM-IV-TR; American Psychological Association, 2000) Scales and whether or not they reached criteria for ADHD, conduct, and/or oppositional defiant disorder on the DSM-IV-TR Symptom Counts of the Conners 3.

Thirteen participants in the CON group exhibited elevated T-Scores (over 65) on the DSM-IV-TR Scales and met criteria for a disorder on the DSM-IV-TR Symptom Counts, thus were excluded from further analyses. One excluded CON participant met DSM-IV-TR criteria for ADHD diagnosis based on both teacher and parent ratings, so he was included in the P-ADHD group. Two participants were excluded from the P-ADHD group due to the absence of a diagnosis of ADHD based on both parent and teacher ratings.

We also used the Conners 3 to identify children in the TBI group who reached criteria for S-ADHD. In addition to meeting criteria for inclusion into the TBI group, the participants in the S-ADHD group needed to exhibit no evidence of P-ADHD prior to the TBI (based on parental report during the recruitment phone call). Although not a full diagnostic interview, retrospective reports about behavior prior to TBI have been used to exclude P-ADHD in previous S-ADHD samples (e.g., Konrad et al., 2000a, 2000b; Schachar et al., 2004). To be eligible for inclusion into the S-ADHD group, participants also needed to meet diagnostic criteria for ADHD (any subtype) on the Conners 3 via teacher and/or parent reports. Given that S-ADHD has yet to be
defined in the DSM, we waived the age requirement for diagnosis as well as the requirement that ADHD symptoms must be present in at least 2 environments (American Psychological Association, 2000), because it is not clear if these criteria are necessary for the classification of participants into the S-ADHD group. Nine participants in the TBI group without evidence of pre-injury P-ADHD met criteria for S-ADHD through parent and/or teacher reports on the Conners 3 (S-ADHD group, 5 female, 4 male; mean age, 11.84 years; mean age at injury, 7.22 years), and 40 participants without evidence of ADHD on the Conners 3 remained in the TBI group (16 female, 24 male; mean age, 11.91 years; mean age at injury, 8.26 years).

4.3 Stop Signal Tasks

The SST is based on a formal model that conceptualizes performance as a race between response execution (go processes) and response inhibition (stop processes; Logan & Cowan, 1984; Logan, 1994; Verbruggen & Logan, 2008); whichever process wins the race determines whether the response will be executed or inhibited. The race model is advantageous because it allows for the measurement of the latency of IC (i.e., the SSRT), which is an unobservable, internally generated act of control (Logan, 1994).

Two versions of the SST were used to measure canceling (“cancellation”) and restraining (“restraint”) a prepotent response (see Figure 1; Logan, 1994; Schachar et al., 2007). Both versions consisted of a primary visual choice reaction time task involving a go signal and a secondary task involving a stop signal (Logan & Cowan, 1984; Logan, 1994). In the primary task, one of two possible go signals (an X or an O) was presented on a computer screen for 1000 milliseconds (ms) following a 500 ms fixation point. Participants were instructed to respond to these stimuli as quickly as possible by making the appropriate button press on a handheld controller. Participants were also instructed to inhibit their responses to the go signal when they
heard the auditory stop signal (a 1000 Hz tone emitted from computer speakers). The stop signal occurred randomly on 25% of trials.

In the restraint version of the task, the stop signal was presented concurrently with the go signal to prevent a response from being executed (Schachar et al., 2007). In the cancellation version, the stop signal occurred at various delays following the go signal to interrupt an already executed response. The delay between the presentation of the go and the stop signal was varied dynamically in this version of the task to ensure that participants would cancel their responses on 50% of the inhibition trials, regardless of whether or not they slowed their go reaction time as a strategy to increase successful cancellation (Logan & Cowan, 1984; Logan, 1994). The initial stop signal delay was set at 250 ms. If a participant successfully inhibited his/her response, then the delay was increased by 50 ms on the subsequent stop trial, and if the participant was unable to inhibit his/her response, then the delay was decreased by 50 ms on the subsequent stop trial. This method ensured approximate control over stop and go processes by increasing or decreasing the ease of successful cancellation.

The latency of IC on both versions of the SST was estimated by determining the SSRT via the integration procedure (Logan, 1994): the go reaction time in non-stop signal trials are rank ordered, the go reaction time that corresponds to the probability of inhibition is determined, and the SSRT is estimated by subtracting the mean delay from this new “integrated go reaction time”. By utilizing this procedure, all faster go reaction times that would have been executed and all slower responses that would have been stopped can be excluded from the final SSRT metric (Schachar et al., 2007).

Each task version was performed under three different reward conditions presented in the same ascending order of magnitude (NO, LOW, HIGH). In the neutral (NO) condition, the words
“Good work! Press a button to keep going” appeared in the middle of the screen. No other specific feedback about task performance was revealed. Following the NO condition, participants were informed that they would be performing the task for a second and third time where they could win points for successful inhibition, and if they could win 400 points by the end of the testing session, they would receive a prize (a $10 gift certificate for the movies). They were also told that each time that they successfully inhibited their responses they would win 2 points in the low reward condition (LOW), which would be followed by a high reward condition (HIGH) where they would win 10 points. Points earned were immediately represented on the screen in a visual analog scale (the scale was left empty in the NO condition). Participants were informed of how many points they had won in each block via a message in the middle of the screen (e.g. “You won 12 points.”). Participants were also told that they would receive bonus points for pushing the buttons as quickly as possible during the primary task. Although no actual bonus points were rewarded, this additional instruction was given in order to reduce the tendency for participants to slow their go reaction time to ensure successful inhibition. The points were recorded by the examiner, and total scores were revealed at the end of the testing session. When 2 children did not win enough points for the prize, their scores were bumped up to 400 via “bonus points” to ensure that all children won the prize.

Each reward condition of the cancellation and restraint versions of the SST involved a total of 120 trials divided into 5 blocks of 24 trials each, with the stop signal randomly occurring on 30 trials. The first block in each task was a practice block, not utilized in subsequent analyses. The order of administration of each version was counterbalanced, with the WASI and another computerized task intervening.
4.4 Statistical Analyses

Participant data from the SST was excluded from statistical analyses if any of the following occurred (Band, van der Molen, & Logan, 2003; Schachar et al., 2004; Shuster & Toplack, 2009): less than 66% accuracy on go trials, mean go reaction time (MRT) less than 100 ms, and for the cancellation version only, percent inhibition less than 12.5% or greater than 87%. Based on these criteria, 1 participant from the CON group, 2 from the TBI group, and 1 participant from the ADHD group were excluded from analyses of the cancellation data, while 1 participant from the CON group and 1 participant from the ADHD group were excluded from analyses of the restraint data.

We examined both IC and response execution. IC was indexed by SSRT and by the number of responses inhibited (percent inhibition). Response execution was indexed by MRT, standard deviation of go reaction time (SDRT), and percent correct on go trials (accuracy). SDRT allowed for a measurement of variability, or the degree to which go responses were consistent across the tasks and reward conditions. We investigated accuracy to not only assess how well participants performed on the go task, but it also allowed us to investigate if reward altered IC at the expense of accuracy (i.e., speed-accuracy trade-off).

Age of test, age of injury, time since injury (for the TBI and S-ADHD groups only) and WASI scores were compared between groups using an analysis of variance (ANOVA). Group differences in performance on each task were compared separately for each dependent variable utilizing repeated measures ANOVAs, with reward condition as the within-subjects factor (NO, LOW, HIGH), group (TBI, S-ADHD, P-ADHD, CON) and order of task administration (cancellation administered first, cancellation administered second) as between-subjects variables.
Given that IC improves with age (see Chapter 2), age at test was added as a covariate in these analyses.

Regression analyses determined the impact of injury variables on performance in the TBI and S-ADHD groups. Age at injury, time since injury, severity score (out of 20), and GCS score were entered as possible predictors of SST performance. The effects of severity of injury using the traditional GCS scoring method were also explored utilizing repeated measures ANOVAs with severity (mild, moderate, severe) as the between-subjects factor and age at testing as the covariate.

5 Results

5.1 Participant Characteristics

Participant characteristics for each group are presented in Table 3. There were no significant age differences between groups, and age of injury and time since injury did not differ between the TBI and S-ADHD groups. Although WASI scores differed between groups (F(3, 110)=4.244, p=0.007), mean IQ scores were within the normal range for all groups and no participants were excluded based on low IQ scores. SES also differed between groups (F(3, 102)=6.797, p<0.001), with the CON group exhibiting greater scores relative to the other groups.

5.2 Cancellation

Percent inhibition was approximately 50% across reward conditions, and was not significantly altered by reward (see Figure 10). Moreover, percent inhibition did not differ between groups. These data indicate that the tracking algorithm was successful at limiting the probability of inhibition to approximately 0.5 across groups and reward conditions.
5.2.1 Group and Reward Effects

The analysis of SSRT revealed a main effect of reward (linear effect; F(2, 198)=4.590, p=0.015) and a significant group effect (F(3, 99)=3.784, p=0.013), but no significant interaction between reward condition and group (see Figure 11). SSRT decreased across reward conditions, and participants in the P-ADHD group exhibited longer SSRT relative to participants in the TBI (p=0.009) and CON (p=0.001) groups. MRT did not differ between groups, nor was there a significant effect of reward or reward by group interaction (see Figure 12). SDRT was not altered by reward, nor was there a significant reward by group interaction (see Table 4). SDRT did differ between groups (F(3, 99)=3.362, p=0.022), with participants in the P-ADHD (p=0.008) and TBI (p=0.013) group exhibiting more variable performance relative to the CON group. Accuracy on go trials differed between groups (F(3, 99)=8.283, p<0.001), with the P-ADHD group exhibiting poorer go trial accuracy relative to both CON and TBI groups (p<0.001) (see Table 4). Percent correct was not altered by reward and there was no significant reward by group interaction.

5.2.2 Order Effects

Order of task administration did not influence SSRT, MRT, and SDRT, nor were there significant interactions between these variables and order. Greater accuracy on was observed when the cancellation version was administered first (F(1, 99), 5.992, p=0.016). A significant interaction between percent inhibition and order (linear effect; F(2, 198)=4.315, p=0.015) indicates that participants were able to inhibit their responses to a greater degree in the NO and LOW conditions when the cancellation version was administered first.
5.3 Restraint

5.3.1 Group and Reward Effects

Percent inhibition increased with increasing reward magnitude (linear effect; $F(2, 202)=5.059$, $p=0.007$), but no significant differences were found between groups (see Figure 13). SSRT was not altered by reward (see Figure 14) and was similar across groups. Despite the lack of significant group effects on the inhibition variables, planned comparisons revealed differences between CON and P-ADHD groups (percent inhibition, $p=0.053$; SSRT, $p=0.03$), suggesting poorer restraint performance in the P-ADHD group relative to typically developing children.

Analysis of MRT yielded no significant effects of reward, group, or an interaction (see Figure 15). SDRT varied across groups ($F(3, 101)=4.330$, $p=0.006$), with the CON group exhibiting less variable performance relative to P-ADHD ($p=0.002$) and S-ADHD ($p=0.021$) groups (see Table 4). Accuracy on the go task decreased with increasing reward magnitude (linear effect; $F(2, 202)=4.072$, $p=0.018$), suggesting poorer accuracy with greater rewards. No group differences in accuracy or group by reward interactions were found (see Table 4).

5.3.2 Order Effects

Order of task administration did not alter SSRT, percent inhibition, or MRT. Participants were more accurate ($F(1, 101)=3.977$, $p=0.049$) and less variable ($F(1, 101)=5.620$, $p=0.02$) when the restraint task was administered first. The presence of an interaction between order and percent inhibition (linear effect; $F(2, 202)=3.613$, $p=0.029$) suggests that a greater number of responses were restrained in the NO condition if restraint was administered first, while the opposite was true in the LOW and HIGH conditions.
5.4 Injury Variables

5.4.1 Cancellation

MRT and SDRT were significantly predicted by age of injury across reward conditions (see Table 5); younger age at injury resulted in slower and more variable response execution in the neutral and reward conditions. MRT during the NO and LOW conditions were additionally predicted by time since injury: greater time since the injury was associated with faster response speed (data not shown). Age at injury, severity, and GCS score were not significant predictors of accuracy on go trials, SSRT, or percent inhibition.

Univariate ANOVAs utilizing GCS severity classification as the between-subjects variable revealed an inconsistent pattern of results across dependent variables. Group differences in SDRT were found in the NO condition (F(2, 43)=4.412, p=0.018), with participants with moderate injuries exhibiting more variable performance relative to participants with mild (p=0.007) or severe (p=0.01) TBIs. Group differences in SSRT were found in the NO (F(2, 43)=3.204, p=0.05) and HIGH (F(2, 43)=3.759, p=0.031) conditions, with participants with severe injuries exhibiting longer SSRTs than those with mild injuries (p=0.019 and p=0.016, respectively).

5.4.2 Restraint

Regression analyses revealed that age of injury was a significant predictor of MRT and SDRT performance across reward conditions (see Table 5), indicating that a younger age of injury results in slower and more variable response execution. MRT during the NO and LOW conditions were additionally predicted by time since injury (data not shown). Age of injury also predicted SSRT in the LOW and HIGH conditions only, with longer SSRT observed in participants who had incurred their TBIs at younger ages. Accuracy in the HIGH condition was
also significantly predicted by age of injury, revealing better accuracy on the go task in the
HIGH condition in those with an older age of injury. Age at injury, severity, and GCS score did
not predict percent inhibition.

Performance on any variables did not vary by GCS severity.

6 Discussion
The broadest objective of the present study was to investigate how reward affects cancellation
and restraint inhibition under comparable task demands in developmental (P-ADHD) and
acquired (S-ADHD) forms of attention disorders. In examining rewarded or unrewarded
cancellation and restraint in children and adolescents with TBI, S-ADHD, P-ADHD, and
typically developing controls, we aimed to articulate the inhibitory control profile of the four
groups. The order of task administration affected the accuracy of go responses and the
percentage of responses that were inhibited, possibly reflecting participant fatigue as the testing
session progressed. The data bear on a number of issues, but particularly how the P-ADHD and
S-ADHD groups differ and whether there are significant differences between children with TBI
with and without identifiable S-ADHD.

6.1 Group Effects
Consistent with our hypotheses and previous research (e.g., Max et al., 2005b), 18 % of
participants in the TBI group reached criteria for S-ADHD. IC in the S-ADHD group was
statistically similar to that in the other groups, but they did exhibit greater variability in go
responses. The TBI group did not differ from controls in terms of either the latency to cancel or
restrain a response, or in the percentage of responses that were inhibited on either task. In
contrast, previous studies have shown slower cancellation in children with S-ADHD than in
typically developing children, but similar SSRT relative to children with TBI only (who were also impaired relative to controls; Konrad et al., 2000a, 2000b). The Konrad et al. (2000a, 2000b) studies included children who had incurred their injuries 6 months to 6 years prior to testing, thereby including participants in the acute phase of injury who might have experienced greater inhibition problems than those in the chronic phase of injury (Leblanc et al., 2005). Rapid functional improvement occurs soon after a TBI, especially in severe injuries, with more gradual recovery over the first few years post-TBI (Yeates, 2000). Performance in our TBI and S-ADHD groups may represent some recovery of IC over time, which, if so, would have attenuated group differences.

A direct comparison of the ADHD groups allowed us to determine whether or not P-ADHD and S-ADHD share a similar expression of disordered behaviour. Poor inhibition performance is a well-replicated finding in children and adolescents with P-ADHD (e.g. Schachar et al., 2007; Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005). Consistent with previous research, participants in the P-ADHD group exhibited longer latencies to cancel and restrain their responses, inhibited fewer responses on the restraint version (made more commission errors), produced more variable responses to go stimuli, and were less accurate in the cancellation go task relative to typically developing controls. The S-ADHD group did not differ significantly from any other group in terms of cancellation or restraint inhibition. However, their performance on the cancellation task may be thought of as “intermediate” between the control, TBI, and P-ADHD groups. That is, they exhibited statistically similar IC performance relative to the CON and TBI groups, but they also did not differ from the most impaired group, suggesting atypical performance in the S-ADHD group. Schachar and colleagues (2004b) revealed an IC deficit in children with S-ADHD and a severe TBI relative to a TBI only group. Because only one participant in the S-ADHD group had incurred a severe TBI, it remains unclear whether children
with more severe injuries would exhibit poorer IC compared to those with less severe injuries and/or those with P-ADHD.

Children and adolescents who experienced TBI at a younger age had slower and more variable responses across reward conditions and tasks. The greater burden of an earlier age at injury is consistent with other studies of childhood TBI (e.g. Dennis, Barnes, Wilkinson, & Humphreys, 1998; Dennis, Wilkinson, Koski, & Humphreys, 1995; Ewing-Cobbs, Fletcher, Levin, Iovino, & Miner, 1998). Compared to older children with equally severe injuries, younger children demonstrate slower recovery of function over time and greater deficits once recovery plateaus (Ewing-Cobbs et al., 1997; Yeates, 2000). Age at injury predicted restraint IC under conditions of low or high reward, but did not predict restraint when no rewards were present nor did it predict cancellation IC under any reward condition (see also Schachar et al., 2004b). Either early injuries do not have a specific effect on inhibition, or a younger age enhances neural compensation for damaged inhibition circuits and/or leads to an over-commitment of neural processing resources that balances the effects of early lesions (Kramer et al., 2008; McAllister, Sparling, Flashman, & Saykin, 2001).

In published reports, the relationship between injury severity and performance outcomes has been contradictory: GCS scores have shown to be both predictive of (Levin et al., 2004; Levin et al., 1993; Konrad et al., 2000a, 2000b) and unrelated to (Leblanc et al., 2005; Schachar et al., 2004b) IC. Utilizing the conventional GCS severity coding, we also found inconsistencies in the relationship between severity and cancellation performance, and no relationship between severity and restraint performance. GCS scores vary over time, so the classification of an injury depends on the timing of assessment (Yeates, 2000). Moreover, categorizing severity based on initial GCS scores ignores injury variables such as the presence of edema, hemorrhaging, or localized
hematomas. Given these difficulties, we created a new severity scale that integrated injury variables presented on pre-surgical, in-patient CT reports with GCS scores, hypothesizing that this new scale might capture the severity of TBI better than GCS alone. Contrary to expectations, scores derived on this new scale did not predict performance on any variable in any reward condition, suggesting that the addition of specific injury-related variables from CT reports does not increase the predictive power of GCS scores on behavioral performance.

6.2 Reward effects

Increases in reward improved the latency to cancel a response in all groups, and increased the number of successfully restrained responses. This is consistent with our previous study that showed that increasing the reward magnitude for successful inhibition improved cancellation and restraint in typically developing children and adolescents (see Chapter 2). We extended that previous study by showing that reward facilitated inhibitory control in children with TBI (with and without S-ADHD) and those with P-ADHD. Reward did not alter the group differences reported above, indicating that all groups benefited similarly from reward.

How reward facilitates IC is not completely known, but our results may allow us to make some predictions about the brain bases of these effects. Reward may be interacting directly with the IC system, or indirectly via a separate system that in turn influences the relationship between reward and inhibition substrates (Padmina & Pesoa, 2010). As elaborated elsewhere (see Chapter 2), we propose that rewards may enhance the preparation of the inhibition response via activation of the neural pathways involving the inferior frontal gyrus (IFG) and/or the basal ganglia. The IFG has been repeatedly implicated in cancellation and restraint (e.g., Chevrier, Noseworthy, & Schachar, 2007; Konishi, Nakajima, Uchida, Sekihara, & Miyashita, 1998; Konishi et al., 1999), and it is thought that this neural structure is involved in a bottom-up, novelty detection system that not
only signals the salience of stimuli, but also feeds into regulatory systems such as working memory to update behavioral plans once contingencies and priorities change (Chikazoe et al., 2009; Downar, Crawley, Mikulis, & Davis 2002; Konishi et al., 1998; 1999; Smith & Jonides, 1998). The basal ganglia are important for the execution of motor responses as well as the gating of sensorimotor information from cortical and limbic areas such that strong reward signals are enhanced, and weak reward signals are dampened (Horvitz, 2002; Mink, 1996).

Given that reward facilitated IC in children and adolescents with TBI, the mesolimbic dopamine system may be intact in the TBI and S-ADHD groups and interacting adaptively with the inhibition system. Our findings are in line with previous research that also showed the beneficial effects of rewards on IC in TBI and S-ADHD groups (Konrad et al., 2000b), and with a study that showed that increasing the magnitude of monetary incentives improved prospective memory in children with mild or severe TBI (McCauley, Pedroza, McDaniel, Chapman, & Levin, 2009). In neither the present study nor the Konrad et al. (2000b) or McCauley et al. (2009) studies is it clear whether rewards stimulated greater allocation of specific cognitive resources to increase proficiency, or whether reinforcement simply served to increase general arousal. The former is more likely to be correct. Relative to the CON group, the TBI group continued to exhibit greater variability in go responses in the cancellation task and the S-ADHD group continued to exhibit greater variability in go responses in the restraint task regardless of reward conditions. Furthermore, MRT was unaffected by reward in both versions of the SST, which indicates that reward did not generally increase arousal.

Rewards facilitated IC in the P-ADHD group across tasks (see also Konrad et al., 2000b). These linear improvements in IC are consistent with previous findings that increasing the value of reinforcement improves SSRT (Slusarek et al., 2001; Huang-Pollock et al., 2007), and that
children with P-ADHD make advantageous decisions with high magnitude (Luman, Oosterlaan, Knol, & Sergeant, 2008) or high frequency (Toplack, Jain, & Tannock, 2005) reinforcement. Children with P-ADHD may use immediate rewards to motivate, decrease distractibility, and focus attention (Sonuga-Barke, 2002). Here, high reward did not normalize the stopping deficit exhibited by the P-ADHD group, so either the IC deficit in P-ADHD is too profound for rewards to significantly improve it, or children with ADHD, despite their preference for immediate incentive, have a higher than normal reward threshold (Douglas, 1999; Haenlein & Caul, 1987; Quay, 1997). Both hypotheses may account for the results, given both the lack of group interaction with reward and the improvements in SSRT (cancellation) and commission errors (restraint) with reward.

6.3 Conclusions
Developmental and acquired forms of ADHD appear to be distinct in terms of IC deficits, with children and adolescents with P-ADHD experiencing greater difficulties with both cancellation and restraint. Our data is in line with the idea that poor IC may be only evident in children with a heritable form of P-ADHD (Crosbie & Schachar, 2001), and that a longer SSRT may be a candidate endophenotype only for this specific group of children (Crosbie et al., 2009). However, the P-ADHD group exhibited longer SSRT and less percent inhibition (restraint version only) relative to controls, which suggests that inhibition is not entirely typical in children with S-ADHD given the lack of significant differences between ADHD groups.

Although problems with attention are common following TBI (e.g., Slomine et al., 2005), our data confirm that long-term inhibition deficits are different from those evident in children with P-ADHD. Compared to the P-ADHD group, the TBI group exhibited significantly faster SSRT on the cancellation task. Like the P-ADHD group, however, children with TBI and S-ADHD were
more variable in their responses to go stimuli, implying that stability of response execution is
disrupted to a similar degree in developmental and acquired disorders of attention. The
inconsistent pattern of responding in the participants with P-ADHD is in line with a number of
studies (e.g. Berwid, Kera, Marks, Santra, Bender, & Halperin, 2005; Lijffijt, Kenemans,
Verbaten, & Engeland, 2005; Schachar, Tannock, Marriott, & Logan, 1995), and may reflect
problems in sustained attention and concentration, motor timing and time estimation (Rubia, et
al., 1999; Rubia, Taylor, et al., 2001; Rubia et al., 2003) and response regulation (Rubia, Smith,
& Taylor, 2007; Sergeant et al., 1999). The exact mechanism of disruption in the TBI groups is
unknown, but because the speed of response execution did not differ between groups, slower
cognitive processing (Kalff et al., 2005) and slower motor speed (Van Meel, Oosterlaan,
Heslenfeld, & Sergeant, 2005) can be excluded as possible mediators of SDRT group
differences.

The data have some treatment implications. Stimulant medication ameliorates P-ADHD
symptoms and improves the latency of cancellation (see Dennis et al., 2008). Although stimulant
effects on attention after childhood TBI are attenuated and time-limited, children with TBI do
exhibit greater improvements in cognition relative to placebo (Jin & Schachar, 2004; Mahalick et
al., 1998). Our data suggest that stimulants may be beneficial in ameliorating the atypical
inhibition performance in children with S-ADHD, and may perhaps also aid in stabilizing the
inconsistent pattern of responses presented by this group. In children with ADHD, reward
improved both cancellation and restraint. Incentives may be a beneficial in the classroom or at
home when children with ADHD are having difficulty stopping their thoughts or actions when it
is adaptive to do so via the reduction of impulsive behaviors, which would potentially result in a
reduction of IC difficulties (Luman, Oosterlaan, & Sergeant, 2005). However, given the lack of
group by reward interaction, it seems unlikely that incentives would fully normalize this deficit.
Children with TBI also benefited from rewards; like typically developing controls, they may require low levels of reinforcement to optimize inhibition.

Broadly, the methods and results in our study support the recent proposal (Levy & Ebstein, 2009) that principled and systematic comparisons of core cognitive phenotypes across disorders inform cognitive processes, putative brain mechanisms, and treatment planning. S-ADHD as a result of childhood TBI results in inconsistent responding to go stimuli and inhibition performance that may be thought of as intermediate between participants with TBI and P-ADHD. Unlike children with P-ADHD, children with S-ADHD do not show significant difficulties with restraint and cancellation inhibition, but they may not possess the typical IC abilities of children with TBI only. Despite similarities in clinical manifestation, S-ADHD and P-ADHD appear to have different cognitive-behavioral phenotypes.
Table 3

**Participant Characteristics**

<table>
<thead>
<tr>
<th></th>
<th>CON</th>
<th>TBI</th>
<th>S-ADHD</th>
<th>P-ADHD</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE AT TEST*</td>
<td>12.44 (3.3)</td>
<td>11.91 (3.4)</td>
<td>11.84 (2.5)</td>
<td>10.70 (3.2)</td>
</tr>
<tr>
<td>WASI Score*</td>
<td>112 (11.0)</td>
<td>105 (10.5)</td>
<td>99 (14.3)</td>
<td>109 (16.8)</td>
</tr>
<tr>
<td>SES Score*</td>
<td>52.8 (6.2)</td>
<td>44.1 (10.1)</td>
<td>44.6 (10.5)</td>
<td>46.2 (11.5)</td>
</tr>
<tr>
<td>HANDEDNESS (R:L)</td>
<td>41:3</td>
<td>38:2</td>
<td>8:1</td>
<td>14:5</td>
</tr>
<tr>
<td>SEX (M:F)</td>
<td>23:21</td>
<td>24:16</td>
<td>4:5</td>
<td>17:2</td>
</tr>
<tr>
<td>AGE AT INJURY*</td>
<td>--</td>
<td>8.26 (3.6)</td>
<td>7.22 (2.4)</td>
<td>--</td>
</tr>
<tr>
<td>TIME SINCE INJURY*</td>
<td>--</td>
<td>3.65 (1.5)</td>
<td>4.62 (1.2)</td>
<td>--</td>
</tr>
</tbody>
</table>

*Mean (standard deviation)*
# Table 4

## Accuracy and Variability of Go Responses (Means and standard deviations)

<table>
<thead>
<tr>
<th></th>
<th>CON</th>
<th>TBI</th>
<th>S-ADHD</th>
<th>P-ADHD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ACCURACY (C)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NO</td>
<td>97.6 (3.9)</td>
<td>97.6 (2.9)</td>
<td>97.1 (3.4)</td>
<td>92.7 (5.6)</td>
</tr>
<tr>
<td>LOW</td>
<td>97.0 (3.8)</td>
<td>96.7 (4.6)</td>
<td>95.3 (5.2)</td>
<td>90.0 (8.5)</td>
</tr>
<tr>
<td>HIGH</td>
<td>96.9 (4.0)</td>
<td>95.7 (6.7)</td>
<td>95.9 (3.8)</td>
<td>90.8 (6.6)</td>
</tr>
<tr>
<td><strong>SDRT (C)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NO</td>
<td>116.8 (34.0)</td>
<td>147.1 (61.0)</td>
<td>128.1 (45.3)</td>
<td>162.8 (58.7)</td>
</tr>
<tr>
<td>LOW</td>
<td>119.6 (34.0)</td>
<td>144.0 (52.5)</td>
<td>144.6 (51.9)</td>
<td>142.2 (30.2)</td>
</tr>
<tr>
<td>HIGH</td>
<td>121.3 (36.9)</td>
<td>138.7 (48.9)</td>
<td>131.9 (30.3)</td>
<td>163.1 (46.0)</td>
</tr>
<tr>
<td><strong>ACCURACY (R)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NO</td>
<td>96.7 (3.5)</td>
<td>96.2 (6.7)</td>
<td>93.7 (7.6)</td>
<td>91.6 (7.8)</td>
</tr>
<tr>
<td>LOW</td>
<td>95.0 (5.9)</td>
<td>95.9 (8.0)</td>
<td>95.2 (4.6)</td>
<td>90.8 (5.0)</td>
</tr>
<tr>
<td>HIGH</td>
<td>95.4 (4.3)</td>
<td>94.3 (9.0)</td>
<td>92.6 (7.0)</td>
<td>91.2 (6.2)</td>
</tr>
<tr>
<td><strong>SDRT (R)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NO</td>
<td>107.1 (40.8)</td>
<td>131.6 (63.4)</td>
<td>171.4 (67.8)</td>
<td>160.1 (79.9)</td>
</tr>
<tr>
<td>LOW</td>
<td>107.6 (47.5)</td>
<td>121.1 (57.8)</td>
<td>144.0 (51.4)</td>
<td>158.6 (70.3)</td>
</tr>
<tr>
<td>HIGH</td>
<td>108.7 (51.7)</td>
<td>125.8 (52.8)</td>
<td>147.8 (71.1)</td>
<td>150.2 (55.4)</td>
</tr>
</tbody>
</table>

**Legend:** Accuracy (C) = Percent correct, Cancellation Version; SDRT (C) = Standard deviation of go reaction time, Cancellation Version; Accuracy (R) = Percent correct, Restraint Version; SDRT (R) = Standard deviation of go reaction time, Restraint Version
Table 5

*Regression Table: Significant Predictor: Age at Injury (all p’s <0.05)*

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>B</th>
<th>SE B</th>
<th>β</th>
</tr>
</thead>
<tbody>
<tr>
<td>CANCELLATION</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRT, NO</td>
<td>-18.67</td>
<td>4.92</td>
<td>-0.519</td>
</tr>
<tr>
<td>MRT, LOW</td>
<td>-15.05</td>
<td>4.68</td>
<td>-0.458</td>
</tr>
<tr>
<td>MRT, HIGH</td>
<td>-14.87</td>
<td>5.23</td>
<td>-0.414</td>
</tr>
<tr>
<td>SDRT, NO</td>
<td>-9.03</td>
<td>2.55</td>
<td>-0.493</td>
</tr>
<tr>
<td>SDRT, LOW</td>
<td>-8.84</td>
<td>2.08</td>
<td>-0.562</td>
</tr>
<tr>
<td>SDRT, HIGH</td>
<td>-7.91</td>
<td>1.78</td>
<td>-0.580</td>
</tr>
<tr>
<td>RESTRAINT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRT, NO</td>
<td>-15.74</td>
<td>3.95</td>
<td>-0.528</td>
</tr>
<tr>
<td>MRT, LOW</td>
<td>-17.91</td>
<td>3.95</td>
<td>-0.578</td>
</tr>
<tr>
<td>MRT, HIGH</td>
<td>-16.10</td>
<td>4.12</td>
<td>-0.521</td>
</tr>
<tr>
<td>SDRT, NO</td>
<td>-8.20</td>
<td>2.68</td>
<td>-0.432</td>
</tr>
<tr>
<td>SDRT, LOW</td>
<td>-9.83</td>
<td>2.04</td>
<td>-0.601</td>
</tr>
<tr>
<td>SDRT, HIGH</td>
<td>-7.66</td>
<td>2.22</td>
<td>-0.474</td>
</tr>
<tr>
<td>SSRT, LOW</td>
<td>-9.82</td>
<td>3.16</td>
<td>-0.436</td>
</tr>
<tr>
<td>SSRT, HIGH</td>
<td>-11.01</td>
<td>3.80</td>
<td>-0.413</td>
</tr>
</tbody>
</table>
Legend: MRT=Mean reaction time (milliseconds); SDRT=Standard deviation of go reaction time (milliseconds); SSRT=Stop signal reaction time (milliseconds); NO=neutral reward condition; LOW=Low reward condition; HIGH=high reward condition
Figure 10

Mean (SE) Percent Inhibition across Groups and Reward Conditions, Cancellation

Percent inhibition was not influenced by reward, nor was there a main effect of group.
SSRT decreased with increasing reward magnitude. Participants in the P-ADHD group exhibited slower SSRT relative to participants in the CON and TBI groups.
Figure 12

Mean (SE) MRT across Groups and Reward Conditions, Cancellation

MRT did not differ between groups, nor was there a significant effect of reward
Figure 13

*Mean (SE) Percent Inhibition across Groups and Reward Conditions, Restraint*

Reward increased the amount of responses inhibited. The P-ADHD group exhibited significantly more commission errors relative to the CON group.
Participants in the P-ADHD exhibited slower SSRT relative to participants in the CON group.

SSRT was not affected by reward.
Figure 15

*Mean (SE) MRT across Groups and Reward Conditions, Restraint*

MRT did not vary by reward condition or by group.
Chapter 4
The Relationship between Multi-Informant Behavioural Ratings and Inhibitory Control Performance on Cancellation and Restraint Tasks in Children with Traumatic Brain Injury

Common sequelae of childhood traumatic brain injury (TBI) include neuropsychological and behavioral disorders of inhibitory control (IC; e.g., Catroppa, Anderson, Morse, Haritou, & Rosenfeld, 2007; Dennis, Wilkinson, Koski, & Humphreys, 1995). The former include difficulties stopping an ongoing action, IC cancellation (Leblanc et al., 2005) and restraining a prepotent response, IC restraint (Levin, Hanten, Zhang, Swank, & Hunter, 2004). The latter include formal diagnoses of secondary attention-deficit/hyperactivity disorder (S-ADHD). Some 15-20% of children with TBI develop these de novo symptoms of ADHD (e.g., Max et al., 2005a, 2005b), diagnosis of which is associated with neurocognitive IC deficits (Konrad, Gauggel, Manz, & Scholl, 2000a, 2000b; Schachar, Levin, Max, Purvis, & Chen, 2004b; see Chapter 2). Problems with IC appear to be somewhat specific in this population: children with chronic-stage TBI and a S-ADHD diagnosis have difficulty canceling a prepotent response but are able to restrain a response before it is executed (Schachar et al., 2004b; see Chapter 3). This paper is concerned with how parents, teachers, and the children themselves view IC behaviours after TBI, as manifested as inattention, hyperactivity, and impulsivity, and with how informant ratings of behavior are related to neurocognitive IC performance.

Parents of children with TBI rate them as inattentive, aggressive, dysexecutive, and dysregulated (Cole et al., 2008; Mangeot, Armstrong, Colvin, Yeates, & Taylor, 2002; Sesma, Slomine, Ding, McCarthy, & CHAT, 2008; Schachar et al., 2004b; Vriezen & Pigott, 2002; Yeates, et al., 2005). Although parents of children with TBI also rate them as exhibiting poor metacognition (i.e., cognition about one’s own cognition; Mangeot, et al., 2002; Sesma et al., 2008; Vriezen &
Pigott, 2002), the discrepancy between parent and self-reports, which would provide insight into the “awareness of deficit”, has not been examined. Further, the relationship between “awareness of deficit” following childhood TBI and neurocognitive function is also unclear. Children with TBI overestimate their memory and learning abilities (Hanten et al., 2004), are impaired in detecting the adequacy of their own knowledge (Dennis, Barnes, Donnelly, Wilkinson, & Humphreys, 1996), and exhibit less post-error slowing than controls after failed inhibition trials, suggesting impaired error monitoring (i.e., poor awareness of errors; Ornstein et al., 2009). Retrospectively, however, they appear able to accurately evaluate their own performance (Hanten et al., 2004).

Parent, teacher, and self-ratings have often been obtained in separate studies, so it is not clear what each informant rates about the same child, and the degree of rating concordance is unknown. The pattern and informant concordance of ratings for children with S-ADHD relative to those with TBI without S-ADHD is unclear. Further, although children with developmental or primary ADHD (P-ADHD) and children with TBI and S-ADHD have superficially similar clinical symptoms, it is unclear how the two groups are rated across different environments. Past studies have indicated that the performance of children with TBI on executive functioning tasks is poorly related to parent executive function ratings (Mangeot, et al., 2002; Vriezen & Pigott, 2002), and impulsivity ratings are unrelated to impulsivity performance (Carrillo-de-la-Pena, Otero, & Romero, 1993; see also McAuley, Chen, Goos, Schachar, & Crosbie, 2010). Perhaps the most significant question, then, is whether informant ratings of behavior, whether concordant or not, predict neurocognitive performance, which, in this context, should involve a theoretically meaningful process rather than an omnibus psychometric measure, and should have both face and ecological validity.
We explored a number of issues:

1. Which IC problems do parents, teachers, and the children themselves endorse in TBI, S-ADHD, P-ADHD, and typically developing children and adolescent groups? How do children with TBI (both with and without a S-ADHD diagnosis) differ from children with a diagnosis of P-ADHD? How aware of their IC problems are children in each group? We rated IC for purposes of this study with measures of inattention, impulsivity, and hyperactivity, as well as measures of ADHD symptoms, based on the parent, teacher, and self-report forms of the Conners 3rd Edition Rating Scales (Conners 3; Conners, 2008).

2. What is the level of concordance for IC ratings across raters, subscales, and groups? Do ratings vary with the rater, and with whether or not the child with TBI had diagnosed S-ADHD?

3. How are informant ratings of IC related to neurocognitive measures of withholding and stopping a response as measured by the restraint and cancellation versions of the stop signal task (SST; Schachar et al., 2007)?

7 Method

7.1 Participants

Participants included children and adolescents aged 7 to 17. A brief interview was conducted with each participant’s parent during an initial recruitment phone call to collect demographic information and ensure eligibility for participation. Participants in the control (CON) group were excluded if they had a reported history of P-ADHD, TBI, neurological or psychiatric disorders, mental retardation, learning disabilities, and sensory or motor impairments. Exclusion criteria for TBI and P-ADHD groups included the presence of a severe psychiatric disorder (e.g. psychosis), mental retardation, and sensory or motor impairments. Participants with Wechsler Abbreviated
Scale of Intelligence (WASI) Full Scale IQ scores under 75 were excluded. The Hollingshead Four-Factor Index of socioeconomic status (SES; Hollingshead, 1975) was calculated from information about parental education and occupation. Family SES scores were calculated by averaging the SES scores of both parents (or from one parent, when this was the only information available).

Sixty-six typically developing children and adolescents were recruited into the CON group through flyers and community advertisements. Thirteen participants were excluded based on clinically significant elevations on the Conners 3 rating scales (see below), and 9 participants cancelled or missed their appointments. The final CON group consisted of 44 participants (21 female, 23 male; mean age, 12.44 years).

Participants in the TBI group (n=63) were recruited through trauma registries at the Hospital for Sick Children in Toronto. Because IC and other cognitive problems abate with increasing time since injury (Leblanc et al., 2005) while ratings of adaptive behaviors remain stable or increase with time (Sesma et al., 2008; Taylor et al., 2002), all children were all in the chronic phase of a single TBI and had had no pre-injury neurological disorders. Inclusion criteria included the presence of a non-inflicted, non-penetrating TBI that occurred 1 to 6 years prior to assessment and hospitalization for the TBI for at least one night. Ten participants cancelled or missed appointments, and 4 were excluded due to parental reports of a pre-injury P-ADHD diagnosis, resulting in a TBI group of 49 participants (21 female, 28 male; mean age, 11.89 years; mean age of injury, 8.07 years). Severity of injury was based on initial post-resuscitation Glasgow Coma Scale (GCS) scores (Teasdale & Jennet, 1974), separating participants into those with mild (n=28), moderate (n=6), and severe (n=16) injuries.
Twenty children from the community who had been diagnosed with ADHD by a health care professional and had a negative history for TBI were recruited into the P-ADHD group. Two participants were excluded due to a lack of parent and teacher endorsement of clinically significant ADHD symptoms required for a diagnosis of ADHD on the Conners 3 (see below). The final P-ADHD group (n=18; 2 female, 16 male; mean age, 10.89 years) included 12 participants that were either drug naïve or were not currently taking any psychiatric medication for their ADHD symptoms. The remaining participants were currently undergoing pharmacological treatment, and were asked to discontinue treatment for 24 hours prior to testing.

Informed consent was obtained prior to testing from each participant’s parent, and assent was obtained from the participants themselves. All procedures in this study were conducted with approval of the Research Ethics Boards at the Hospital for Sick Children and the University of Toronto.

7.2 Questionnaires: Conners 3rd Edition

The Full Form of the Conners 3 (Conners, 2008) was administered to each participant’s parent (Conners-P, 110 items) and teacher (Conners-T, 115 items). Participants over the age of 8 were administered the self-report scales (Conners-SR, 99 items). Each scale has moderate to high internal consistency, test-retest reliability, and inter-rater reliability (Conners, 2008). The Conners-P and Conners-SR were completed as part of a larger study examining IC following TBI, and the Conners-T was mailed to each participant’s teacher.

For purposes of the present questions about IC, scales of interest from the Conners 3 were those that reflected IC disturbances, specifically those measuring inattention and hyperactivity/impulsivity. From the Conners 3 Content Scales, we used the Inattention (IN) and Hyperactivity/Impulsivity (HY) subscales. The DSM-IV-TR Symptom Scales assess symptoms
associated with ADHD, so we examined ratings from the ADHD inattentive (DSM-AN) and the ADHD hyperactive/impulsive (DSM-AH) subscales. Raw scores on each Content and DSM-IV-TR Symptom subscales were converted into T-scores, adjusted for each participant’s age and sex. All T-scores have a mean of 50, with a standard deviation (SD) of 10. T-scores greater than 1.5 SD above the mean (i.e., over 65) are considered to be elevated for age and sex (Conners, 2008). The Conners 3 also includes DSM-IV-TR Symptom Counts for all ADHD subtypes (inattentive, hyperactive/impulsive, and combined subtypes). Symptom Counts represent the explicit DSM-IV-TR symptoms required for a diagnosis of either subtype.

Thirteen participants in the CON group exhibited elevated T-Scores on the DSM-IV-TR Symptom Scales and met criteria for a disorder on the DSM-IV-TR Symptom Counts, thus were excluded from further analyses. Two participants were excluded from the P-ADHD group due to the absence of parent and teacher ratings of significant ADHD symptoms that are required for an ADHD diagnosis.

The Conners 3 was also used to identify children in the TBI group who reached criteria for S-ADHD. These participants met criteria for inclusion into the TBI group, had no diagnosed P-ADHD prior to the TBI, and had met diagnostic criteria for ADHD (any subtype) on the Conners-P and/or Conners-T. Because it is not clear if the DSM criteria for P-ADHD are necessary for the classification of participants as S-ADHD, and because age at onset of any S-ADHD can be no earlier than the age at TBI, we waived the age requirement for diagnosis as well as the requirement that ADHD symptoms must be present in at least 2 environments (American Psychological Association, 2000). Nine participants in the TBI group without evidence of pre-injury P-ADHD met criteria for S-ADHD through parent and/or teacher ratings (S-ADHD group, 5 female, 4 male; mean age, 11.84 years; mean age at injury, 7.22 years), and
40 participants without evidence of ADHD on the Conners 3 remained in the TBI group (16 female, 24 male; mean age, 11.91 years; mean age at injury, 8.26 years).

7.3 Neurocognitive testing: Stop Signal Tasks

The SST is an IC task based on a formal model conceptualizing performance as a race between “go” and “stop” processes (Logan & Cowan, 1984; Logan, 1994; Verbruggen & Logan, 2008). These processes “race” against each other and the process that “wins” the race determines the outcome (i.e., response execution or inhibition; Logan & Cowan, 1984; Logan, 1994). The race model allows for the measurement of the latency of IC (i.e., the stop signal reaction time, SSRT), which is an unobservable, internally generated act of control (Logan, 1994). Figure 16 shows a cartoon of the cancellation and restraint versions of the SST utilized in the present study (Logan, 1994; Schachar et al., 2007). Both versions consist of a primary visual choice reaction time task involving a go signal and a secondary task involving a stop signal that indicated the need to inhibit a response (Logan & Cowan, 1984; Logan, 1994). In the cancellation version, the stop signal was presented after a delay following the go signal in order to interrupt an already executed response, and was varied dynamically to ensure inhibition on approximately 50% of the stop trials. In the restraint version of the task, the stop signal was presented concurrently with the go signal to prevent a response from being executed (Schachar et al., 2007).

The latency to inhibit a response (SSRT) on both versions of the SST was determined via the integration procedure (Logan, 1994). First, the go reaction times in non-stop signal trials were rank ordered, and the go reaction time that corresponded to the probability of inhibition was determined. The SSRT was estimated by subtracting the mean delay from this new “integrated go reaction time.” Participant data from the SST were excluded if there was less than 66% accuracy on go trials, mean go reaction time (MRT) was less than 100 milliseconds, or percent
inhibition was less than 12.5% or greater than 87% (for the cancellation version; only Schachar et al., 2004; Shuster & Toplak, 2009). Based on these criteria, 3 participants were excluded from analyses of cancellation data (n=2, TBI; n=1, P-ADHD), and 2 participants were excluded from restraint analyses (n=1, CON; n=1, P-ADHD).

7.4 Statistical Analyses

Age of injury, time since injury (for TBI and S-ADHD groups), age at test, WASI scores, and SES scores were compared between groups utilizing an analysis of variance (ANOVA) with group (CON, TBI, P-ADHD, S-ADHD) as the between subjects variable.

Ratings that met criteria for inconsistent responding on the Inconsistency Index of the Conners 3 were considered invalid and were subsequently excluded from future analyses. Group differences in ratings were analyzed separately for each scale using ANOVAs with SES as a covariate. Because we used parent and teacher ratings to define the S-ADHD group, confirm the inclusion of participants in the P-ADHD group, and exclude participants in the CON group with clinically significant elevations, making comparisons across all four groups on these scales would not be meaningful. Instead, we limited the comparison between groups on the Conners-P and Conners-T to the following: CON vs. all groups; TBI vs. P-ADHD; S-ADHD vs. P-ADHD. Pearson correlations were conducted to explore associations between rating scales, the relationship between SST performance and ratings, and the relationship between SST performance and the number of ADHD symptoms.

For each subscale, the discrepancy between raters was obtained by calculating the difference score between two raters (e.g., subtracting the IN T-score on the Conners-P from the IN T-score on the Conners-T). Negative or positive scores indicated that one rater rated a participant more negatively or more positively than another. Group differences in discrepancy scores were
examined with separate ANOVAs for each discrepancy rating, with SES as a covariate and group as the between-subjects factor. Concordance in discrepancy ratings was defined as scores within 1 SD of the mean of each subscale discrepancy rating. We also rated each discrepancy rating on a binary scale that indicated whether or not each rating for each participant was concordant or not (i.e., whether it fell within 1 SD of the mean). We analyzed this concordance data with a series of non-parametric Kruskal-Wallis tests, and post-hoc analyses were conducted with separate Mann-Whitney U tests with the alpha level adjusted to 0.008 to adjust for multiple group comparisons.

Group differences in SST performance were conducted with separate ANOVAs with group and order of task administration (cancellation first, cancellation second) as between-subjects variables, and age as a covariate. Stepwise linear regression analyses were conducted to examine the diagnostic utility of inhibition measures on the SST. We examined whether or not SSRT and percent inhibition (restraint only) predicted parent, teacher, and/or concordance of parent and teacher classification of ADHD subtypes on the DSM-IV-TR Symptom Counts. Percent inhibition from the cancellation data was not entered as a predictor because the tracking algorithm was designed to limit the probability of inhibition to approximately 0.5. Severity of injury was unrelated to ratings by any informant, or to performance on the SST (data not shown), so will not be discussed further.

8 Results

8.1 Participant Characteristics

Participant characteristics are presented in Table 6. Age at assessment did not differ between groups, and age of injury and time since injury was similar between the TBI and S-ADHD groups. IQ scores differed between groups (F(3, 109)=4.207, p=0.007), but all mean scores were
within the normal range. SES was greater in the CON group relative to all other groups (F(3, 105)=6.797, p<0.001; planned comparisons, all p’s<0.05), and so was used as a covariate in subsequent analyses.

8.2 Validity of Ratings

Parent ratings were available for all but 2 participants in the CON group (CON, n=44; TBI, n=40; S-ADHD, n=9; P-ADHD, n=18). We received 61% of the teacher rating scales (CON, n=27; TBI, n=22; S-ADHD, n=7; P-ADHD, n=12), and self-reports were completed by 77% of participants (CON, n=36; TBI, n=29; S-ADHD, n=8; P-ADHD, n=12). Based on criteria for invalid responses on the Inconsistency Index of the Conners 3, 12 parent reports (CON, n=3; S-ADHD, n=3; P-ADHD, n=5), 3 teacher reports (P-ADHD), and 9 self-reports (CON, n=2; TBI, n=4; S-ADHD, n=1; P-ADHD, n=2) were excluded from further analyses.

8.3 Group Differences across Raters

See Table 7 for a summary of group differences across the Conners-P, Conners-T, and Conners-SR.

8.4 Conners-P: Group Differences

Group differences in parent ratings were found for all Content and DSM-IV-TR Symptom Scales (all p’s<0.001; see Figure 17). Parent ratings for the CON group were age-typical (i.e., mean T-scores below 50). Although we found differences between parent ratings of CON and TBI participants on a number of subscales, the mean T-scores of the TBI group were also within the normal range.

Parents of typically developing children and adolescents rated their children as exhibiting significantly lower T-scores on the IN (F(3, 92)= 73.393), HY (F(3, 92)= 56.686), DSM-AN
(F(3, 92)=74.093), and DSM-AH (F(3, 92)=50.03) subscales compared to the clinical groups. In addition, parent ratings of TBI participants were lower on all subscales compared to the P-ADHD group. Parent ratings were generally similar in the two ADHD groups, except for the IN subscale where participants with P-ADHD were rated as exhibiting greater impairments than the S-ADHD group.

### 8.5 Conners-T: Group Differences

Teacher ratings differed significantly between groups on Content and DSM-IV-TR Symptom Scales (all p’s<0.001; see Figure 18). No differences were found between CON and TBI teacher ratings on any subscale, and all teacher ratings of these participants were within the normal range. Teachers rated participants in the CON and TBI groups as exhibiting significantly lower scores on the IN (F(3, 56)=17.703), HY (F(3, 56)=21.56) and DSM-AH (F(3, 56)=20.343) subscales relative to the ADHD groups. Greater impairments on the DSM-AN (F(3, 56)=21.685) subscale were found for the P-ADHD group compared to the other groups. The two ADHD groups were rated similarly on the IN, HY, and DSM-AH subscales.

### 8.6 Conners-SR: Group Differences

Typically developing children yielded self-report measures within the normal range (see Figure 19). Despite differences in self-report measures between the CON and TBI group on a number of subscales, T-scores on all scales were within the normal range for the TBI group. Moreover, no group rated itself with difficulties (i.e. no mean T-scores were above 65) in any domain. Groups rated themselves similarly on the HY and DSM-AH subscales. The CON group rated themselves as having fewer difficulties on the IN (F(3, 67)=4.585, p=0.006) and DSM-AN (F(3, 67)=5.072, p=0.003) subscales than any of the other groups.
8.7 Concordance between the Conners-P and Conners-T

Significant correlations were found between parent and teacher ratings on all Content and DSM-IV-TR Symptom Scales. Following correction for attenuation, all subscales yielded medium to large correlations between raters: IN, r=0.681; HY, r=0.694; DSM-AN, and r=0.672; DSM-AH, r=0.710. These data indicate fair, although not perfect, agreement between parent and teacher ratings of behavior.

Parent-teacher discrepancy scores across subscales were analyzed to further investigate concordance between raters (see Table 8). Negative scores specify that teachers endorsed a greater number of difficulties, whereas positive scores indicate that parents reported more difficulties. All discrepancy measures for the CON group were within 1 SD of the mean for all subscales, suggesting considerable concordance between teachers and parents. Concordance was also found for discrepancy ratings in the TBI, S-ADHD, and P-ADHD groups. Significant group differences between discrepancy ratings were found for the IN (F(3, 56)=3.210, p=0.03), HY (F(3, 56)=4.114, p=0.011), and DSM-AH (F(3, 56)=5.238, p=0.003) subscales, with marginal significance for the DSM-AN (F(3, 56)=2.747, p=0.052) subscale. Parents identified more problems than teachers (there were more positive discrepancy scores) in the TBI and P-ADHD groups compared to the CON group discrepancy scores.

We also assigned a rating to each subscale depending on whether or not parents and teachers met concordance (i.e., scores within 1 SD of the mean), with a 1 indicating concordance, and 0 indicating non-concordance. We then analyzed group differences utilizing a Kruskal-Wallis test, and significant findings were further analyzed utilizing Mann-Whitney U tests with α levels adjusted to 0.008 to adjust for multiple group comparisons. No significant group differences were found for any subscale.
8.8 Concordance between Conners-P and Conners-SR

Significant correlations were found between parent and self-report ratings on both Content Scales and the only significant correlation found on the DSM-IV-TR Symptom Scales was for DSM-AN. Following correction for attenuation, significant correlations were: IN, r=0.423; HY, r=0.303; and DSM-AN, r=0.441. These findings suggest modest agreement between parent and self-report ratings of a subset of behaviors assessed.

Table 9 displays the parent-self-report discrepancy scores. Concordance between parent and self-reports across all scales were found for the CON and TBI groups. Both ADHD groups were rated by their parents as exhibiting more disturbances on the Conners 3 relative to self-report ratings. Parent and self-report ratings in the P-ADHD group were not concordant. In the S-ADHD group, concordance was found only for the inattention subscales. Significant group differences were found for all subscales (IN: F(3, 64)=12.822, P<0.001, HY: F(3, 64)=15.319, p<0.001, DSM-AN: F(3, 64)=17.762, p<0.001, DSM-AH: F(3, 63)=12.495, p<0.001). Planned comparisons revealed more positive discrepancy scores (i.e., greater impairments reported by parents) in the P-ADHD and S-ADHD groups relative to both the CON and TBI groups in subscales assessing inattention (IN and DSM-AN) and hyperactivity/impulsivity (HY and DSM-AH). The P-ADHD group exhibited more positive discrepancy scores relative to the S-ADHD group on scales measuring inattention (IN and DSM-AN).

Significant group differences in concordance ratings were found for the IN ($\chi^2$=8.290, df=3, p=0.034), HY ($\chi^2$=20.494, df=3, p<0.001), DSM-AN ($\chi^2$=12.114, df=3, p=0.006), and DSM-AH ($\chi^2$=11.666, df=3, p=0.007) subscales. Post-hoc tests revealed differences between the CON and P-ADHD groups on the IN (U=36.5, p=0.004), HY (U=12.0, p<0.001), DSM-AN (U=30.5, p=0.001), and DSM-AH (U=33.5, p=0.002) subscales. The TBI group differed from the P-
ADHD group on the HY (U=21.0, p=0.001) and DSM-AN (U=31.0, p=0.006) subscales. No other significant differences were found. In brief, the P-ADHD group exhibited poorer concordance on ratings of inattention and hyperactivity/impulsivity relative to the CON and TBI groups.

8.9 Concordance between Conners-T and Conners-SR

No significant correlations were found between teacher and self-report ratings on any Content or DSM-IV-TR Symptom Scales. Table 10 displays the teacher-self-report discrepancy scores. Concordance was found for all discrepancy scores in the CON group. Concordance was found across all subscales for the TBI group. In the S-ADHD group, concordance was found for all scales with the exception of hyperactivity/impulsivity ratings (HY and DSM-AH), and near-perfect concordance was reached on ratings of DSM symptoms of inattention. In the P-ADHD group, there was concordance across all subscales except for the DSM-AN scale.

Significant group differences between discrepancy ratings were found for the HY (F(3, 37)=3.848, p=0.017), DSM-AN (F(3, 27)=3.715, p=0.02), and DSM-AH (F(3, 37)=3.247, p=0.033) subscales. Planned comparisons revealed less positive discrepancy scores in the CON and TBI groups relative to the S-ADHD group on the HY and DSM-AH subscales, and relative to the P-ADHD group on the DSM-AN subscale.

Concordance analyses (Kruskal-Wallis tests) were significant for the DSM-AN (χ²=7.469, df=3, p=0.05) subscale, yet post-hoc tests did not reveal significant differences between groups at the adjusted alpha level.

A summary of group differences in discrepancy measures is presented in Table 11.
8.10 IC Performance: Cancellation and Restraint

8.10.1 Cancellation

The tracking algorithm successfully limited the probability of inhibition to approximately 0.5 across groups. There was a significant group effect on SSRT (F(3, 100)=2.858, p=0.041). Planned comparisons revealed that the P-ADHD group exhibited longer SSRT relative to participants in the TBI (p=0.026) and CON (p=0.005) groups. The S-ADHD group did not differ from any other group, suggesting intermediate SSRT performance in this group across the task. MRT was similar between groups, and there were no task order effects.

8.10.2 Restraint

Inhibition measures did not differ between groups, but planned comparisons revealed marginal differences in SSRT between CON and P-ADHD groups (p=0.051), suggesting poorer restraint performance in the P-ADHD group relative to typically developing children. There were no group differences in MRT. Task order did not alter SSRT, percent inhibition, or MRT.

8.11 Relationship between SST Performance and Conners 3 Ratings

The relationship between rating scales and SST performance are presented in Table 12. In the CON group, significant correlations were: SSRT in cancellation and Conners-T ratings of IN, HY, DSM-AN, and DSM-AH; percent inhibition in restraint and Conners-T ratings of IN, HY, DSM-AN, and DSM-AH; MRT in cancellation and Conners-SR ratings of HY and DSM-AH; SSRT in restraint and Conners-SR ratings of HY and DSM-AH. Significant correlations in the TBI group were: percent inhibition in restraint and Conners-P ratings of HY; percent inhibition in restraint and Conners-SR ratings of IN. In the P-ADHD group, significant correlations were: percent inhibition in restraint and Conners-P ratings of IN; SSRT in restraint and Conners-P
ratings of DSM-AN; MRT in cancellation and Conners-T ratings of HY and DSM-AH; SSRT in cancellation and restraint and Conners-T ratings of HY and DSM-AH.

8.12 Relationship between the number of ADHD Symptoms and IC Performance

8.12.1 Cancellation

Significant correlations were found between SSRT and the number of Conners-P inattentive (r=0.265, p=0.048) and hyperactive/impulsive symptoms (r=0.316, p=0.018). SSRT was significantly correlated with Conners-T inattentive (r=0.335, p=0.043) and hyperactive/impulsive symptoms (r=0.323, p=0.051). Conners-SR ADHD symptoms were uncorrelated with SSRT.

8.12.2 Restraint

Percent inhibition was significantly correlated with the number of Conners-P hyperactive/impulsive symptoms (r=-0.268, p=0.042). Conners-T and Conners-SR ADHD symptoms were uncorrelated with SSRT.

8.13 Is IC performance related to ADHD status?

Regression analyses were performed to examine whether neurocognitive IC performance predicted rater classification into ADHD subtypes. Thus cancellation and restraint inhibition (SSRT and percent inhibition) were entered as potential predictors of parent, teacher, or self-report classification of participants into the ADHD inattentive, hyperactive/inattentive, or combined subtypes on the DSM-IV-TR Symptom Counts. We conducted separate linear stepwise regression analyses for each type of rating scale.
8.13.1 Cancellation

Table 13 displays the results from the regression analyses for cancellation. SSRT significantly predicted parent classification of ADHD, inattentive ($r^2=0.056, p=0.015$), hyperactive/impulsive ($r^2=0.056, p=0.015$), and combined ($r^2=0.082, p=0.003$) subtypes. SSRT also predicted teacher classifications of ADHD, inattentive ($r^2=0.170, p=0.001$), hyperactive/impulsive ($r^2=0.075, p=0.027$), and combined ($r^2=0.071, p=0.032$) subtypes. No inhibition variable predicted self-report classification into any ADHD subtype.

8.13.2 Restraint

Table 13 displays the regression results for restraint. Neither SSRT nor percent inhibition on the restraint task significantly predicted parent classification of ADHD inattentive or hyperactive/impulsive subtype. Percent inhibition significantly predicted parent classification of ADHD, combined subtype ($r^2=0.040, p=0.036$). Restraint inhibition predicted teacher ADHD classification: percent inhibition predicted ADHD, inattentive subtype ($r^2=0.134, p=0.002$), and SSRT predicted ADHD, hyperactive/impulsive ($r^2=0.059, p=0.049$) and combined ($r^2=0.066, p=0.038$) subtypes. No inhibition variable predicted self-report classification into any ADHD subtype.

8.14 Agreement between Parent and Teacher Ratings and SST Performance

Linear regression analyses were conducted to examine if IC performance predicted parent and teacher agreement of classification of participants into ADHD subtypes. Agreement between parent and teacher ratings was defined as both raters identifying each participant as 1) meeting criteria for inattentive or hyperactive/impulsive or combined ADHD subtype or 2) not meeting criteria for any ADHD subtype. SSRT for both tasks and percent inhibition from the restraint
task were entered into regression analyses as potential predictors, with separate analyses run for
cancellation and restraint. Agreement between raters in classifying children and adolescents as
meeting criteria for ADHD, combined subtype was significantly predicted by SSRT in the
cancellation task \( (r^2 = 0.020, p = 0.052) \). No other IC measures were significant predictors of
agreement of classification.

9 Discussion
This paper addresses three issues about IC that concerned how it is rated behaviorally by
multiple informants (parent, teacher, and self), the concordance of ratings across raters, and the
relation of neurocognitive cancellation IC and restraint IC performance to informant ratings of
IC behavior. The purpose of the paper was to understand more about IC following childhood
TBI; in particular, to delineate similarities and differences in IC within and between four groups:
children with TBI, children with TBI and S-ADHD, children with P-ADHD, and a typically
developing control group. The data bear on a number of issues: Parent and teacher IC profiles;
rating concordance; self-report IC profile, which informs the level of awareness of deficits in
children with TBI; the relation between IC ratings and cancellation and restraint; the diagnostic
utility of neurocognitive IC performance for ADHD ratings; and key differences between
primary and secondary forms of ADHD.

9.1 Parent and teacher IC profiles
Parents and teachers of children with ADHD rated them as inattentive, hyperactive, and
impulsive. A diagnosis of S-ADHD following TBI, not TBI alone, increases the identification of
IC problems by parents and teachers. Our data extend previous work on IC ratings in childhood
TBI. Although Yeates and colleagues (2005) showed that parent ratings of attention problems
and ADHD symptoms were greater for participants with TBI relative to non-head injured
controls, the TBI group was not divided into those with and without S-ADHD, so group differences may reflect inclusion of children with clinically significant symptoms. Indeed, children with S-ADHD exhibit more attentional difficulties than children with TBI without ADHD (Slomine, Salorio, Grados, Vasa, Christensen, & Gerring, 2005).

The absence of significant ADHD symptoms in the TBI group implies that these participants are behaving normally and/or that any acute IC impairment is now attenuated. By 2 years post-injury, performance measures of inattention and impulsiveness improve (Wassenberg, Max, Lindgen, & Schatz, 2004) and normal IC performance is achieved (Leblanc et al., 2005), despite the presence of deficits in the acute phase of injury. A proposed “recovery of function” in the TBI group might be associated with atypical activity in neural circuits that support behaviour. For example, children with TBI exhibit similar attention performance and activate the same neural networks subserving attention as non-head injured controls, but exhibit hyperactivation in the same areas (Kramer et al., 2008). According to McAllister and colleagues (2001), putative brain mechanisms may include compensation or greater activation of neural resources due to effortful processing, or an over-commitment of neural resources that does not alter performance but improves subtle deficits that have occurred as a result of the TBI (McAllister, Sparling, Flashman, & Saykin, 2001).

Despite elevated IC ratings by parents and teachers for both ADHD groups, the rating profiles were not identical in the two groups. The groups differed in terms of parent ratings of inattention on the Content Scales and teacher ratings of inattention on the DSM-IV-TR Symptom Scale, with greater difficulties identified in children with P-ADHD. This finding is surprising given that the inattentive ADHD subtype predominates in S-ADHD (Levin, Hanten, Max, Li, Swank, Ewing-Cobbs, et al., 2007; Max et al., 2005a; 2005b) and that the most common behavioral
problem endorsed by parents and teachers of children with S-ADHD is a short attention span (Schachar et al., 2004b). Moreover, hyperactive symptoms in children with S-ADHD tend to decline over the first few years following TBI (Levin et al., 2007), suggesting that hyperactivity is generally more characteristic of P-ADHD than of S-ADHD. Of the 9 participants, 4 met criteria for the Inattentive subtype, 4 met criteria for the Hyperactive/Impulsive subtype, and 2 met criteria for ADHD Combined subtype, so this conclusion should be tempered by the relatively small sample size in the S-ADHD group. Although teachers and parents flag ADHD rather than TBI, primary and secondary forms of ADHD are rated differently, suggesting that at some level these disorders are recognized as being phenotypically distinct in real-world contexts.

9.2 Rating concordance

Parents and teachers showed moderate to high agreement, suggesting that these informants reliably identified similar behaviors in children and adolescents. These data are consistent with previous work that showed high correlations between teacher and parent S-ADHD ratings (Schachar et al., 2004b). In contrast, concordance between ratings of ADHD symptoms in children with P-ADHD have exhibited only partial or modest agreement (i.e., low to medium correlations; DuPaul, Ervin, Hook, & McGoey, 1998; Hartman, Rhee, Willcutt, & Pennington, 2007; Malhi, Singhi, & Sidhu, 2008; Murray et al., 2007; Sprafkin, Gadow, Salisbury, Schneider, & Loney, 2002; Sullivan & Riccio, 2007; Willcutt, Hartung, Lahey, Loney, & Pelham, 1999), which may be related to the situational specificity of ADHD symptoms, or the fact that parents and teachers observe different but equally valid behaviors (Gomez, 2007; Hartman et al., 2007). Classroom observations may represent a more rule-governed ecology than observations made at home, resulting in more ADHD behaviors displayed in the home environment.
9.3 Self-report IC profile

Generally, there was poor agreement between child and others’ perception of the child’s behavior. This implies that declarative knowledge about one’s own cognitive and behavioral (dis)abilities, or metacognitive knowledge, is still relative immature in our sample of participants aged 7-17 years old. Metacognitive knowledge interacts with other processes such as metacognitive monitoring, or the conscious awareness and online evaluation of thoughts and behaviors, and metacognitive control, or the self-regulation and adjustment of cognition and behavior (Mazzoni & Nelson, 1998; Toglia & Kirk, 2000). Overall competence in each of these domains increases with age (Schneider, Vise, Lockl, & Nelson, 2000) and is associated with increased competence in other aspects of cognition (see Hanten et al., 2004).

Adults with TBI do not always acknowledge injury-related deficits (Hart, Whyte, Kim, & Vaccaro, 2005; O’Keeffe, Dockree, Moloney, Carton, & Robertson, 2007; Vanderploeg, Belanger, Duchnick, & Curtiss, 2007; Spatt, Zebenholzer & Oder, 1997). We present new evidence that children with TBI in the chronic phase of recovery exhibit “awareness” of their behaviors. To be sure, the TBI group performed normally on the Conners 3 subscales. It may be that these children experienced “unawareness” in the acute phase of injury, but this has since recovered with time since injury, which would be consistent with findings from the adult TBI literature (Hart et al., 2009; Lanham, Weissenburger, Schwab, & Rosner, 2000; Powell, Machamer, Temkin, Dikmen, 2001; Vanderploeg et al., 2007).

In the S-ADHD group, correlations between parent and self-report ratings were small, and concordance was found only for subscales that measured inattention. Relative to self-report ratings, parents endorsed a greater number of ADHD symptoms in the S-ADHD group. Thus, children with S-ADHD exhibit “unawareness” of deficits that are diagnostic of the disorder, in
particular for hyperactive/impulsive behaviours. This parallels what is observed in adults with TBI, who exhibit poor awareness for behavioral and affective difficulties (Bivona et al., 2008; Hart, Sherer, Whyte, Polansky, & Novack, 2004; Hart et al., 2009; Sherer et al., 1998). Although acknowledgement of deficits is not always predictive of better outcomes (Bach & David, 2006), poor self-awareness in TBI populations has been linked to poor rehabilitation and adaptive outcomes, occupational and relational difficulties, increased maladaptive behaviour, and greater family distress (Prigatano, Borgaro, Baker, & Wethe, 2005; Sherer et al., 1998; Trudel et al., 1998; Wise et al., 2005). We did not directly assess these measures here, but note that the development of S-ADHD is associated with high psychosocial adversity, and poor adaptive and family functioning (Gerring et al., 1998; Max et al., 2004; Max et al., 2005b).

Crosson and colleagues (Crosson et al., 1989) have proposed a hierarchical approach to awareness of deficits: emergent awareness, or the ability to detect cognitive and behavioural deficits as they occur; intellectual awareness, which is similar to metacognitive knowledge; and anticipatory awareness, or predicting when problems will occur as a result of one’s own deficits. Previous data has shown that children with TBI are impaired in emergent awareness or metacognitive monitoring as evidenced by an error monitoring deficit on the SST (Ornstein et al., 2009); that they overestimate their abilities and competencies is consistent with deficits in anticipatory awareness (Hanten et al., 2004). We add to this knowledge base in the present study by showing that metacognitive knowledge is impaired in a subset of children with TBI who also have S-ADHD. Our data suggest the presence of a monitoring deficit that may be due to an inability to accurately integrate self-knowledge with self-monitoring (Hanten et al., 2004), and implies a relationship between poor awareness of behaviors in everyday life with ecologically valid laboratory-based tasks.
Children in the P-ADHD group also exhibited little awareness of deficits, and their ratings correlated poorly with those of parents and teachers, in agreement with studies that showed that children with P-ADHD report fewer hyperactive/impulsive symptoms and oppositional behaviors relative to parents and teachers (Loeber, Green, Lahey, Stouthamer-Loeber, 1991) and display poor awareness of IC performance on the SST (Stevens, Quittner, Zuckerman, & Moore, 2002). Deficits in metacognitive knowledge may coincide with difficulties that children with P-ADHD have with metacognitive monitoring and control on the SST (Schachar et al., 2004a).

In sum, discrepancy analyses revealed that children with TBI without S-ADHD did not exhibit “unawareness of deficits”, but children with S-ADHD failed to identify a number of problematic behaviors that parents and teachers flagged. The implication of these results is that multi-informant ratings can be used to accurately assess the behaviour of children with TBI across contexts, and “unawareness of deficits” is a symptom of S-ADHD (and P-ADHD) but not childhood TBI in general.

9.4 Relationship between Multi-Informant Ratings and Inhibitory Control Performance

Cancellation and restraint are fundamentally different forms of IC. Each follows a distinct developmental trajectory (Williams, Ponesse, Schachar, Logan, & Tannock, 1999; Johnstone et al., 2007) and is depends on separate, but overlapping neural systems involving the prefrontal cortex and basal ganglia (e.g., Chevrier, Noseworthy, & Schachar, 2007; Kelly et al., 2004; Konishi, Nakajima, Uchida, Sekihara, & Miyashita, 1998; Konishi et al., 1999). Slower SSRT in the cancellation task is a well-documented deficit in children with P-ADHD (see Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005) and is thought to reflect frontostriatal dysfunction (e.g., Aron & Poldrack, 2005; Kieling, Goncalves, Tannock, & Castellanos, 2008). Compared to
controls, children with P-ADHD also experience deficient restraint performance as evidenced by longer SSRT and less percent inhibition (i.e., more commission errors) in the restraint version of the SST (Schachar et al., 2007; see Chapter 2). Because longer SSRT has been proposed as a candidate endophenotype for P-ADHD (Crosbie, Perusse, Barr & Schachar; 2008), we selected this performance measure as a potential predictor of IC ratings. In addition, we examined the possible relationship between endophenotypic behavior of P-ADHD and ratings of ADHD symptoms.

Children with TBI exhibited slower cancellation SSRT, but only if they were in the acute phase of injury or had S-ADHD and/or a severe injury (Konrad et al., 2000a, 2000b; Leblanc et al., 2005; Schachar et al., 2004b). Conversely, normal restraint performance on the SST was documented in both children with TBI and those with S-ADHD (see Chapter 3). Therefore, poor IC is common in P-ADHD and may reflect the complex neuropsychology underlying the disorder, whereas TBI may confer a time-limited deficit in cancellation that persists beyond the acute phase of injury only if a child develops S-ADHD.

Greater elevations in parent and teacher ratings of DSM-IV-TR ADHD inattentive and hyperactivity/impulsivity symptoms were associated with poorer cancellation SSRT, whereas more hyperactivity/impulsivity symptoms were related to poorer IC on the restraint task, as reported earlier (Konrad et al., 2000a). Our data suggest that stopping an ongoing response efficiently requires intact attention, such as paying attention to details, following through on instructions, keeping one’s mind continually on a task and resisting distraction. These traits may ensure that the finishing time of the stop process occurs before the finishing time of the go process, which would result in successful inhibition (Logan, 1994). Our data also suggest that successful restraint may involve controlled, measured behaviors such as staying seated, not
fidgeting or squirming, waiting for the next trial to occur before a response is made, resisting impulses, and making deliberate movements once a stimulus appears on the screen. These traits may enable greater top-down control of behavior, which is thought to be required for successful restraint (e.g., Kelly et al., 2004).

No inhibition variable in the cancellation or restraint version predicted self-report classification into any ADHD subtype. Cancellation speed consistently predicted parent and teacher classification of ADHD across subtypes, whereas the speed of restraint predicted teacher classification of hyperactive/impulsive and combined subtypes. However, cancellation SSRT only accounted for approximately 6-8% and 8-17% of the variance in parent and teacher classifications, respectively, and restraint SSRT only accounted for 6-7% of the variance in teacher classifications. Toplak and colleagues (2009) showed that IC during the SST predicted ADHD status; however, parent and teacher ratings of inhibition functioning predicted ADHD to a much greater degree than did SSRT (Toplak, Bucciarelli, Jain, & Tannock, 2009), which suggests that SSRT alone is an inadequate predictor of parent and teacher ratings of ADHD.

Nevertheless, these relationships indicate that rater classification of diagnosable ADHD subtypes is predicted by slower IC, just as performance on attention tasks in children with TBI is inversely related to severity of parent ratings of ADHD symptoms (Yeates et al., 2005).

Agreement between parent and teacher ratings in the classification of children into the combined subtype was significantly predicted by SSRT in cancellation, accounting for approximately 6% of the variance. No other indices of IC were significant predictors of agreement of classification. Cancellation IC predicted the concordance of parent and teacher ratings only if a child was rated as exhibiting both inattentive and hyperactive/impulsive symptoms, which suggests that SSRT
does not reliably predict the agreement between teachers and parents to classify children into ADHD subtypes.

9.5  Key differences between P-ADHD and S-ADHD

Poor IC is a candidate endophenotype for P-ADHD, reflecting an inheritable trait that represents the underlying neural dysfunction conferred by the disorder. Poor IC performance was correlated with ratings of IC from both parents and teachers, with parents endorsing greater deficits across subscales. On the other hand, children with S-ADHD seem to selectively exhibit atypical performance on the cancellation version of the SST that is less severe than that in P-ADHD. Moreover, IC performance in the S-ADHD group is not correlated with IC ratings and, relative to children with P-ADHD, parents and teachers rate them as exhibiting fewer IC problems. Considered together, these data suggest that S-ADHD is a distinct disorder from P-ADHD despite similar expression of DSM-IV-TR symptomology. Lesion data also suggest differences between these disorders in terms of underlying pathology (e.g., Max et al, 2005b). Congruent with this idea, stimulants ameliorate IC deficits in P-ADHD, but have a more limited effect in S-ADHD, helping only certain symptoms within a short time frame (Jin & Schachar, 2004; Mahalick et al., 1998). Because performance on IC tasks in the S-ADHD group was unrelated to IC in everyday life, our findings suggest that performance indices of IC are imperfect tools for characterizing the disorder. Future studies are needed to further elucidate the central deficits of S-ADHD, and whether or not injury severity, early biomarker, and neuroanatomical variables are important in the identification and classification of behavioral and neurocognitive IC dysfunction in these children.
Table 6

**Participant Characteristics**

<table>
<thead>
<tr>
<th></th>
<th>AGE AT TEST</th>
<th>AGE AT INJURY</th>
<th>TIME SINCE INJURY</th>
<th>WASI IQ SCORE</th>
<th>SES</th>
</tr>
</thead>
<tbody>
<tr>
<td>CON</td>
<td>12.0 (3.3)</td>
<td>--</td>
<td>--</td>
<td>112.3 (11.0)</td>
<td>52.8 (6.2)</td>
</tr>
<tr>
<td>TBI</td>
<td>1.2 (3.4)</td>
<td>8.3 (3.6)</td>
<td>3.7 (1.5)</td>
<td>105.0 (10.5)</td>
<td>44.1 (10.1)</td>
</tr>
<tr>
<td>P-ADHD</td>
<td>10.9 (3.2)</td>
<td>--</td>
<td>--</td>
<td>108.3 (17.0)</td>
<td>46.2 (11.5)</td>
</tr>
<tr>
<td>S-ADHD</td>
<td>11.8 (2.5)</td>
<td>7.2 (2.4)</td>
<td>4.6 (1.2)</td>
<td>99.0 (14.3)</td>
<td>44.6 (10.5)</td>
</tr>
</tbody>
</table>

*All scores represented as means (standard deviation)*
Table 7

**Summary of Group Differences across the Conners-P, Conners-T, and Conners-SR**

<table>
<thead>
<tr>
<th></th>
<th>Conners-P</th>
<th>Conners-T</th>
<th>Conners-SR</th>
</tr>
</thead>
<tbody>
<tr>
<td>IN</td>
<td>CON &lt; TBI &lt; S-ADHD &lt; P-ADHD</td>
<td>CON = TBI &lt; S-ADHD = P-ADHD</td>
<td>CON &lt; TBI = S-ADHD = P-ADHD</td>
</tr>
<tr>
<td>HY</td>
<td>CON &lt; TBI &lt; S-ADHD = P-ADHD</td>
<td>CON = TBI &lt; S-ADHD = P-ADHD</td>
<td>NS</td>
</tr>
<tr>
<td>DSM-AN</td>
<td>CON &lt; TBI &lt; S-ADHD = P-ADHD</td>
<td>CON = TBI = S-ADHD &lt; P-ADHD</td>
<td>CON &lt; TBI = S-ADHD = P-ADHD</td>
</tr>
<tr>
<td>DSM-AH</td>
<td>CON &lt; TBI &lt; S-ADHD = P-ADHD</td>
<td>CON = TBI &lt; S-ADHD = P-ADHD</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Legend: NS = no significant group differences; < = fewer elevations on the subscale*
Table 8

*Parent-Teacher Discrepancy Ratings (Means and standard deviations)*

<table>
<thead>
<tr>
<th></th>
<th>IN</th>
<th>HY</th>
<th>DSM-AN</th>
<th>DSM-AH</th>
</tr>
</thead>
<tbody>
<tr>
<td>CON</td>
<td>-2.1 (10.3)</td>
<td>-3.9 (8.8)</td>
<td>-2.3 (9.7)</td>
<td>-4.0 (7.9)</td>
</tr>
<tr>
<td>TBI</td>
<td>6.1 (11.2)*</td>
<td>6.8 (10.9)*</td>
<td>5.8 (11.3)*</td>
<td>7.8 (10.0)*</td>
</tr>
<tr>
<td>P-ADHD</td>
<td>12.0 (7.5)*</td>
<td>8.4 (22.7)*</td>
<td>9.6 (11.3)*</td>
<td>8.0 (22.1)*</td>
</tr>
<tr>
<td>S-ADHD</td>
<td>3.2 (20.0)</td>
<td>3.2 (10.3)</td>
<td>7.6 (23.8)</td>
<td>2.8 (12.7)</td>
</tr>
</tbody>
</table>

* Significant differences relative to CON group
Table 9

*Parent-Self-Reports Discrepancy Ratings (Means and standard deviations)*

<table>
<thead>
<tr>
<th></th>
<th>IN</th>
<th>HY</th>
<th>DSM-AN</th>
<th>DSM-AH</th>
</tr>
</thead>
<tbody>
<tr>
<td>CON</td>
<td>-4.4 (11.4)</td>
<td>-7.8 (11.6)</td>
<td>-3.6 (10.9)</td>
<td>-8.2 (12.4)</td>
</tr>
<tr>
<td>TBI</td>
<td>-4.1 (13.6)</td>
<td>-4.3 (15.7)</td>
<td>-4.1 (12.2)</td>
<td>-5.0 (15.6)</td>
</tr>
<tr>
<td>P-ADHD</td>
<td>27.3 (14.4)*</td>
<td>27.5 (11.8)*</td>
<td>30.2 (13.6)*</td>
<td>23.5 (16.3)*</td>
</tr>
<tr>
<td>S-ADHD</td>
<td>11.0 (12.6)*</td>
<td>16.8 (10.4)*</td>
<td>13.6 (11.1)*A</td>
<td>17.6 (9.3)*</td>
</tr>
</tbody>
</table>

* Significant differences relative to the CON and TBI groups

A Significant differences relative to the P-ADHD group
Table 10

*Teacher-Self-Reports Discrepancy Ratings (Means and standard deviations)*

<table>
<thead>
<tr>
<th></th>
<th>IN</th>
<th>HY</th>
<th>DSM-AN</th>
<th>DSM-AH</th>
</tr>
</thead>
<tbody>
<tr>
<td>CON</td>
<td>-1.6 (9.0)</td>
<td>-2.8 (10.1)</td>
<td>-1.4 (9.0)</td>
<td>-3.8 (10.5)</td>
</tr>
<tr>
<td>TBI</td>
<td>-9.9 (16.3)</td>
<td>-9.8 (12.1)</td>
<td>-10.5 (11.5)</td>
<td>-11.3 (14.5)</td>
</tr>
<tr>
<td>P-ADHD</td>
<td>6.0 (18.2)</td>
<td>-5.0 (15.8)</td>
<td>13.5 (14.1)*</td>
<td>-3.7 (15.0)</td>
</tr>
<tr>
<td>S-ADHD</td>
<td>-3.2 (25.3)</td>
<td>10.2 (9.4)*</td>
<td>-0.6 (25.5)</td>
<td>8.8 (11.3)*</td>
</tr>
</tbody>
</table>

* Significant differences relative to the CON and TBI groups
Table 11

*Summary of Discrepancy Ratings*

<table>
<thead>
<tr>
<th></th>
<th>Conners-P &gt; Conners-T</th>
<th>Conners-P &gt; Conners-SR</th>
<th>Conners-T &gt; Conners-SR</th>
</tr>
</thead>
<tbody>
<tr>
<td>IN</td>
<td>TBI and P-ADHD vs. CON</td>
<td>P-ADHD and S-ADHD vs. CON and TBI</td>
<td>NS</td>
</tr>
<tr>
<td>HY</td>
<td>TBI and P-ADHD vs. CON</td>
<td>P-ADHD and S-ADHD vs. CON and TBI</td>
<td>S-ADHD vs. CON and TBI</td>
</tr>
<tr>
<td>DSM-AN</td>
<td>TBI and P-ADHD vs. CON</td>
<td>P-ADHD and S-ADHD vs. CON and TBI</td>
<td>CON and TBI vs. S-ADHD</td>
</tr>
<tr>
<td>DSM-AH</td>
<td>TBI and P-ADHD vs. CON</td>
<td>P-ADHD and S-ADHD vs. CON and TBI</td>
<td>P-ADHD vs. S-ADHD</td>
</tr>
</tbody>
</table>

Legend: NS = no significant group differences; < = fewer elevations on the subscale; > = greater elevations on the subscale
Table 12

*Correlation Coefficients (r) between SST Performance and Ratings*

<table>
<thead>
<tr>
<th>RATER</th>
<th>GROUP</th>
<th>SCALE</th>
<th>CANCELLATION</th>
<th>RESTRAINT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>SSRT  MRT</td>
<td>SSRT PI MRT</td>
</tr>
<tr>
<td>Conners-P</td>
<td>TBI</td>
<td>HY</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>P-ADHD</td>
<td>IN</td>
<td></td>
<td>-0.330*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DSM-AN</td>
<td></td>
<td>0.587*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-0.621*</td>
<td></td>
</tr>
<tr>
<td>Conners-T</td>
<td>CON</td>
<td>IN</td>
<td>0.578**</td>
<td>-0.621**</td>
</tr>
<tr>
<td></td>
<td>CON</td>
<td>HY</td>
<td>0.392*</td>
<td>-0.460*</td>
</tr>
<tr>
<td></td>
<td>CON</td>
<td>DSM-AN</td>
<td>0.477**</td>
<td>-0.443*</td>
</tr>
<tr>
<td></td>
<td>CON</td>
<td>DSM-AH</td>
<td>0.433*</td>
<td>-0.515**</td>
</tr>
<tr>
<td></td>
<td>P-ADHD</td>
<td>HY</td>
<td>0.696* 0.330**</td>
<td>0.676*</td>
</tr>
<tr>
<td></td>
<td>P-ADHD</td>
<td>DSM-AH</td>
<td>0.729* 0.767*</td>
<td>0.678*</td>
</tr>
<tr>
<td>Conners-SR</td>
<td>CON</td>
<td>HY</td>
<td>-0.416*</td>
<td>0.356*</td>
</tr>
<tr>
<td></td>
<td>CON</td>
<td>DSM-AH</td>
<td>-0.402*</td>
<td>0.353*</td>
</tr>
<tr>
<td></td>
<td>TBI</td>
<td>IN</td>
<td></td>
<td>-0.427*</td>
</tr>
</tbody>
</table>

* *p<0.05, **p<0.01*
Table 13

Regression Results

<table>
<thead>
<tr>
<th>PREDICTOR</th>
<th>DV</th>
<th>B</th>
<th>SE B</th>
<th>B</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSRT</td>
<td>PAI</td>
<td>-0.001</td>
<td>&lt;0.001</td>
<td>-0.237</td>
</tr>
<tr>
<td>Cancellation</td>
<td>PAH</td>
<td>-0.001</td>
<td>&lt;0.001</td>
<td>-0.236</td>
</tr>
<tr>
<td></td>
<td>PAC</td>
<td>-0.001</td>
<td>&lt;0.001</td>
<td>-0.286</td>
</tr>
<tr>
<td></td>
<td>TAI</td>
<td>-0.001</td>
<td>&lt;0.001</td>
<td>-0.412</td>
</tr>
<tr>
<td></td>
<td>TAH</td>
<td>-0.001</td>
<td>&lt;0.001</td>
<td>-0.274</td>
</tr>
<tr>
<td></td>
<td>TAC</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>-0.266</td>
</tr>
<tr>
<td>PI</td>
<td>PAC</td>
<td>0.004</td>
<td>0.002</td>
<td>0.200</td>
</tr>
<tr>
<td>Restraint</td>
<td>TAI</td>
<td>0.007</td>
<td>0.002</td>
<td>0.367</td>
</tr>
<tr>
<td>SSRT</td>
<td>TAH</td>
<td>-0.001</td>
<td>&lt;0.001</td>
<td>-0.244</td>
</tr>
<tr>
<td>Restraint</td>
<td>TAC</td>
<td>-0.001</td>
<td>&lt;0.001</td>
<td>-0.256</td>
</tr>
</tbody>
</table>

Legend: DV = dependent variable; B = unstandardized coefficient; SE B = standard error of B; \( \beta \) = standardized coefficient; PAI = Parent classification of ADHD inattentive subtype; PAH = Parent classification of ADHD hyperactive/impulsive subtype; PAC = Parent classification of ADHD combined subtype; TAI = Teacher classification of ADHD inattentive subtype; TAH = Teacher classification of ADHD hyperactive/impulsive subtype; TAC = Teacher classification of ADHD combined subtype
Trials 1 and 2 represent “go trials”. In both versions of the SST, one of two possible go signals (an X in Trial 1, an O in Trial 2) is presented on a computer screen for 1000 milliseconds (ms) following a 500 ms fixation point. Participants are instructed to respond to these stimuli as quickly as possible by making the appropriate button press on a handheld controller. Trial 3 represents a “stop trial”. Participants are instructed to inhibit their responses to the go signal when they hear the auditory stop signal (SS; a 1000 Hz tone), which occurs randomly on 25% of trials (Logan, 1994). In the restraint version, the go and SS are presented concurrently (i.e., the delay between the onset of the go and SS was 0 ms). In the cancellation version, the delay...
between the presentation of the go and the SS was varied dynamically to ensure that participants would inhibit their responses on 50% of the inhibition trials, regardless of whether or not they slowed their go RT as a strategy to increase successful cancellation (Logan & Cowan, 1984; Logan, 1994). The initial SS delay was set at 250 ms, and when a participant successfully inhibited his/her response, the delay was increased by 50 ms on the subsequent stop trial, and when the participant failed to inhibit his/her response, the delay was decreased by 50 ms on the subsequent stop trial.
Ratings of the CON and TBI groups were within the normal range. The ADHD groups were rated as exhibiting a greater number of deficits across subscales relative to the CON group, with the P-ADHD group rated as exhibiting greater elevations on the IN subscale relative to the S-ADHD group.
Ratings of the CON and TBI groups were within the normal range. The ADHD groups were rated as exhibiting a greater number of deficits across subscales relative to the CON group, with the P-ADHD group rated as exhibiting greater elevations on the DSM-AN subscale relative to the S-ADHD group.
No self-report ratings in any group were considered clinically significant. Similar ratings were obtained from all groups for the hyperactivity/impulsivity subscales, and participants in the CON group rated themselves as exhibiting significantly fewer inattention problems relative to the other groups.
Chapter 5
General Discussion

The goal of the trio of studies in this dissertation was to understand IC in children with S-ADHD. In the Introduction, I outlined a several questions organized in a series of steps designed to address the general goal. This general discussion concerns what the data mean in terms of a number of broader issues, including: the developmental course of IC and reward processes; how IC problems manifest across a range of childhood disorders and the interpretation of IC behavioral phenotypes and IC neurocognitive phenotypes; the ecological validity of IC tasks; some avenues for future research; and – the key question - what, if anything is unique about IC in S-ADHD and how does it differ from P-ADHD? Before discussing these issues, a summary of the main results will be presented.

10 Summary of Studies

Chapter 2 investigated the effects of reward on cancellation and restraint inhibition in typically developing children and adolescents. Participants aged 7-17 years old performed both versions of the SST under 3 reward conditions (NO, LOW, HIGH). Rewards facilitated the speed and probability of inhibition across task versions without significantly altering response execution. Compared to children, adolescents exhibited faster and less variable go responses, were more accurate when responding to go stimuli, and exhibited faster latencies to cancel and restrain a response when encountering a stop signal.

Following the demonstration of age-related changes in inhibition in typically developing children and adolescents, Chapter 3 examined how children with S-ADHD cancel and restrain responses under different reward conditions. Here, the goal was to delineate S-ADHD from both TBI (without S-ADHD) and P-ADHD, with the aim of elucidating the behavioural characteristics of
the S-ADHD group. Children with TBI did not exhibit IC deficits across tasks, and, like the CON group, their performance improved when successful inhibition was rewarded. The P-ADHD group exhibited poor cancellation and restraint, and variable performance across tasks and reward conditions. Although performance improved with increasing reward magnitude, their IC impairments persisted. The S-ADHD group exhibited normal restraint IC, but moderately abnormal cancellation IC. Rewards also improved IC performance in this group. Younger age of injury in the TBI and S-ADHD groups predicted slower and more variable response execution performance across task versions, and slower restraint IC in the reward conditions of restraint. No other injury variables were consistently related to performance.

Chapter 4 investigated behavioural ratings of IC and the relationship between ratings and neurocognitive IC performance on the cancellation and restraint versions of the SST. Parent, teacher, and self-report ratings from the Conners 3 were analyzed between groups (CON, TBI, S-ADHD, and P-ADHD). Ratings of inattention and hyperactivity/impulsivity, as well as DSM-IV-TR ADHD symptoms were examined. Participants in the CON and TBI groups were rated by parents and teachers as exhibiting behaviours within the typical range. The CON group was rated as exhibiting fewer problems than either of the ADHD groups, with the P-ADHD group rated as more inattentive than the S-ADHD group. Moderate to high concordance was found between parent and teacher reports, each of which was poorly concordant with self-reports suggesting poor metacognition across development. Relative to children with TBI without S-ADHD, the P-ADHD and S-ADHD groups were unaware of their own deficits. Ratings of IC deficits were correlated with poorer IC performance in the P-ADHD group, but not in the S-ADHD group. Poorer IC predicted parent and teacher classification of participants into ADHD subtypes, although IC did not predict rating concordance.
11 Reward and Inhibitory Control in Normal Children

Adolescents exhibited faster and more accurate IC and response execution relative to younger children, consistent with previous research (Hale, 1990; Johnstone et al., 2007; Williams et al., 1999). Improvements in IC are thought to reflect maturation in regulatory control centers of the brain; specifically in the ventrolateral prefrontal cortex and its connections with subcortical structures that are involved in the preparation, execution, and coordination of voluntary behaviour (the basal ganglia; Liston et al., 2006; Rubia et al., 2007). Age-related improvements may be also supported by the maturation of other regulatory processes such as working memory, decision-making, and performance monitoring (e.g., Roncadin, Pascual-Leone, Rich, & Dennis, 2007; Velanova, Wheeler, & Luna, 2009).

Reward facilitated both cancellation and restraint, and the lack of interaction between age group and reward suggests that reward facilitated IC to a similar degree throughout child and adolescent development. Strikingly, these effects occurred in the absence of a significant influence of reward on response execution, which confirms that reward motivated the process it was designed to effect, rather than exerting a global effect on arousal. Previous studies examining reward and IC contain a variety of limitations such as rewarding both IC and “go” processes, including rewards and punishments within the same paradigm, and not including appropriate control groups. By solely rewarding successful IC in studies that included carefully chosen comparison groups (see Chapter 3), the current dissertation avoided these methodological pitfalls and thereby clarifies the locus of reward effects in two IC paradigms.

Like the IC system, the neural circuits subserving reinforcement learning, including the dopamine system, are immature in children (Meng, Ozawa, Itoh, & Takashima, 1999; Segawa, 2000; Spear, 2000). Compared to adults, children and adolescents exhibit decreased activation of
the ventral striatum when approaching rewards (Bjork et al., 2004), but greater and more diffuse activity in the ventral striatum and orbitofrontal cortex after they have received the reward (Ernst et al., 2005; Galvan et al., 2006; May et al., 2004). The dopamine system, responsible for approach, incentive processing, and prediction errors (Schultz, 1997), continues to develop into adulthood, with hyperactivity of this system apparent in adolescence (Meng et al., 1999; Seeman et al., 1987; Segawa, 2000; Spear, 2000). An immature reward system may bias adolescents toward greater reward-seeking and may undermine a still developing IC system, resulting in poor decision-making (Galvan, 2010; Geir & Luna, 2009). However, the lack of an interaction effect between reward and age in Chapter 2 suggests that reward improved IC similarly across the developmental span studied here. The lack of interaction may be mediated by the relatively less mature IC system in children, which may have equated the effects of reward on IC processes between age groups by counteracting the effects of a hyperactive reward system in adolescents.

Despite differences in the development, neural substrates, and inhibition processes assessed by restraint and cancellation (e.g., Johnstone et al., 2007; Schachar et al., 2007), reward did not differentially alter these IC processes. The facilitation of reward on IC may be due to the effects of dopaminergic signals in the striatum and orbitofrontal cortex interacting directly with substrates of the IC system. Alternatively, there may be an interaction between reward centers and other areas of the brain that influence the interaction of inhibition and reward (see Padmala & Pessoa, 2010). As elaborated in Chapter 2, we suggest that reward signals may affect the preparation of the inhibition response in both cancellation and restraint at the level of the inferior frontal gyrus (IFG) and/or basal ganglia. Stop signals that signify the potential of reward receipt are arguably more salient than non-rewarding stop signals, thus facilitating the preparation of the inhibition response via activation of the IFG (Chikazoe et al., 2009). At the same time, dopaminergic signals in the ventral and dorsal striatum may have strengthened the strong signals
associated with the reward conditions (see Horovitz, 2002), thereby facilitating IC by altering motor planning or programming prior to the response (Beste et al., 2010).

12 Reward and Inhibitory Control in TBI and ADHD

As with the effects found in Chapter 2, rewards facilitated both cancellation and restraint in children and adolescents in the TBI, S-ADHD, and P-ADHD groups. The lack of group by reward interactions reveals that the reinforcing effects of rewards are similar in typical development and in some acquired and developmental disorders of childhood. These data also imply that the mesolimbic dopamine system is intact in participants with TBI, with or without S-ADHD, and is able to interact adaptively with the IC system.

Increasing reward magnitude failed to “normalize” IC performance in the P-ADHD group, suggesting that their IC deficits might be resistant to reward. To be sure, rewards decreased the latency of cancellation and commission errors in the P-ADHD group, so these children are not entirely impervious to reinforcement, which agrees with the idea that children with P-ADHD may have a higher than normal reward threshold despite a preference for immediate incentives (Douglas, 1999; Haenlein & Caul, 1987; Quay, 1997; Sergeant et al., 1999; Sonuga-Barke, 2002). Neuroimaging studies corroborate the “reward hypothesis” in P-ADHD, illustrating an association between ADHD status with the motivational components of approach behaviour: hypoactivation has been observed in the striatum and orbitofrontal cortex when anticipating rewards, with normal striatal response and greater activity in the orbitofrontal cortex and left prefrontal cortex in response to receipt of a reward (Scheres, Milham, Knutson, & Castellanos, 2007; Strohle, Stoy, Wrase, Schwarzer, Schlagenhauf, et al., 2008).

Compared to rewards, punishment may represent a more salient form of reinforcement to children with P-ADHD, and so may have a greater impact on IC. For example, these children
make better decisions on gambling-type tasks when the magnitude and frequency of punishments (but not rewards) is increased (Luman et al., 2008; Toplak et al., 2005). Indeed, increasing the magnitude of punishments has been shown to normalize the IC deficit in children with P-ADHD (Slusarek, Velling, Bunk, & Eggers, 2001); however this study also rewarded correct go trials, which clouds interpretation of the data. Future studies might clarify the effects of punishment across cancellation and restraint utilizing the paradigms presented in the current dissertation, but instead of rewarding successful inhibition, deducting points for failed inhibition. The next step would be to compare performance under conditions of punishment to performance under conditions of reward in order to establish whether there are group by condition by task interactions, which would reveal whether children with P-ADHD behave differently in response to different forms of reinforcement.

In sum, the data suggests that rewards affected both restraint and cancellation to improve IC across acquired and developmental disorders in a similar manner. This general effect shows that reward can be used as an incentive for behavioral control in the classroom where stringent rules for behavior are present, and perhaps even clinically when aiding children with IC difficulties. External rewards may provide a means to shape behavior in an adaptive manner in children with normal and disordered attention, especially if delivered shortly following the desired behaviour.

13 Differences between S-ADHD and TBI without S-ADHD

An important finding is that a diagnosis of S-ADHD presents a different behavioral profile from TBI without such a diagnosis. Abnormal cancellation performance in the S-ADHD group was not observed in the TBI group. Relative to participants with TBI, participants with S-ADHD were rated as exhibiting a significantly greater number of IC behaviours at home and at school.
Moreover, “awareness of deficits”, as indicated by discrepancy ratings between self and parent ratings, was present in the S-ADHD but not the TBI group. Thus, the long term sequelae of S-ADHD are distinct from those following TBI without S-ADHD.

Lesion variables and premorbid familial and behavioral functioning may be responsible for differences between the TBI groups. A subsequent diagnosis of S-ADHD is associated with damage to the orbitofrontal cortex, the basal ganglia as a whole or specifically the right putamen, and the left or bilateral thalamus (Gerring et al., 2000; Herkovits, et al., 1999; Max et al., 2005a). However, some investigations have failed to find a significant relationship between lesion location and diagnosis of S-ADHD (e.g., Max et al., 2005b; Max et al., 2004). Children diagnosed with S-ADHD at 6 months post-TBI were more likely to have poorer SES than those without S-ADHD (Max et al., 2005a), but not at 12 or 24 months post-TBI (Chapter 3; Max et al., 2005b). Pre-injury adaptive functioning and psychosocial adversity were not related to S-ADHD in the acute phase (Max et al., 2005a), but were related to diagnosis in the chronic phase of injury (Gerring et al., 2000; Max et al., 2005b; Max et al., 2004). It is clear that research lacunae include an understanding of what makes children susceptible to developing S-ADHD beyond the consequences of a TBI in childhood.

14 Relationship between Ratings of IC and Neurocognitive measures of IC

One of the objectives of Chapter 4 was to examine whether ratings of IC are related to neurocognitive IC performance. That is, do individuals perceive IC deficits in children at home and at school in a manner that reflects poor neurocognitive performance? Are IC variables predictive of classification into ADHD subtypes (i.e., do they show diagnostic utility)?
Correlation analyses revealed that difficulties with impulse control and/or difficulties sitting still are related only to IC deficits across tasks, whereas additional difficulties with attention are related only to poor stopping (cancellation). These findings further support the idea that IC is not a unitary construct. Importantly, the data show that not all children with ADHD experience deficits across all domains of IC, which have a direct implication in clinical settings when making predictions of function based on symptomatology.

Poor IC performance on the SST only accounted for a small proportion of the variance in parent and teacher classification of participants into ADHD subtypes. Moreover, deficits in IC did not consistently predict greater agreement of ADHD classification between teachers and parents. In light of these findings, caution is needed when considering neurocognitive measures of IC as predictors of informant ratings of ADHD subtypes.

15 Future Directions

Problems in the self-regulation of behavior can negatively influence academic, social, and occupational successes. Recognizing these deficits in TBI is essential for identifying children who require intervention and treatment after they have returned to home and school activities. Even better would be identifying, shortly after the TBI, children most likely to develop S-ADHD and/or persistent IC problems. Although prospective studies of IC after TBI are vital for examining changes in function over time, children can become more familiar with tasks with repeated exposure, leading to practice effects. An important future direction then would be to identify biomarkers in the early acute phase of the injury that can predict future outcomes. Biomarkers are objectively measured characteristics, such as protein levels present in serum or electrophysiological activity, that act as surrogate markers of brain injury that can complement more expensive neuroimaging methods (Haqqani et al., 2007). A good biomarker for S-ADHD
and/or IC deficits should reflect the presence of such difficulties, and should inform the progression of deficits, the severity of prognosis, and the efficacy of any interventions.

In addition to the development of S-ADHD, childhood TBI is also associated with new-onset disruptive behaviors and behavioral disorders such as oppositional defiant disorder and conduct disorder. Parent ratings of verbal and physical aggression in children with TBI increase as time since injury increases, with approximately 20% of patients exhibiting borderline clinical or clinically significant levels of aggression (Cole et al., 2008). These increases may be due to the emergence of S-ADHD, as high levels of affective lability and aggression are common in children who have developed S-ADHD compared to those with TBI without S-ADHD, and these two traits tend to co-occur (Gerring et al., 1998; Max, Koele, Castillo, et al., 2000). Moreover, new-onset oppositional defiant disorder/conduct disorder/disruptive behavioural disorder are apparent in approximately 35% of participants with S-ADHD during the chronic phase of recovery (Max et al., 2005b), and are the most frequent comorbidities of S-ADHD as measured by both parental interviews and ratings scales (McKinlay, Grace, Horwood, Fergusson, & MacFarlane, 2009; Max et al., 1998; Max et al., 2004). Future studies are needed to assess whether these increases in aggressive behaviors are present across contexts, and whether their co-occurrence with S-ADHD is related to changes in IC functioning. The Conners 3 may be a helpful tool for answering these questions, because it includes scales that assess aggression, oppositionality, and poor conduct.

Current neuroimaging suggests that reward systems may be intersecting with IC systems to affect behaviour (Padalma & Pesoa, 2010). Therefore, a third major focus of future study would be to replicate the methods presented in Chapters 2 and 3 under an fMRI protocol in order to examine this phenomenon in children and adolescents across IC tasks. In particular, the
hypotheses presented in Chapter 2 needs to be explicitly tested. That is, does reward facilitate preparation of the inhibition response via stimulation of the IFG/basal ganglia to affect outcome? This type of experiment would clarify how rewards affect behaviour, providing insights into normal brain functioning across development. There would likely be an effect of age, given lags in the maturation of the frontostriatal system.

Neuroimaging studies, combined with the data from the present study, suggest some directions to investigate the neural bases of inhibitory control in S-ADHD. Disrupted inhibition in P-ADHD may be related to abnormalities of frontostriatal circuitry (e.g. Aron & Poldrack, 2005; Kieling, Goncalves, Tannock, & Castellanos, 2008) including volume reductions and functional abnormalities in the basal ganglia (caudate nucleus and globus pallidus) and parts of the prefrontal cortex (e.g., Castellanos et al., 1996; Durston et al., 2004; Filipek et al., 1997; Rubia et al., 2009; Rubia et al., 1999; Seidman et al., 2006; Sowell et al., 2003; Vaidya, Bunge, Dudukovic, Zalecki, Elliott, & Gabrieli, 2005). Children with S-ADHD and lesions to the right ventrolateral prefrontal cortex and basal ganglia (especially the striatum) would be expected to exhibit longer SSRT on the cancellation task without significant deficits on the go trials (Aron, Fletcher, Bullmore, Sahakian, & Robbins, 2003; Chambers et al., 2007; Chevrier et al., 2007; Rieger, Gauggel, & Burmeister, 2003; Rubia et al., 1997, 2000). Conversely, participants with damage to the dorsal aspects of the prefrontal cortex, especially to the left side, may exhibit greater impairments with restraint (Levin et al., 1993).

Another important imaging direction would be to assess reward-IC interactions in children with TBI, S-ADHD, and P-ADHD. Based on predictions from Chapter 2 and the findings from Chapter 3, one would expect an attenuated preparation response in P-ADHD across tasks, but an increase in activation during reward trials relative to non-reward trials. The TBI group may
exhibit an abnormal pattern of activation despite normal performance on both cancellation and restraint. Kramer and colleagues (2008) discovered that children with TBI who perform normally on attention tasks activate similar areas of the brain to controls when performing the task; however, the TBI group exhibited hyperactivation in these networks (Kramer et al., 2008), suggesting that normal performance had been effected by neural compensation involving an over-commitment of resources (McAllister et al., 2001). Thus greater activity in the IFG/basal ganglia in response to rewards may be observed in the TBI group relative to controls. While this general pattern of results may also be present in children with TBI and S-ADHD, differences may exist between the TBI groups in terms of activation of frontostriatal networks during cancellation, with an attenuated response in the S-ADHD group.

16 Limitations

Limitations of the dissertation include those related to sampling methodology, diagnostic measures, issues of power and group sizes, and severity of injury in the TBI and S-ADHD groups.

Participants in the S-ADHD group were selected based on parent or teacher endorsement of clinically significant ADHD symptoms on the Conners 3, with only those children with TBI who met DSM-IV-TR criteria for the disorder included into the S-ADHD group. Although it would have been desirable to conduct psychiatric interviews with the parents of each child in the TBI group in addition to assessing the child directly in order to determine the presence of ADHD symptoms, current resources (including financial and time resources) precluded this procedure. However, a diagnosis of S-ADHD via a psychiatrist or clinical interview does not necessarily lead to greater identification of children with S-ADHD (Chapter 3 revealed that 18% of children with chronic phase TBI had developed S-ADHD, consistent with prevalence rates in the
literature), nor does it improve the relationship between diagnosis and neurocognitive behaviour (see Willcutt et al., 2005). Hence, it is felt that the overall findings of the dissertation may not have been significantly tempered by the sampling and research diagnosis methodology.

The absence of P-ADHD in the S-ADHD and TBI groups was probed via retrospective reports during a brief telephone interview conducted with each parent during the initial recruitment call. This interview involved the probing of whether specific DSM-IV-TR symptoms of ADHD were present pre-injury: if a parent had reported that 6 or more inattentive and/or hyperactive/impulsive symptoms were present in the child pre-TBI, then the child was not included in the subsequent experiments. While retrospective reports of behaviour are not ideal, this procedure has been used in previous studies to exclude children from S-ADHD groups due to the presence of pre-injury ADHD symptoms (e.g., Konrad et al., 2000a, 2000b; Schachar et al., 2004). Short of conducting a longitudinal, prospective study, I felt that this was the best way to avoid including children with both primary and secondary forms of ADHD in the S-ADHD group.

The final S-ADHD group consisted of 9 participants. This small sample size makes it difficult to further subdivide the participants into different severity or age groups. In order to achieve a greater sample size, I would have needed to recruit and test a much larger group of children with TBI, which would have required much greater financial and time resources than I had available for the dissertation. One concern with having a small clinical group is that the increased variability that these children exhibit, similar to the increased variability present in the P-ADHD group (see Chapter 3), may have led to a liberal F test thus resulting in an increased Type 1 error rate and an inflated alpha level (Tabachnick & Fidell, 2007). Unequal n’s between groups also leads to the concern of having insufficient power to detect the presence or absence of an effect. A
number of adjustments could have been made, including subtracting cases from cells with greater
$n$ until all cells were equal (Tabachnick & Fidell, 2007). However, because the unequal $n$ in the
current studies was a direct reflection of the population incidence of children with S-ADHD (i.e.,
only represented in 15-20% of cases of TBI), to artificially equalize $n$ is to distort differences
between groups and may result in a loss of the generalizability of results (Tabachnick & Fidell,
2007).

There are a number of statistical approaches that attenuate the influence of unequal and small
group sizes. I felt that conducting non-parametric tests would not have been appropriate, as the
variables of interest were not presented in nominal or ordinal scales. Including covariates in the
analysis, as I did in Chapter 3 (age) and Chapter 4 (SES), act to increase the power of the
analyses (Tabachnick & Fidell, 2007). Another method is to assign heavier weighting to cells
with larger sample sizes when computing marginal means and lower-order interactions
(Tabachnick & Fidell, 2007), and SPSS version 15 (the statistical software used in the
dissertation) conducts this procedure as a default in the general linear model. Thus, the repeated
measures ANOVAs conducted in the current experiments appropriately took into account the
unequal sample sizes across groups when calculating differences across reward conditions,
groups, and behavioural ratings. To be sure that my findings were meaningful beyond being
statistically significant, I explored the effect sizes and power estimates associated with each main
effect (with the $\alpha$ level adjusted to 0.0125 to account for multiple group comparisons), and the
results suggested medium effect sizes and power estimates across studies. For example, in
Chapter 3, the main effect of reward condition yielded a small to medium effect size associated
with medium power, and the main effect of group yielded a medium to large effect size
associated with medium to high power. In sum, despite the presence of a small S-ADHD group
and unequal n’s in the group comparisons, the results in the dissertation are nevertheless meaningful as reflected by adjustments made to the general linear model, and by the effect sizes and estimates of power yielded by each analysis.

Another potential limitation is the distribution of injury severity in the TBI and S-ADHD groups (see Appendix 2). In the TBI group, 52.5% of the participants had incurred a mild injury, whereas 10% and 37.5% of participants had incurred a moderate and severe injury, respectively. While this may appear as though the sample was biased toward those with mild injury, this distribution reflects the reality that most pediatric TBI patients incur mild injuries, with some estimates that approximately 76% of hospital admissions for TBI being for mild injuries (Lescohier & DiScala, 1993). To ensure that the performance of children in the mild TBI group did not account for the lack of effect between TBI and control groups on the IC measures (i.e., that their presence did not cause a Type II error), I re-analyzed the SST data limiting the TBI group to those with moderate and severe injuries, then re-analyzed the data again just including children with severe TBI. These additional analyses did not change the findings reported earlier, suggesting that the severity of injury does not influence the manner in which children with chronic phase TBI without S-ADHD are able to cancel or restrain their responses. Like children with moderate and severe TBI, children with mild TBI exhibit poor IC acutely following the injury, but this deficit recovers to normal levels by the chronic phase of injury (Leblanc et al., 2005).

The severity distribution in the S-ADHD group made it impossible to examine the influence of severity on SST performance, but one would expect a stronger cancellation deficit in children with more severe injuries relative to the TBI group (see Schachar et al., 2004b). Thus it remains unclear whether children with more severe injuries would exhibit poorer IC compared to those
with less severe injuries and/or those with P-ADHD. Subsequent studies with larger group sizes may clarify these issues.

17 S-ADHD: A Separate Disorder from P-ADHD?

The major goal of this dissertation was to better characterize S-ADHD, with a particular emphasis on comparisons with P-ADHD. Both groups exhibit symptoms of inattention and/or hyperactivity/impulsivity that are clinically significant, and there is some evidence to suggest that like P-ADHD, children with severe TBI and a research diagnosis of S-ADHD also experience problems canceling their ongoing actions (Schachar et al., 2004). However, no study to date had directly compared these groups of patients, so it was unknown whether children with S-ADHD present with similar deficits to those with P-ADHD or whether they have a disorder with a substantially different behavioral profile.

Through principled study of acquired and developmental forms of ADHD, this dissertation has shown that S-ADHD is not just a form of P-ADHD that develops due to TBI. Rather, S-ADHD is separable in terms of qualitative IC deficits (they do not exhibit problems with restraint) but also in terms of quantitative IC deficits (their atypical cancellation performance is not as severe). This group was also rated by parents and teachers as exhibiting fewer inattention problems relative to children with P-ADHD, who exhibited the greatest impairments on the Conners 3. Moreover, poor IC on the SSTs was related to ratings of IC behaviors in the P-ADHD group, but not in the S-ADHD group.

The differences between S- and P-ADHD concern the nature and magnitude of IC deficits, which may reflect the underlying mechanisms unique to each disorder. Children with P-ADHD exhibit a number of neural abnormalities in frontostriatal circuitry (e.g. Aron & Poldrack, 2005; Kieling et al., 2008) including volume reductions in the basal ganglia (caudate nucleus and globus
pallidus), anterior cingulate cortex, and parts of the prefrontal cortex (Castellanos et al., 1996; Filipek et al., 1997; Seidman et al., 2006), especially the right inferior frontal cortex (Durston et al., 2004; Sowell et al., 2003). Moreover, poor inhibition displayed by ADHD groups is correlated with smaller right frontal cortices (Casey et al., 1997), anterior cingulate cortex, and right lentiform nucleus (McAlonan, Cheung, Chua, Oosterlaan, Hung, et al., 2008), and with decreased activity in the right IFG (Rubia, Cubillo, Smith, Woolley, Heyman, & Brammer, 2009; Rubia et al., 1999; Vaidya, Bunge, Dudukovic, Zalecki, Elliott, & Gabrieli, 2005), orbitofrontal cortex (Rubia et al., 2009), and left caudate nucleus (Durston et al., 2003; Rubia et al., 1999; Vaidya et al., 1998). Associations between IC performance and brain injury location and volume in children has yet to be explored in children with S-ADHD, but one would expect that frontal lesions would be an important focus of investigation.

A child with S-ADHD may exhibit increased activity and impulsive behaviours across contexts, and have difficulty when trying to stop an ongoing action, leading to selective deficits in self-control. This child would appear to be qualitatively and quantitatively different from a child with P-ADHD, who may be severely inattentive in addition to being hyperactive/impulsive, exhibiting general deficits across different forms of inhibition, leading to overall problems in self-regulation. The clinical implications of these findings are that children with S-ADHD do not present with “classic ADHD” difficulties, which means that assessment and treatment procedures need to be tailored to this group to account for such differences.
References


*Biological Psychiatry, 57*, 1285-1292.


*Neuropsychological Rehabilitation, 16*, 397-414.


Carrillo-de-la-Pena, M. T., Otero, J. M., & Romero, E. (1993). Comparison among various


attention deficit hyperactivity: effects on classroom behavior and academic performance.

*Journal of Applied Behavior Analysis, 31, 579-592.*


Ewing-Cobbs, L., Fletcher, J. M., Levin, H. S., Francis, D. J., Davidson, K., & Miner, M. E.


investigation of the concordance between individuals with traumatic brain injury and
family or friend ratings on the Katz adjustment scale. *Journal of Head Trauma
Rehabilitation, 15*, 1123-1138.

in adolescent mice: Psychobiological determinants and early epigenetic influence.

Leblanc, N., Chen, S., Swank, P. R., Ewing-Cobbs, L., Barnes, M., Dennis, M., et al. (2005)
Response inhibition after traumatic brain injury (TBI) in children: impairment and

during inhibition of hand and eye movements. *Neuroscience and Biobehavioral
Reviews, 27*, 9893-9900.

Developmental changes in performance on tests of purported frontal lobe

Levin, H. S., Culhane, K. A., Mendelsohn, D., Lilly, M. A., Bruce, D., Fletcher, J. M., et al.,
(1993). Cognition in relation to magnetic resonance imaging in head-injured children and
adolescents. *Archives of Neurology, 50*, 897-905.

Symptoms of attention-deficit/hyperactivity disorder following traumatic brain injury in


hyperactivity disorder. *Journal of Abnormal Child Psychology, 35*, 229-238.


Proceedings of the National Academy of Sciences of the United States of America, 95, 12061-12068.


Appendices

Appendix 1

*TBI Severity Coding*

**A. GLASGOW COMA SCALE RATING** (lowest post-resuscitation rating, ± sedation)

<table>
<thead>
<tr>
<th>Rating</th>
<th>Description</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-5</td>
<td>Unconscious, coma, TBI grade 3</td>
<td>4</td>
</tr>
<tr>
<td>6-8</td>
<td>Clouded awareness to unconscious, TBI grade 2-3</td>
<td>3</td>
</tr>
<tr>
<td>9-12</td>
<td>Clouded awareness, cerebral contusion TBI grade 1-2</td>
<td>2</td>
</tr>
<tr>
<td>13-14</td>
<td>Cerebral commotion, TBI grade 1</td>
<td>1</td>
</tr>
<tr>
<td>15</td>
<td>Conscious</td>
<td>0</td>
</tr>
</tbody>
</table>

**TOTAL GCS**

| 15 |

**B. FOCAL CONTUSION/HEMORRHAGE** (based on all available presurgical CT)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Focal intracranial contusion</td>
<td>1</td>
</tr>
<tr>
<td>Intraparenchymal/intracerebral</td>
<td>1</td>
</tr>
<tr>
<td>Intraventricular bleed</td>
<td>1</td>
</tr>
<tr>
<td>Subarachnoid hemorrhage</td>
<td>1</td>
</tr>
<tr>
<td>Subdural hemorrhage</td>
<td>1</td>
</tr>
<tr>
<td>Epidural hemorrhage</td>
<td>1</td>
</tr>
<tr>
<td>Extradural/extra-axial blood</td>
<td>1</td>
</tr>
<tr>
<td>None/not reported</td>
<td>0</td>
</tr>
</tbody>
</table>
C. DIFFUSE INJURY *(based on all available presurgical CT)*

<table>
<thead>
<tr>
<th>Condition</th>
<th>Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Punctate hemorrhage or petechia</td>
<td>1</td>
</tr>
<tr>
<td>Swelling/edema/effacement of sulci/attenuation of gray-white matter</td>
<td>1</td>
</tr>
<tr>
<td>Ventricles abnormal/compressed/displaced/asymmetric</td>
<td>1</td>
</tr>
<tr>
<td>Cisterns abnormal/obliterated/hyperintense</td>
<td>1</td>
</tr>
<tr>
<td>Midline shift</td>
<td>1</td>
</tr>
<tr>
<td>Brain herniation (uncal, subfalcine, other)</td>
<td>1</td>
</tr>
<tr>
<td>Mass effect</td>
<td>1</td>
</tr>
<tr>
<td>None/not reported</td>
<td>0</td>
</tr>
</tbody>
</table>

D. SKULL FRACTURE *(based on all available presurgical CT)*

<table>
<thead>
<tr>
<th>Condition</th>
<th>Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linear/depressed/diastased skull # in frontal, parietal, occipital, temporal bone</td>
<td>1</td>
</tr>
<tr>
<td>Basilar skull fracture</td>
<td>1</td>
</tr>
<tr>
<td>None or not reported</td>
<td>0</td>
</tr>
</tbody>
</table>
### A) Injury Severity Characteristics

<table>
<thead>
<tr>
<th>GROUP</th>
<th>SEVERITY</th>
<th>DISTRIBUTION OF GCS SCORES</th>
</tr>
</thead>
<tbody>
<tr>
<td>TBI</td>
<td>MILD</td>
<td>15 (n = 14) 14 (n = 7)</td>
</tr>
<tr>
<td></td>
<td>MODERATE</td>
<td>11 (n = 2) 10 (n = 1) 9 (n = 1)</td>
</tr>
<tr>
<td></td>
<td>SEVERE</td>
<td>8 (n = 3) 7 (n = 3) 6 (n = 4) 5 (n = 2) 4 (n = 1) 3 (n = 2)</td>
</tr>
<tr>
<td>S-ADHD</td>
<td>MILD</td>
<td>15 (n = 4) 14 (n = 2)</td>
</tr>
<tr>
<td></td>
<td>MODERATE</td>
<td>12 (n = 1) 10 (n = 1)</td>
</tr>
<tr>
<td></td>
<td>SEVERE</td>
<td>3 (n = 1)</td>
</tr>
</tbody>
</table>
### B) TBI and S-ADHD Group Characteristics

<table>
<thead>
<tr>
<th>GROUP</th>
<th>SEVERITY</th>
<th>N</th>
<th>AGE (SD)</th>
<th>AGE AT INJURY (SD)</th>
<th>TIME SINCE INJURY (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S-ADHD</td>
<td>MILD</td>
<td>6</td>
<td>11.03 (2.6)</td>
<td>6.50 (2.5)</td>
<td>4.53 (1.3)</td>
</tr>
<tr>
<td></td>
<td>MODERATE</td>
<td>2</td>
<td>13.25 (2.23)</td>
<td>8.95 (2.6)</td>
<td>4.29 (0.4)</td>
</tr>
<tr>
<td></td>
<td>SEVERE</td>
<td>1</td>
<td>13.92</td>
<td>8.08</td>
<td>5.84</td>
</tr>
<tr>
<td>TBI</td>
<td>MILD</td>
<td>21</td>
<td>11.90 (2.9)</td>
<td>8.19 (4.2)</td>
<td>3.71 (1.4)</td>
</tr>
<tr>
<td></td>
<td>MODERATE</td>
<td>4</td>
<td>12.17 (4.3)</td>
<td>7.71 (5.1)</td>
<td>4.46 (1.1)</td>
</tr>
<tr>
<td></td>
<td>SEVERE</td>
<td>15</td>
<td>11.84 (4.1)</td>
<td>8.51 (4.2)</td>
<td>3.33 (1.6)</td>
</tr>
</tbody>
</table>

Legend: N, number of participants; SD, standard deviation