THE NEURO-PSYCHO-PHYSIOLOGICAL DEFICITS OF CHILDREN WITH SLUGGISH COGNITIVE TEMPO SYMPTOMS

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The Neuro-psycho-physiological Deficits of Children with Sluggish Cognitive Tempo Symptoms

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CERTIFICATE OF ORIGINALITY

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Abstract

Background. Children with Sluggish Cognitive Tempo are often reported to have symptoms such as day-dreaming, drowsiness and slowness to respond to the environment. Previous studies did not examine the underlying mechanism which may lead to the sustained attention deficits observed in people with SCT. It has been proposed that the hypo- or hyper-arousal maybe related to SCT symptoms and may possibly explain the sustained attention deficits in individuals with SCT. However, no previous study has been conducted to examine this hypothesis. It is also unclear how these neuropsychological and neurophysiological deficits may relate to the social difficulties exhibited by these children.

Aim. This thesis aimed to investigate the neuro-psycho-physiological factors associated with SCT symptoms. Three studies were conducted in order to identify the nature of SCT. Study I aimed to examine the neurophysiological correlates of SCT symptoms. It is hypothesized that deficit arousal state and regulation would be associated with higher SCT symptoms. Study II aimed to identify the linkage between arousal regulation deficits and sustained attention difficulties in High SCT group. It is hypothesized that deficient arousal state and regulation would predict the severity of sustained attention deficits in High SCT group. Study III aimed to identify the role of attention deficits in social difficulties (social problems and withdrawn behaviour) in High SCT group. It is hypothesized that scores in the sustained attention measures would predict the severity of social problems and withdrawn behaviour in High SCT group.

Methods. In the Study I, thirty children aged 6-12 years old were recruited and their heart rate variability (HRV) was measured in resting condition (reflecting their basal arousal state) and warning signal condition (reflecting their arousal regulation capacity). The association between the severity of SCT symptoms and HRV in both conditions were examined. In the Study II, eighty-eight children aged 6-13 were recruited (41 children with SCT and 47 children with typical development). Their physiological responses quantified by HRV and EEG in resting and warning signal conditions were recorded. Cued Continued Performance Test (CCPT) were also conducted in order to assess their sustained attention abilities. HRV and EEG measures were used to predict their performance of the CCPT in High SCT group and in Low SCT group. In the Study III, eighty-eight children aged 6-12 years were recruited (40 children in the High SCT group and 48 children in the Low SCT group). CCPT were conducted in both groups and their parents were asked to fill in the Child Behavioural Checklist (CBCL). CCPT measures were used to predict the scores of the Social Problems subscale and Withdrawn Behaviour subscale in the CBCL.

Results. In the Study I, SD2 nu in the resting condition significantly predicted the SCT symptoms after controlling the ADHD symptoms. Specifically, higher SD2 nu (reflecting lower arousal) was found to be positively associated with higher SCT symptoms. SCT symptoms were also significantly predicted by the changes of SD2 nu and pNN50 between resting and warning signal condition. SCT symptoms were found to be positively associated with the change in SD2 nu between resting and warning signal conditions (reflecting hyperarousal during stimulation). There results supported the notion that SCT were related to arousal deficiencies. In the Study II, high theta power in warning signal condition than in resting condition was found to be associated with higher number of omission errors of the CCPT in the High SCT group. Higher SD1 nu in

the warning signal condition than in resting condition was found to associated with higher commission errors of the CCPT in the High SCT group. These results reflect that sustained attention deficits in children with high SCT symptoms were related to hyper-sensitivity towards stressful auditory stimulus (such as those in the warning signal condition). In the Study III, number of omission errors of the CCPT significantly predicted the severity of the social problems and withdrawn behaviour in children with high SCT symptoms. This result supported the linkage between sustained attention deficits and social difficulties in SCT.

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Chapter 1: Introduction

1.1 Background

Sluggish Cognitive Tempo (SCT) has been used to describe a group of symptoms that are characterized by inconsistent alertness (e.g., daydreaming) and slowed behaviour/thinking (e.g., drowsiness, and slow respond) among children and adults (Barkley, 2013a; Becker et al., 2016). These symptoms are often associated with impairments in real life such as internalizing behaviour difficulties (e.g., anxiety problem), social problems and academic learning difficulties (Barkley, 2013b; Tamm et al., 2016).

Previously, it has been suggested that SCT may be a pure form of attention-deficit/hyperactivity disorder (ADHD) Inattentive subtype (Milich, Balentine & Lynam, 2001). However, findings of recent research suggested that SCT may be a separate disorder from any form of another form of childhood psychopathologies (Barkley, 2013; Becker et al., 2016).

Although SCT has been gradually understood as a separate disorder, its underlying neuropsychological and neurophysiological mechanisms are still not clearly understood. Executive functioning deficits have been suggested to be one of the neuropsychological factors that could explain SCT deficits. Recent laboratory research results suggested that SCT symptoms did not seem to relate to those executive functioning deficits which are related to different subtypes of ADHD (Bauermeister et al., 2012; Skirbekk et al., 2011). SCT symptoms seem to be related to sustained attention deficit, as reflected by the laboratory attention tests (Wahlstedt & Bohlin, 2010; Willcutt et al., 2014). However, previous studies have rarely examined the underlying mechanism which may lead to the sustained attention deficit observed in SCT and whether sustained attention deficit could explain the common problem (e.g., social difficulties) seen in individuals with high SCT symptoms.

The activity of the arousal system has been proposed to be related to sustained attention abilities in humans (Petersen &Posner, 2012). Sustained alertness towards stimulus is related to increased activity of locus coeruleus (LC), which was found to be the source of norepinephrine (NE) (Aston-Jones & Cohen, 2005). NE was also found to be the chemical switch that could turn on the prefrontal cortex (PFC) during an alert state (Brennan & Arnsten, 2008). Therefore, the sustained attention deficit found in individuals with SCT symptoms may be due to the under-activity of the arousal system in these individuals, but no previous study was conducted to examine this hypothesis. LC was found to have a reciprocal pathway with the autonomic nervous system (ANS) (Samuels & Szabadi, 2008; Wood & Valentino, 2017). However, no previous research has examined the relationship between ANS activity and SCT symptoms.

The primary aim of the present study is to investigate the neuro-psycho-physiological factors associated with SCT symptoms. By doing so, we could understand the nature of these SCT symptoms. The lack of understanding of the nature of these symptoms may have multiple drawbacks: Firstly, clinicians may find it difficult to accurately assess symptoms of SCT in their patients because those underlying factors are not well understood. Secondly, clinicians subsequently could not provide appropriate treatment for children who exhibit symptoms of SCT because of a lack of valid assessment methods. Therefore, researchers must identify the factors contributing to SCT and examine how these factors distinguish SCT from other mental disorders.

1.2 Statement of Purpose

This report consisted of three studies to identify the nature of SCT symptoms. Study I aimed to examine the neurophysiological correlates of SCT symptoms in school-aged children.

Study II aimed to identify the linkage between arousal regulation deficit and sustained attention difficulties in children with SCT. Study III aimed to identify the role of attention deficits in social problem and withdrawn behaviour among individuals with SCT symptoms. Specifically, this thesis has found specific parameters of attention measures that contribute to social problems and withdrawn problems in children with high SCT symptoms.

1.3 Organization of Chapters

This thesis consists of six chapters. Chapter 2 describe the definition of SCT, its common associated difficulties, the possible neuropsychological and neurophysiological factors associated with this condition, and the proposed conceptual model of the present study.

Chapter 3 describes the research method and results of Study I, in which the experimental protocol applied for eliciting autonomic responses and the measures of heart rate variability (HRV) are explained in detail. The findings regarding the association between autonomic response (HRV) and SCT symptoms were reported.

Chapter 4 describes the research method and the results of Study II which examined the relationship between arousal regulation and sustained attention deficits in children with high SCT symptoms. The findings provide a neurophysiological explanation of sustained attention deficit which was commonly found in children with SCT. This may help us to have a better understanding of the nature of SCT from a neurophysiological perspective.

Chapter 5 describes the research method and the results of Study III which examined the relationship between sustained attention deficit and social problem/withdrawn behaviour among children with high SCT symptoms. The findings showed the relationship between attention measures and social problems/withdrawn behaviour among children with high SCT symptoms and their healthy peers.

Chapter 6 offers a discussion and conclusion based on the findings of the above-mentioned three studies. The key findings and new knowledge generated by the study as well as recommendations for further research and clinical practice are highlighted.

Chapter 2: Literature Review

2.1 What is SCT?

SCT is defined as a construct comprised of two dimensions of symptoms: (1) daydream/slow, and (2) sleepy/sluggish/underactive (Barkley, 2013a; Penny et al., 2009). Symptoms associated with SCT include daydreams, sleepy/drowsy, underactive/slow moving, easily confused, staring blankly, lost in thoughts, in a fog, tired/lethargic, sluggish, spacey/alertness from moment to moment, slow thinking and responding, apathetic/unmotivated, low initiative and persistence, absentminded, easily bored, slow work/task completion, loses train of thought/loses cognitive set, and poor listening/difficulty with directions (Becker et al., 2017). Among these symptoms, 13 of them were loaded consistently on SCT factor in the previous studies (mean loading of at least .70 across all samples) (Becker et al., 2017) (Figure 1). Penny et al. (2009) conducted a principal component analysis on 14 items SCT parent scale and obtained three factors namely Slow, Sleep and Daydream. These three factors collectively accounted for 70.2% of the variance in the SCT symptoms.

2.2 Is SCT a Subtype of ADHD?

SCT symptoms are often associated with impairments in the real life such as internalizing behavioural difficulties (e.g., anxiety), social problem and academic learning (Barkley, 2013b; Tamm et al., 2016). Despite its clinical significance, the nature of the SCT is still poorly understood. Previously, it has been suggested that SCT may be a purer form of ADHD Inattentive (ADHD-I) subtype (Milich, Balentine & Lynam, 2001).

Figure 1. SCT symptoms commonly loaded on SCT factor in previous studies (Becker et al., 2016).

SCT symptoms	
1.	Sluggish
2.	Tired/lethargic
3.	Slow thinking/processing
4.	Lost train of thoughts/cognitive set
5.	Sleepy/drowsy
6.	Spacey
7.	In a fog
8.	Underactive/slow moving
9.	Daydreams
10.	Lost in thoughts
11.	Stares blankly
12.	Easily confused
13.	Apathetic/unmotivated

2.2.1 SCT symptoms are separated from ADHD symptoms.

ADHD is a developmental disorder that is characterized by age-inappropriate difficulties with overactivity, impulsivity, inattention, and disorganization. Three major subtypes are specified by the Diagnostic and Statistical Manual of Mental Disorders 5th Edition (DSM-5; American Psychiatric Association, 2013): Combined presentation (ADHD-C), predominantly inattentive presentation (ADHD-I) and predominantly hyperactivity/impulsive presentation (ADHD-H).

As early as 1960s and 1970s, SCT was considered as a kind of attention disorder under ADHD-I (Becker, Marchall & McBurnett, 2014). In the 1980s, more empirical evidence (Lahey et al., 1988) supported that SCT is separated from ADHD-I. For example, Lahey et al. (1988) conducted a study to examine ADHD symptoms on 1340 children (school-based sample; aged 7-12). It was found that SCT symptoms were loaded on a separate construct named as “sluggish tempo” (referring to those symptoms of SCT) rather than on the constructs of inattention or

hyperactivity-impulsivity. Recent studies supported that the best fit model of ADHD is that SCT items are loaded on a factor separating from DSM-IV ADHD-I and ADHD-H (Becker et al., 2016; Garner et al., 2014; Lee et al., 2015; Willcutt et al., 2014). For example, Garner et al. (2014) conducted a study using Vanderbilt ADHD Diagnostic Parent Rating Scale, Vanderbilt ADHD Diagnostic Teacher Rating Scale and SCT items in CBCL to examine whether SCT symptoms were independent from the ADHD global factor[1]. They recruited samples from clinical setting. It was found that the best model of ADHD has the following characteristics: (a) SCT symptoms were loaded on a SCT factor independent of ADHD global factor; (b) inattention and hyperactivity/impulsivity symptoms were loaded on ADHD independent factors (e.g., ADHD-I or ADHD-H and ADHD global factor; and (c) SCT factor, inattention factor and hyperactivity/impulsivity factor were correlated with each other. Based on their results, Garner et al. (2014) suggested that SCT factor seemed to be structurally distinct from ADHD-I as well as from overall ADHD even though it is positively correlated with ADHD-I.

Lee et al. (2015) also conducted a similar study as Garner et al. (2014) to examine whether SCT symptoms were independent from the ADHD. In Lee et al.'s study (2015), they recruited community sample and employed the Child and Adolescent Disruptive Behavior Inventory (Burns & Lee, 2011) which comprised of SCT symptoms, ADHD-I symptoms, ADHD-H symptoms, ODD symptoms. Similar to the result of Garner et al.'s study (2014), the best fit model was the one in which: (1) SCT symptoms were loaded on the factor that was separated from the ADHD symptoms, and (2) the SCT symptoms were correlated with the symptoms of ADHD-I. The finding of these studies further suggested that SCT symptoms are distinct from ADHD symptoms even in

[1] ADHD global factor includes all 18 symptoms of ADHD described in the DSM-5

community sample. However, these studies cannot reflect the underlying deficits of SCT that are common with or distinct from ADHD.

2.2.2 SCT symptoms are empirically distinct from but highly related to affective disorders.

Previous studies frequently found that SCT symptoms were associated with internalizing symptoms (e.g., anxiety and depression) (Bauermeister et al., 2012; Becker & Langberg, 2014; Penny et al., 2009). Smith & Langberg (2017) also found that self-rated SCT symptoms[2] were associated with anxiety and depression; all three self-rated SCT factors (Slow, Sleepy and Daydreamer) were all significantly associated with higher levels of anxiety (Smith & Langberg, 2017) whereas self-rated SCT Slow and Daydreamer factors were significantly associated with higher levels of depression (Smith & Langberg, 2017). It is also found that anxiety and depression symptoms were more uniquely related to SCT symptoms compared to ADHD. Higher scores on SCT trait factor predicted significantly higher scores in anxiety and depression after controlling for ADHD-I symptoms whereas ADHD-I symptoms did not significantly predict anxiety and depression after controlling for the SCT symptoms (Becker, Burns, Leopold, Olson & Willcutt, 2018). SCT only-group and SCT-ADHD groups were also found to have significantly higher scores than ADHD only group on mother-rated anxiety and depression (Servera, Sáez, Burns & Becker, 2018). Burns & Becker (2019) also found similar results.

SCT symptoms were often found to be significantly associated with internalizing symptoms (Bauermeister et al., 2012, Garner et al., 2010 & Penny et al., 2009). However, recent findings suggested that SCT symptoms were independent of symptom structures of affective disorders. For example, Becker et al. (2014) conducted a confirmatory factor analysis (CFA) on

[2] Rated by 14 items SCT scale (Penny et al., 2009)

Child Behavior Checklist for 6-18 (Achenbach, 2001) with 680 clinically distressed sample and that study found that SCT symptoms constituted a construct distinct from the constructs of other childhood psychopathology including ADHD, depression and anxiety. More recent research also found that SCT items were found to be mainly loaded on SCT latent construct rather than other constructs of affective disorder (e.g., depression and anxiety) (Becker et al., 2016).

All the above evidence supported that SCT was empirically distinct from internalizing symptoms of anxiety and depression but was strongly related to anxiety and depression symptoms. The results of the previous research (e.g., Becker et al., 2018) have frequently found that SCT was a predictor of later internalizing symptoms, which supported the notion that the relationship between SCT symptoms and internalizing symptoms were unidirectional and SCT symptoms may heighten the risk to develop internalizing symptoms.

2.3 Social Difficulties in Children with SCT

Among different clinical features of SCT, social difficulties have been consistently found to be associated with SCT symptoms. Social difficulties refer to two core challenges: social rejection and difficulties in initiating or maintaining social relationships with others (Bierman & Welsh, 2000). Previous studies have often found associations between social difficulties and SCT symptoms while the influence of demographics and other psychopathology on the severity of social difficulties was controlled (Becker & Langberg, 2012; Becker, Luebbe, Fite, Stoppelbein & Greening, 2013; Willcutt, et al., 2014).

A longitudinal study to examine whether SCT symptoms would predict poorer social functioning over a six-month period in a sample of elementary school students after controlling for baseline social functioning and other psychiatric disorders (Becker, 2014). Results of this teacher-rated study indicated that SCT could strongly predict the participants' poorer later

functioning across domains of social popularity, social preference, and peer relations (Becker, 2014). Therefore, SCT symptoms may have strong impact on the development of social difficulties in these children. However, it is not clear why and how these SCT symptoms may contribute to the social difficulties exhibited by these children.

Similar results were also found in other studies; SCT symptoms were often found to be linked to social withdrawal, social isolation, and low initiative in social situations (Marshall, Evans, Eiraldi, Becker & Power, 2014; Sáez, Servera, Burns & Becker, 2019). Such results were consistent with the previous study using computerized chat room task[3] in which SCT symptoms alone predicted fewer responses, reduced ability to attend to subtle social cues, weaker memory for the conversation, and smaller proportion of hostile responses (Mikami, Huang-Pollock, Pfiffner, McBurnett & Hangai, 2007). The authors explained that the weak performance in the task exhibited by children with SCT symptoms may be due to their attention and memory deficits. However, the direct linkage between attention deficits and social difficulties in children with SCT symptoms is yet to be examined.

A recent study (Becker, Garner, Tamm, Antonin & Epstein, 2017) found that the nature of social difficulties between children with SCT symptoms and ADHD were different, and the SCT symptoms were uniquely associated with social behaviours (e.g., passive/low social engagement, withdrawal, and isolation). In contrast, ADHD-H symptoms were significantly associated with social difficulties such as improper responding, active peer rejection and weak self-control in social situations. ADHD-I symptoms were not associated with social difficulties. To conclude, passive social engagement, withdrawal and isolation were often found to be associated with SCT

[3] In Chat Room Task, participants were asked to interact with a computer program through instant messaging in a chat room which simulating interactions between four peers

symptoms comparing to the social deficits manifested in children with ADHD. However, it is unclear why these children would exhibit such tendencies in social functioning.

Despite the growing evidence showing that SCT is a disorder independent from other childhood psychopathologies and is associated with social difficulties and emotional disturbances, the nature of this disorder is yet to be well understood (Barkley, 2013). To understand the multifaceted nature of SCT, it is necessary to investigate on how this condition is related to different biologically based constructs, such as, negative valence systems, positive valence systems, cognitive systems, social processes, arousal and regulatory system. Such research direction may provide us ample and important data to establish a comprehensive theoretical model of SCT. It may help differential diagnosis and provide effective treatment. In the current study, SCT will be studied in a framework delineated by the Research Domain of Criteria (RDoC).

2.4 Understanding SCT through Research Domain Criteria (RDoC)

2.4.1 Multifacet's analysis - RDoC?

Research Domain Criteria (RDoC) was launched by the National Institute of Mental Health (NIMH) in 2009 in order to devise a new way of classifying mental illnesses using different dimensions of observable behavioural and neurobiological measures (NIMH, 2016). In the present form of RDoC, there are five domains: Negative Valence Systems, Positive Valence Systems, Cognitive Systems, Systems for Social Processes, and Arousal/Regulatory Systems (NIMH, 2016). Each of these domains has its own constructs which can be studied by different units of analysis such as genes, molecules, cells, circuits, physiology, behaviour, and self-reports (NIMH, 2016). RDoC also specifies well-validated paradigms which are empirically associated with each of these constructs and units of analysis (NIMH, 2016). Previous research effort has

been focused on attention and executive functions difficulties to explain the SCT symptoms (Barkley, 2013; Baytunca, Inci, Ipci, Kardas, Bolat & Ercan, 2018; Wahlstedt and Bohlin, 2010). In RDoC, attention has been conceptualized as one of the constructs in the Cognitive Systems while executive functions are related to two of the constructs in the Cognitive Systems: Cognitive Control and Working Memory. In other words, SCT so far has been studied only in the Cognitive Systems construct. SCT has not been studied in other domains in the RDoC. In fact, Becker & Willcutt (2018) proposed that RDoC may be a meaningful approach to understand SCT. They argued that RDoC may guide researchers to investigate SCT in different levels of analysis (e.g., physiological measures) beyond the behavioural presentation of its symptoms and related impairment (Becker & Willcutt, 2018). As a result, data drawing from previous studies investigating different RDoC constructs and different level of analysis may inform the development of a comprehensive model of SCT (Becker & Willcutt, 2018). In addition, results from these studies may also help us to understand how SCT is different from or similar to other psychopathology, especially ADHD and anxiety disorders, by examining which RDoC domains are associated with SCT and other disorders (Becker & Willcutt, 2018). Negative Valence Systems, Cognitive Systems and Arousal/Regulatory Systems are RDoC domains that have been suggested to be related to SCT (Becker & Willcutt, 2018). However, previous studies have rarely examined SCT in terms of those constructs within Negative Valence Systems and Arousal/Regulatory Systems.

The main aim of the present investigation was to examine the possible relationship between SCT symptoms and the deficient processes in the Negative Valence Systems and the Arousal/Regulatory Systems. Understanding such relationship would not only enable us to identify the underlying causes of SCT but also help us to understand how various biological

constructs delineated by RDoC may contribute to the presence of psychological symptoms. This may offer support for the use of RDoC to conceptualize psychological disorders.

2.4.2 Negative Valence Systems and SCT.

The NIMH RDoC team has proposed five constructs under the Negative Valence Systems: Responses to acute threat (Fear), responses to potential harm (anxiety), responses to sustained threat, frustrative non-reward and loss (NIMH, 2016). Among these constructs, responses towards acute threat and potential harm, as well as response toward sustained threat, may be related to SCT symptomology (Becker & Willcut, 2018). Previous research has shown that fear/shyness (reflected avoidance/escape response towards aversive stimulus such as punishment) was the only predictor of SCT symptoms while ADHD symptoms were more associated with Impulsivity/ Fun seeking which reflected higher sensitivity to reinforcement (Becker, Fite, Garner, Greening, Stoppelbein & Luebbe, 2013). The results of this research provided initial evidence that SCT symptoms may be related to those constructs in Negative Valence Systems. However, further evidence is needed to support this notion particularly with different level of analysis such as physiological measures.

2.4.3 Cognitive Systems and SCT.

RDoC Cognitive Systems are comprised of five different constructs: Attention, Perception, Declarative Memory, Cognitive Control and Working Memory. Based on the day-dreamy and easy-to-be-confused characteristics of SCT, SCT seemed to be related to the Attention, Cognitive Control and Working Memory constructs. Those sub-constructs in Cognitive Control (e.g., Goal Selection, Response Inhibition and Performance Monitoring, etc.) and Working Memory in RDoC resemble those components which are often regarded as executive functions in the literature.

Previous studies have found numerous brain anatomical and functional abnormalities associated with SCT. Higher SCT symptoms in school aged children have been found to be associated with larger regional gray matter volumes in areas of the frontal lobe particularly in the dorsal region centered at the boundaries between the premotor and prefrontal cortex (Camprodon-Rosanas, et al., 2019). Such alterations in dorsal aspect of the frontal lobes may lead to difficulties in general executive function and sustained attention during complex tasks (Camprodon-Rosanas et al., 2019). In addition, SCT symptoms were also found to be associated with lower anticorrelation between dorsal frontal area and Default Mode Network (DMN). This result was not surprising given daydreaming was a key symptom of SCT and DMN has been involved in mind-wandering activities (Fox, Spreng, Ellamil, Andrews-Hanna & Christoff, 2015). Fassbender, Krafft & Schweitzer (2015) has also found that higher number of SCT symptoms were associated with hypoactivity in the left superior parietal lobe (SPL) suggesting difficulties in reorienting attention. Based on the results of the brain abnormalities research on SCT, it was expected that individuals with SCT may have significant difficulties in attention and executive functioning abilities.

Previous studies have examined whether executive function deficits could be the explanation of the SCT symptoms. Wahlstedt and Bohlin (2010) conducted a study which comprised of 209 children drawn from the community sample. ADHD-I symptoms were associated with deficits in inhibitory control, working memory, and reaction time variability, whereas SCT symptoms were associated with difficulties in sustained attention only. In the study of Willcutt et al. (2014), the researchers recruited children from the community and also found that only sustained attention weakness remained significantly associated with SCT symptoms after inattention and hyperactivity/impulsive symptoms were controlled in the analysis; they also

did not find any significant relationship between severity of SCT symptoms and performance in executive functioning tasks (e.g., Response Inhibition, Working Memory, Naming Speed and Response Variability). To examine the association between SCT and neurocognitive measures, Skirbekk et al. (2011) conducted the Attention Network Test, Verbal Memory and Working Memory test, and Spatial Memory and Working Memory test on 64 children who are diagnosed with ADHD or ADHD/Anxiety. In their study, SCT symptoms were found to be associated only with the variability score of the spatial memory test when symptoms of ADHD or ADHD/Anxiety were controlled in the analysis. In a more recent study, Baytunca, Inci, Ipci, Kardas, Bolat & Ercan (2018) compared the neurocognitive outcomes of 107 children either with ADHD only, ADHD with SCT, or in the control group by using the CNS Vital Signs Battery. They found that ADHD with SCT group performed worse than the ADHD only group in Shifting Attention test and in Stroop test which both reflected cognitive flexibility (Baytunca et al., 2018). Their results also suggested that ADHD group with SCT symptoms had significantly worse performance on the Continuous Performance Test than the ADHD-only group and the Control group indicating ADHD with SCT symptoms group had more difficulty in sustained attention ability than ADHD-only group. Baytunca et al. (2018) did not find that the SCT group had worse performance on other neuropsychological domains such as processing speed, visual/auditory memory, psychomotor speed, and reaction time compared to other two groups. Bauermeister et al. (2012) recruited 140 children aged 6-11 of community sample and also found that there were no significant correlations between SCT and executive functioning (including working memory, memory retrieval, processing speed, interference control and planning/problem solving abilities). All these evidence suggested that severity of SCT does not associate with those executive functioning deficits which have been shown to be associated with different subtypes of ADHD.

Instead, SCT was commonly found to be related to sustained attention deficit and possibly cognitive flexibility reflected by the laboratory tests.

Another line of research used rating scales to investigate the relationship between EF deficits and severity of SCT symptoms. It is because the rating scales may be better in tapping individual EF performance in the real-life setting. Using sample of 1800 children from 6 to 17 years, Barkley (2013b) compared the parental EF rating between four groups of children (healthy control, SCT only, ADHD only and ADHD with SCT symptoms). It was found that ADHD only group and ADHD with SCT group had significantly higher deficit score than SCT only group on all domains of EF (Self-management to Time, Self-Organization and Problem Solving, Self-Restraint (inhibition), Self-Motivation, and Self-Regulation of Emotion) while these two groups and the SCT only group had significant higher deficit scores than the control group on all the above EF domains. This result reflected that SCT seem to have more EF difficulties than the normal population, but these EF deficits seem to be in a milder form compared to those of ADHD. Using the regression analysis, Barkley (2013b) also found that SCT only significantly accounted for small variance on the Self-Organization scale (4.8%) and only contributed less than 1 percent of the variance on the Self-Restraint, Self-Motivation and Self-Regulation of Emotion. No significant contribution by SCT symptoms to the Self-Management to Time was found in that study. In contrast, ADHD-I symptoms accounted for the vast majority of variance on all these dimensions. Once again, SCT was shown to be less related to those EFs which were often associated with ADHD subtypes particularly ADHD-I. Therefore, EFs may not be the strong underlying factors of the daily life deficits in SCT comparing to ADHD.

Becker and Langberg (2014) used Behavioural Rating Inventory of Executive Functioning (BRIEF) (parent/teacher's report) to examine the EFs of children with ADHD at

home and school environment. Like the results of Barkley (2013), Becker and Langberg (2014) found that both of the parent or teacher's rating on the SCT symptoms was not a significant predictor of their rating on the Behavioural Regulation Index (BRI) which assessed problems in Behavioural Inhibition, Shifting and Emotional Regulation. However, both of their ratings on SCT symptoms were found to be a significant predictor of the ratings on the Metacognition Index (MI) which assessed problems in Initiation, Working Memory, Planning/Problem Solving, Organization of Materials and Self-Monitoring. Although MI was found to be associated with the severity of SCT symptoms, it should be noted that ADHD-I was also found to be the strongest predictors of MI in both parent and teacher report (Becker & Langberg, 2014). It is possible that the individuals with SCT symptoms may have EF deficits but less severe than those with ADHD, especially on metacognitive abilities. However, it is still unclear whether there is any other underlying factor contributing to the EF deficits and other SCT symptoms.

Research using laboratory tests and rating scale suggested that SCT symptoms were often found to be associated with more real life executive functioning deficit reflected by parent/parent rating scales but not in laboratory EF tests. The reason which causes such discrepancy may be because EF rating scales has been seen as a better ecological measure than laboratory measures (Barkley & Fischer, 2011; Jimenez et al., 2015). EF has been seen as hierarchically organized construct with increasing level of complexity of functioning (Barkley & Fischer, 2011). Higher level of EF manages the lower level of the EF to achieve long term and complex EF goals (Barkley & Fischer, 2011). For example, set shifting, working memory and inhibition may be at the lower level of the EFs. But at the higher level of EFs, we may strategically utilize all these basic EFs in planning or problem solving. In other words, EF laboratory tests seem to tap the individual's lower level of EFs, while the EF rating scale can tap the higher level EFs especially

on how we apply EFs in pursuing short term and long-term real-life goals. Therefore, the apparent discrepant findings between laboratory EF tests and EF rating scales in SCT may simply reflect that they were just different levels of measurement of EFs among individuals with SCT. Based on the finding of the laboratory tests and the rating scales, SCT may have sustained attention deficit at the lower level of cognitive functioning which may lead to problems at the higher level of EF functioning in the real life, especially metacognitive abilities. Therefore, it is not that SCT was not related to EF as shown by some previous studies. It is just that the underlying deficits of SCT may lie among different levels of this EF hierarchy model and sustained attention. However, the underlying mechanism leading to attention deficits in SCT remains unclear.

2.4.4 Arousal/Regulatory Systems and SCT.

RDoC Arousal/Regulatory Systems has comprised of Arousal, Sleep-Wakefulness and Circadian Rhythms constructs. Arousal is defined as the continuum of the sensitivity of the individual towards external and internal stimulus while circadian rhythms are defined as self-sustaining oscillations which organize the timing of the biological system to optimize one's physiology, behaviour and health (NIMH, 2016). Sleep and wakefulness are defined as internal state which reflect the coordinated changes in the dynamic functional organization of the brain which optimize one's physiology, behaviour and health (NIMH, 2016).

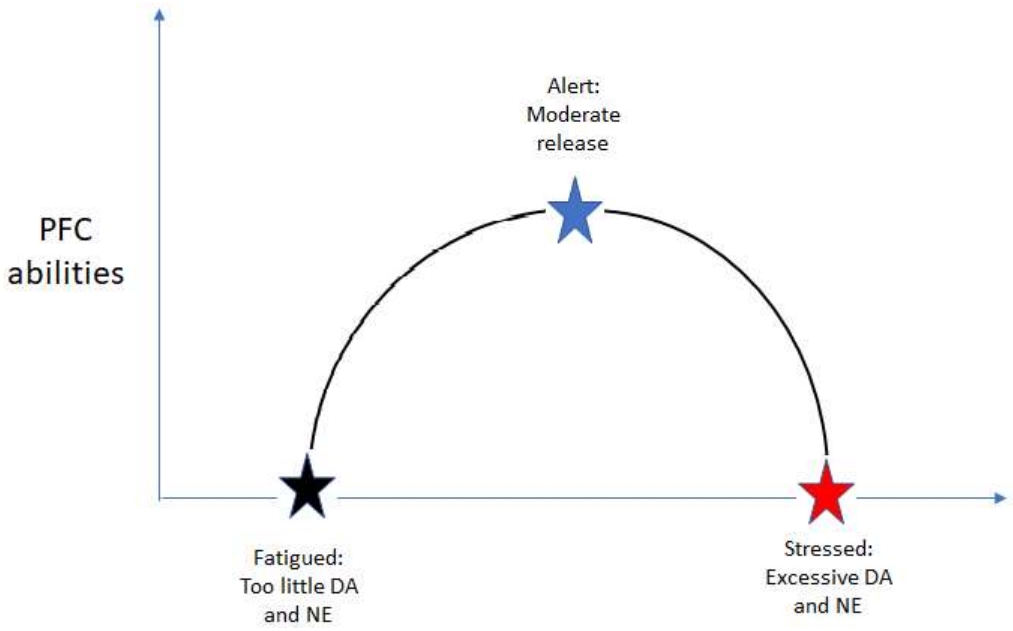
Among these three constructs of the RDoC Arousal/Regulatory Systems, Arousal Systems has been suggested to be related to SCT symptoms. Barkley (2013a) suggested that SCT may be related to arousal abnormalities because of its symptoms associated with sleepiness and low energy. However, no previous research has examined the linkage between abnormalities in Arousal State/Regulation and SCT symptoms.

2.5 Theoretical Models Explaining SCT

There is a lack of theoretical model to explain SCT. Other than viewing SCT through the constructs of RDoC, this study also applied Posner model of attention and Thayer's neurovisceral integration model to reveal the potential neurobiological deficits behind SCT symptoms.

Arousal and alertness are closely related (Petersen & Posner, 2012). Norepinephrine (NE) has been related to the alerting system. Increasing or decreasing the NE can increase or decrease the warning signal effect (enhance the speed of orienting attention and faster responding to the signal) (Petersen & Posner, 2012). Alertness towards warning signal is accompanied by activity in the locus coeruleus (LC) which is found to be the source of NE (Aston-Jones & Cohen, 2005) and such warning signal effect can be blocked by drugs which decrease the release of NE. Sustained vigilance (tonic alertness) has been found to be related to the mechanisms of the right cerebral cortex (Posner & Petersen, 1990). Sturm and Willmes's study (2001) showed that right hemisphere and thalamic set of areas are involved in both phasic and tonic alerting. NE, along with dopamine (DA), can exert an inverted U influence on different prefrontal cortex functions including attention and EF (Brennan & Arnsten, 2008) (see Figure 1). Too little or too much release of NE and DA can impair prefrontal cortex (PFC) functions (Brennan & Arnsten, 2008). Therefore, NE and DA may act as a chemical switch which turns on the PFC during alert state and turn off the PFC during drowsy and stressful state (Brennan & Arnsten, 2008). Therefore, previous findings on those EF and attention difficulties in individuals with SCT symptoms may be due to the low arousal level in their brain.

Figure 2. Inverted U influence of NE and DA on PFC function (adapted from Brennan & Arnsten, 2008)



LC has a reciprocal pathway with the autonomic nervous system (ANS) (Samuels & Szabadi, 2008; Wood & Valentino, 2017). LC neurons can receive and process cardiovascular related information and change LC activity, where LC activity impacts on the cardiovascular function (Wood & Valentino, 2017). For example, during hypotensive stress, the pattern of LC discharge could be changed to high tonic state so as to supports an individual to have increased arousal, extraneous attention and behavioural flexibility (Valentino & Wehby, 1988). Previous study has also showed that activity in the LC, which is the source of NE in the brain, can produce a cardiovascular response. For example, Wang et al. (2014) found that photo-stimulation of LC neurons in mouse increased inhibitory neurotransmission to the parasympathetic cardiac vagal neurons in the brainstem and therefore decreased the parasympathetic affluent to the heart. To control the autonomic functions, LC has also been found to have direct projections to the spinal cord and projections to autonomic nuclei including the dorsal motor nucleus of the vagus, the nucleus abiguus and the rostroventrolateral medulla (Samuels & Szabadi, 2008). This evidence support the two-way pathway between LC and ANS. Therefore, changes in the arousal state in

the brain may lead to changes in the ANS activity. It is possible that measuring the changes in the ANS can reflect though not equivalent to the changes in the brain arousal system in human.

The autonomic nervous system (ANS) has been suggested to play a crucial role in the modulation of physiological arousal during tasks required executive functioning and attention (Suess, Porges & Plude, 1994; Thayer & Lane, 2000). The ANS comprises of the sympathetic nervous system (SNS; mainly use NE as primary neurotransmitter) and parasympathetic nervous system (PNS; use acetylcholine as primary neurotransmitter) (Janig, 2008). SNS and PNS have innervated to different organs in human. SNS and PNS work interactively. SNS is responsible for resources mobilization while PNS is responsible for restorative/vegetative function (Thayer et al., 2009). Sustained attention has been found to be dependent on the brain stem regions to decrease the parasympathetic vagal tone (through the vagal nerve) so as to facilitate the sympathetic influence in the ANS system which enable the immediate mobilization of the individual during real life tasks (Suess, Porges & Plude, 1994).

Thayer et al. (2009) suggested that the PFC exerts influence on subcortical structures (e.g., amygdala and thalamus) so that an individual is able to control the psychophysiological resources in attention and executive functions, so that he/she can organize behaviour efficiently in order to deal with the challenge in the environment. Lane et al. (2009) found that the level of PNS functioning (as reflected by high frequency of heart rate variability, HRV) in resting condition correlated with the level of blood flow in cortical regions (the right superior prefrontal cortex, the left rostral anterior cingulate cortex, the right dorsolateral prefrontal cortex and the right parietal cortex) when different emotions were induced to the participants through film clips and recall of personal experiences. Hansen et al. (2003) found that resting ANS functioning (as reflected by heart rate variability) is associated with cognitive performance in various attention

and executive functioning tasks in 53 adults aged 18 to 34 years (e.g., n-back working memory task). The ability to regulate the ANS activity was also found to have better attention performance during challenge conditions in ninety-nine children and adolescents aged 8 to 17 years (Chapman et al., 2010).

Two recent meta-analysis studies were conducted to examine the relationship between ANS functioning and executive functioning (Holzman & Bridgett, 2017; Zahn et al., 2016). Both studies applied HRV indexes to reflect ANS functioning. It was found that resting HRV was found to be significantly associated with executive functioning (Holzman & Bridgett, 2017; Zahn et al., 2016). The finding of these studies suggested a two-way relationship between ANS functioning and cognitive functioning (such as executive functioning and attention). Therefore, it is possible that abnormalities in ANS functioning, caused by suboptimal level of arousal, may be related to their sustained attention and executive functioning difficulties in real life among children with high SCT symptoms.

2.6 Conceptual Framework of this Study

Although SCT has been gradually recognized as a separate condition from ADHD, we still do not have a comprehensive model to explain its symptoms or associated problem such as social difficulties. Previous studies from multiple dimensions shows SCT symptoms may be related to arousal abnormalities, sustained attention deficit and executive functioning deficits. Using RDoC framework, we can formulate a model which can account for the mixture of cognitive, affective, behavioural and physiological factors related to the SCT symptoms and its associated problem. SCT seemed to be associated with Cognitive Systems (such as attention and executive functions) and with Arousal/Regulatory Systems (such as abnormalities in arousal state and regulation which can be reflected by ANS abnormalities).

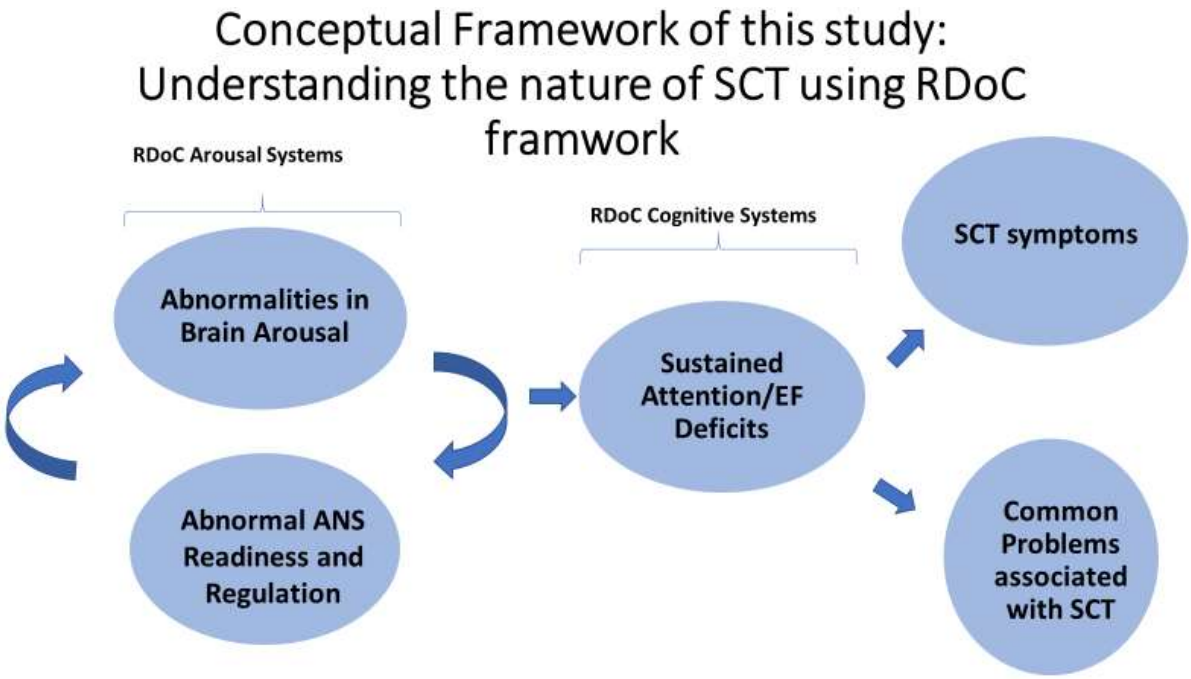
In the current study, SCT is conceptualized as a condition with functional deficits in brain arousal and ANS state and regulation related to the deficits in attention and executive functioning. Therefore, the conceptual framework of the current study (Figure 2) includes components in both brain arousal and ANS state and regulation to explain the SCT deficits. Brain arousal is defined as the brain state related to the level of NE in the cortical area in the PFC which is regulated by the LC (Petersen & Posner, 2012). ANS readiness is defined as the physiological readiness in ANS of an individual to prepare for the challenge in the real life and can be measured by one of the well-recognized methods, the resting HRV (Thayer & Lane, 2009). The ANS regulation is defined as the ability to regulate one's physiological activity when dealing with real life changes and challenge. The ANS readiness and ANS regulation are two components of ANS functioning. Executive functioning is defined as a range of cognitive abilities which enable people to focus on tasks, make plans, solve problems and multitasking (Ahmed & Stephen, 2011), and it is responsible for regulating and monitoring one's goal directed behaviour (Biderman et al., 2004; Schoemaker et al., 2012). Sustained attention is defined as the ability to produce and maintain optimal vigilance during task (Petersen & Posner, 2012).

This framework postulates that among individuals with high SCT symptoms, abnormalities in brain arousal state and regulation (e.g., under-arousal due to lower level of norepinephrine) may be related to abnormal ANS readiness (as reflected by the resting HRV in the current study) and ANS regulation ability (as reflected by the change of HRV from one condition to another condition in the current study). Such chained actions between the arousal system and ANS may be related to the deficits in executive functioning and attention among

individuals with SCT. Subsequently, SCT symptoms and its associated problems (such as social difficulties) arise.

Under this framework, it is expected that severity of SCT symptoms would be associated with the level of ANS readiness. Due to their possible arousal difficulties, it is also expected that severity of SCT symptoms would be associated with different regulation pattern in ANS when receiving stimulation. Moreover, common associated problem with SCT such as social difficulties would be related to their deficits in sustained attention and executive functioning.

Figure 3. Conceptual framework of SCT symptoms in the present study.



2.7 Knowledge Gap and Significance of this Study

Previous studies have found that SCT symptoms were associated with some cognitive deficits such as sustained attention and executive functioning. However, the relationship between other biological systems such as Arousal/Regulatory Systems and Negative Valence Systems with SCT systems is unclear. The present study was the first attempt to examine the relationship between SCT symptoms, arousal state and regulation using physiological measures (such as HRV measures) and cognitive deficits. The results gathered from this study may inform us to build a comprehensive model of SCT which can serve a framework to invent new assessment and treatment of SCT.

2.8 Aims, Research Questions and Hypotheses of this Study

The overall aim of the present study was to examine the nature of SCT symptoms. Specifically, the current study aimed to find out whether the Arousal/Regulatory Systems and Cognitive Systems delineated by the RDoC framework would be related to the symptoms of SCT. The research questions of this study are: (1) What is the neurophysiological correlates of SCT symptoms? (2) What is the relationship between arousal regulation and sustained attention in SCT? and (3) What is the role of attention deficits in the social difficulties in SCT?

To answer the research questions, the present study was comprised of three studies. Study I aimed to examine the neurophysiological correlates of SCT symptoms in school aged children. Study II aimed to identify the linkage between arousal regulation deficit and sustained attention difficulties in children with SCT. Study III aimed to identify the role of attention deficits in the social difficulties (social problem and withdrawn behaviour) among individuals with SCT symptoms.

The hypotheses of Study I are:

1. Resting HRV measures (measures of ANS readiness) would exhibit a significant relationship with SCT symptoms;
2. Changes in HRV measures from a resting to warning signal condition (measure of ANS regulation) would have a significant relationship with SCT symptoms;
3. ANS readiness and ANS regulation would significantly predict severity of SCT symptoms among school-aged children after controlling ADHD symptoms.

The hypotheses of Study II are:

1. Abnormalities in cortical activities measured by EEG would predict the severity of sustained attention deficits in children with high level of SCT symptoms;
2. ANS readiness and ANS regulation measured by HRV measures would predict the severity of sustained attention deficits in children with high level of SCT symptoms.

The hypotheses of Study III are:

1. Scores in the sustained attention measures would predict the severity of the social problems measured by the parent rating scale among children with high level of SCT symptoms;
2. Scores in the sustained attention measures would predict the severity of withdrawn behaviour measured by the parent rating scale among children with high level of SCT symptoms.

Chapter 3

Study I: Neuro-Physiological Correlates of SCT Symptoms in Children

Remarks: Part of the Study I has been published in peer-reviewed journal:

Yung, T. W. K., Lai, C. Y. Y., Chan, J. Y. C., Ng, S. S. M., & Chan, C. C. H. (2020). Neurophysiological correlates of sluggish cognitive tempo (SCT) symptoms in school-aged children. European Child & Adolescent Psychiatry, 29(3), 315-326.

SCT is conceptualized as a condition resulted from abnormalities in arousal regulation. As there is a reciprocal link between brain arousal system (e.g., LC) and ANS (Samuels & Szabadi, 2008; Wood & Valentino, 2017), it is expected that changes in the LC would cause the corresponding changes in the ANS (ANS readiness and ANS regulation measured by the HRV). Therefore, if SCT is associated with the arousal abnormalities, SCT symptoms should associate with ANS readiness and ANS regulation, which could be both reflected by HRV measures. The aim of the Study I is to examine the neurophysiological correlates of SCT symptoms in school aged children. The hypotheses of Study I are:

1. Resting HRV measures (measures of ANS readiness) would exhibit a significant relationship with SCT symptoms;
2. Changes in HRV measures from a resting to warning signal conditions (measure of ANS regulation) would have a significant relationship with SCT symptoms;
3. ANS readiness and ANS regulation would significantly predict severity of SCT symptoms among school-aged children after controlling ADHD symptoms.

3.1 Method

3.1.1 Participants.

Thirty primary school students aged 6–12 (mean age = 104.2 months, standard deviation [SD] = 20.1; 56.7% female; mean IQ score = 102.92, SD = 9.95) were recruited via posters sent to primary schools and parent chat groups in Hong Kong. Using G*Power, the required sample size for the present study was 20. Therefore, the current sample size was sufficient. Most of the participants were recruited from primary schools (93.3%), and the remainder (6.7%) were recruited via the parent chat group channel. Parents who expressed an interest in joining the study were instructed to contact the researcher. Each parent received information on the nature and purpose of the study and a written consent form. The consent forms were signed prior to the collection of data.

The participants involved in this study were required to meet the following inclusion criteria: (a) aged 6–12 years and (b) a full-scale IQ score >80. Potential participants who met the following criteria were excluded: (a) any psychiatric diagnosis, including ADHD, oppositional defiant disorder, conduct disorder, or dyslexia; (b) a T-score >85 in the Chinese version of the Strength and Weaknesses of ADHD Symptoms and Normal Behavior scale (SWAN; Swanson et al., 2012); (c) a T-score >70 in any subscale of the Child Behavior Checklist (CBCL) (Chinese version) (Achenbach, 2001); (d) any uncorrected visual or auditory problems; and (e) a history of diabetes or cardiac and/or respiratory problems. Children with an ADHD diagnosis or elevated symptoms of ADHD were excluded because these symptoms would have confounded the neurophysiological measures used in the study (i.e., HRV measures). Those with other psychiatric disorders (e.g., childhood anxiety or oppositional defiant disorder/conduct disorder) were excluded because these disorders have also been found to be associated with different

patterns of HRV (Rozenman, Sturm, McCracken, & Piacentini, 2017; Schoorl, Rign, De Wied, Van Goozen & Swaab., 2016).

3.1.2 Procedure and experimental setup.

Before the data collection, the children's demographic information (i.e., name, date of birth, and gender) and medical histories were obtained from their parents. Each participant was then asked to attend two 1.5-hour testing sessions conducted in a laboratory free from visual or auditory distractions. Additional requirements were set to safeguard the quality of the HRV measures, including (a) an illumination level of 10 lux, (b) a room temperature of 23–25 ºC, and (c) a background noise level of 40–45 dB. During the first session, each participant completed an IQ test and neuropsychological tests. During the second session, each participant completed the HRV measures. The participants were reminded to avoid the following before the second session: (a) the intake of caffeinated drinks; (b) the intake of food for 1.5 hours before testing; (c) participating in vigorous activities for 24 hours before testing; and (d) the use of any treatment or medication that could affect ANS activity. Breaks were offered before or during the tests.

3.1.3 Measuring Instruments.

Each participant underwent four neuropsychological tests and neurophysiological measures of HRV.

3.1.3.1 Neuropsychological tests.

- *Wechsler Intelligence Scale for Children, Fourth Edition (Hong Kong) short-form (WISC-IV; Wechsler, 2010).* This short version of the WISC-IV consists of four subscales: similarities, matrix reasoning, coding and digit span. The raw scores obtained from these subscales are combined to calculate a total raw score. This total raw score is then converted into a full-scale IQ score.

- *Child Behavior Checklist for Ages 6–18 (CBCL/6-18) (Achenbach, 2001).* The CBCL/6-18 is an assessment tool designed for parents to rate the emotional and behavioural problems of children between the ages of 6 and 18. Each item on the scale is rated by the respondent using a 3-point scale, where 0 represents "not true", 1 indicates "somewhat or sometimes true", and 2 signifies "very true or often true". The CBCL consists of eight subscales including withdrawn behaviour, anxiety/depression, somatic complaints, social problems, thought problems, attention problems, rule-breaking behaviour, and aggressive behaviour. The total raw score for each scale is then converted into a standardized score. Previous study has shown that the CBCL exhibits good to excellent test-retest reliability (intra-class correlation coefficient: .66–.87) and good discriminant validity (Leung et al., 2006).
- *SWAN—Chinese version.* SWAN is a rating scale used by teachers and parents to assess ADHD symptoms (Swanson et al., 2012). The Chinese-translated version of the scale was utilized and validated for children in Hong Kong (Education Bureau of HKSAR, 2010). The scale consists of 18 items that evaluate a child's control of their attention, impulses, and activity. These items are divided into two subscales, with nine items each, focusing on inattention and hyperactivity/impulsivity. Total scores and subscale scores are calculated by summing the raw item scores and can be expressed as T-scores. Higher scores indicate a lower presence of ADHD symptoms. For this study, only the total SWAN scores were utilized. The parent and teacher versions of SWAN have demonstrated excellent internal consistency (alpha > .9) and good discriminant validity (AUC > .8) for both total and subscale scores (Education Bureau of HKSAR, 2010).
- *SCT Scale (Penny, Washbusch, Klein, Corkum, & Eskes, 2009).* The 14-item parent and teacher scale is utilized to assess symptoms of Sluggish Cognitive Tempo (SCT) in children.

Each item is rated on a 7-point scale, ranging from 0 ("not at all") to 6 ("very much"). Consistent with previous research conducted by Becker, Garner, Tamm, Antonini, and Espstein (2019) and Holdaway and Becker (2018), the present study selected 10 items from the scale instead of using the full scale. These 10 items demonstrated consistent loadings on the SCT factor but not the ADHD inattention factor, as reported by Becker et al. (2016). This selection of items formed a cohesive 10-item construct that aligned with the characteristics of the participants and the study's hypotheses. The internal consistency of the original 14-item SCT scale, as measured by both parent (alpha > .8) and teacher ratings (alpha > .9), was found to be high according to Penny et al. (2009). In the present study, the 10-item version also exhibited a high level of internal consistency, with a Cronbach's alpha of .898.

3.1.3.2 Neurophysiological tests.

- *HRV measures*. HRV measures ANS activity (Task Force of the European Society of Cardiology & North American Society of Pacing and Electrophysiology, 1996). Here, HRV was used to evaluate SNS and PNS activity under each experimental condition (resting and warning signal conditions; refer to the next section for details). The sampling rate of 5 kHz was set using an H2 heart rate monitor (Polar Electro, Finland).

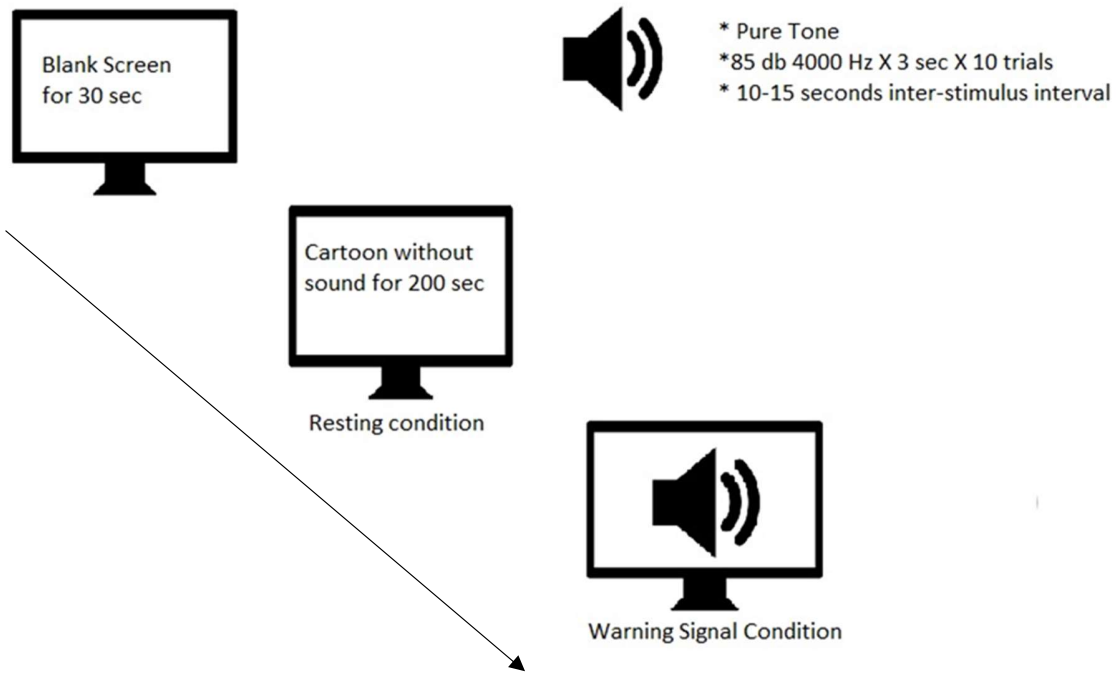
3.1.4 Experimental paradigm.

3.1.4.1 Warning signal paradigm.

Figure 3 depicts the experimental paradigm used in this study. This paradigm was adapted from Gomez, Lai, Chan, and Tsang (2018) and Lai (2013), who modified the sensory challenging protocol proposed by Miller et al. (1999). The paradigm described by Gomez et al. (2018) and that of the present study differed mainly in the former's inclusion of a recovery condition. The recovery condition was omitted here because the study focused solely on the change in HRV from the resting condition to the warning signal condition[4]. In the experimental protocol, the HRV was measured continuously across the two conditions: resting and warning signal. During the resting condition, each participant was shown a silent animated video for 200 seconds. Subsequently, the monitor screen turned blank, and the participant was exposed to a warning signal condition block comprising 10 trials of a 4-kHz pure tone at 85 dB. The duration of each trial was 3 seconds. A pseudorandomized interval of 10–15 seconds was set to avoid adaptation to the stimulus.

[4] The warning signal condition was used in the current study to examine the change of the arousal level from resting condition to the stimulation condition (the warning signal). Aston-Jones & Cohen (2005) found that warning signal was accompanied by the increase of the activity in the LC which was the source if NE.

Figure 4. Experimental paradigm of Study I (adapted from Gomez, Lai, Chan & Tsang, 2018; Lai, 2013). This figure shows the resting and warning signal conditions used in the study.



3.1.4.2 HRV signal processing.

HRV is a measure that quantifies the variation in the time intervals between consecutive heartbeats (Shaffer & Ginsberg, 2017). The raw HRV data was initially processed using aHRV software (Nevrokard, Slovenia) to convert it into tachograms. The tachograms were visually inspected to identify any ectopic beats, movement artifacts, or abnormal noise signals. Afterward, the data was divided into specific time events based on the experimental paradigm. Any values that fell 20% below or above the mean of the preceding 25 beats were considered artifacts during short-term recording and were corrected through interpolation. Data with a correction rate exceeding 3% compared to the total normalized HRV data samples were

discarded, following the recommendations of the Task Force of the European Society of Cardiology and North American Society of Pacing and Electrophysiology (1996).

Previous studies have used three major types of HRV measurement, following the recommendations of the Task Force of the European Society of Cardiology and North American Society of Pacing and Electrophysiology (1996): time domain, frequency domain, and non-linear measurements. Time domain indices quantify the variability in the measured time interval between successive heartbeats (Shaffer & Ginsberg, 2017) and can be derived from direct measurements of the NN intervals or the instantaneous heart rate and from the differences between NN intervals. The most common measures are the root mean square of successive RR interval differences (RMSSD) and the percentage of successive RR intervals that differ by more than 50 ms (pNN50). Both measures are closely correlated with PNS activity (Shaffer & Ginsberg, 2017).

Frequency domain measurements estimate the distribution of absolute or relative power into four frequency bands: ultra-low frequency (ULF;< .003 Hz), very low frequency (VLF; .0033–.04 Hz), low frequency (LF; .04–.15 Hz), and high frequency (HF; .15–.4 Hz). In this study, autoregressive modeling was used to stratify HRV into these four frequency bands. Absolute power is calculated as dividing ms squared by cycles per second (ms^2/Hz). Relative power is determined as the percentage of total HRV power or in normalized units (nu).The absolute power for a specific frequency band is divided by the summed absolute power of the LF and HF bands (Shaffer & Ginsberg, 2017). In this study, the frequency domain measurements were expressed in terms of relative power (nu), as this enabled the direct comparison of frequency domain measurements between participants. Notably, HF has been found to reflect

PNS activity, whereas LF may reflect both SNS and PNS activity (Task Force of the European Society of Cardiology & North American Society of Pacing and Electrophysiology, 1996).

Finally, non-linear measurements indicate the unpredictability of a time series, which arises from the complexity of the sympatho-vagal mechanism that regulates HRV (Shaffer & Ginsberg, 2017). The standard deviation of the Poincaré plot perpendicular to the line of identity (SD1) and along the line of identity (SD2) are commonly used in this context (Shaffer & Ginsberg, 2017). A Poincaré plot can be created by plotting every RR interval against the prior interval (Shaffer & Ginsberg, 2017), and can be analyzed by fitting an ellipse to the plotted dots. SD1 represents the width of this ellipse, and is thought to reflect short-term variability in HRV, a measure of PNS activity (Tulppo, Mäkikallio, Takala, Seppänen, & Huikuri, 1996). SD2 represents the length of the ellipse and is thought to reflect long-term variability in HRV (Brennan, Palaniswami, & Kamen, 2001; Guzik Piskorski, Krauze, Schneider, Wesseling, Wykretowicz, & Wysocki, 2007; Shaffer & Ginsberg, 2017). In several studies, a decrease in SD2 has been associated with an increase in sympathetic activity (Castaldo, Montesinos, Melillo, James, & Pecchia, 2019; De Vito, Galloway, Nimmo, Maas, & McMurray, 2002; Rahman, Habel, & Contrada, 2018; Tulppo et al., 1996). However, changes in SD2 may also be modulated partly by changes in parasympathetic activity (Rahman et al., 2018). Both SD1 and SD2 can be expressed in nu.

3.1.5 Data analysis.

Partial correlation analysis was used to examine the correlations between the resting HRV measures (RMSSD, pNN50, SD1 nu, SD2 nu, LF nu, and HF nu) and SCT scores (Hypothesis 1). This method was also used to measure the correlations between changes in these HRV measures from the resting to warning signal conditions and SCT scores (Hypothesis 2)

when controlling for the ADHD symptoms included in SWAN. The changes in HRV measures were calculated by deducting the value of resting HRV measures from the value of HRV measures in warning signal condition. Strong correlations were observed between the HRV variables (r = .64–.94). Therefore, to minimize multicollinearity, stepwise regression was conducted to examine the contributions of the different HRV variables to the severity of SCT symptoms. All the analyses were conducted using SPSS 23.0 (IBM, U.S.A.), and the significance level was set at .05.

3.2 Results

3.2.1 Associations of resting HRV measures with SCT scores.

Partial correlation analysis was used to test the associations of the resting ANS measures with the participants' SCT scores. The means and standard deviations of the resting HRV measures and rating scale scores were shown in the Table 1. When controlling for SWAN ADHD scores, SCT scores exhibited a significant positive relationship with SD2 nu (p = .022) (Table 2). No other significant correlations between the participants' SCT scores and other resting HRV measures were observed (Table 2).

3.2.2 Associations of changes in HRV from resting to warning Signal condition with SCT scores.

Partial correlation analysis was also used to test the associations between the magnitude of changes in the HRV measures from the resting to warning signal conditions and the participants' SCT scores. The means and standard deviations of the changes in the HRV measures and rating scale scores were shown in the Table 3. When controlling for SWAN ADHD scores, the change in SD2 nu from resting to warning signal condition was significantly

associated with the SCT score (r = .402, p = .031) (Table 4). Moreover, the change in pNN50 from resting to warning signal condition exhibited a marginally significant association with the SCT score (r = *.362,* p = .053). No significant correlations were observed between changes in the other HRV measures and the participants' SCT scores.

3.2.3 Use of Resting HRV measures to predict SCT symptoms.

The intercorrelations between resting HRV measures and behavioural rating scale scores were shown in the Table 5. Stepwise regression was conducted to determine the ability of HRV measures to predict the SCT score after entering the Swan ADHD score into the model to control for ADHD symptoms (Step 1). Subsequently, the HRV measures (RMSSD, pNN50, SD1 nu, SD2 nu, LF nu, and HF nu) were entered using the stepwise method (entry probability = .05; removal probability = .10) (Step 2) (Table 6). The SWAN ADHD score did not contribute significantly to the regression model [$F(1,28) = 2.601$, $p > .05$]. The stepwise analysis identified only the resting SD2 nu as a significant predictor in the regression model. This measure explained 16.5% of the variance in SCT scores [$F(2,27) = 4.497$, $p < .05$].

Table 1
Resting HRV Measures and Behavioral Rating Scales (n = 30)

Variable	Mean	*SD*
SCT score	23.33	9.26
Swan ADHD score	75.10	14.01
RMSSD	62.61	18.81
pNN50	39.34	13.51
SD1 nu	5.61	1.79
SD2 nu	10.21	3.30
HF nu	65.00	13.34
LF nu	48.94	24.91

Note. RMSSD = root mean square of successive RR interval differences; pNN50 = percentage of successive RR intervals that differ by more than 50 ms; SD1 nu = Poincaré plot standard

deviation perpendicular to the line of identity in normalized units; SD2 nu = Poincaré plot standard deviation along the line of identity in normalized units; LF nu = low-frequency HRV in normalized units; HF nu= high-frequency HRV in normalized units.

Table 2

Partial Correlation Coefficients between Resting HRV Measures and SCT Scores when Controlling for SWAN ADHD Scores (n = 30)

	HRV measures					
	RMSSD	pNN50	SD1 nu	SD2 nu	LF nu	HF nu
SCT score	0.154	0.289	0.304	.425*	0.003	0.023

Note. RMSSD = root mean square of successive RR interval differences; pNN50 = percentage of successive RR intervals that differ by more than 50 ms; SD1 nu = Poincaré plot standard deviation perpendicular to the line of identity in normalized units; SD2 nu = Poincaré plot standard deviation along the line of identity in normalized units; LF nu = low-frequency HRV in normalized units; HF nu = high-frequency HRV in normalized units.
* $p < .05$.

Table 3

Changes in HRV Measures and Behavioral Rating Scale Scores (*n* = 30)

Measure	Mean	*SD*
SCT score	23.33	9.26
Swan ADHD score	75.10	14.01
RMSSD	-2.76	10.49
pNN50	-1.04	10.24
SD1 nu	-.30	1.02
SD2 nu	-1.07	2.27
HF nu	-.04	14.21
LF nu	-3.97	36.02

Note. RMSSD = root mean square of successive RR interval differences; pNN50 = percentage of successive RR intervals that differ by more than 50 ms; SD1 nu = Poincaré plot standard deviation perpendicular to the line of identity in normalized units; SD2 nu = Poincaré plot standard deviation along the line of identity in normalized units; LF nu = low-frequency HRV in normalized units; HF nu = high-frequency HRV in normalized units.

Table 4

Partial Correlation Coefficients Between Magnitude of Change in HRV Measures From Resting to Warning Signal Conditions and SCT Scores when Controlling for SWAN ADHD Score

	HRV measures					
	RMSSD	pNN50	SD1 nu	SD2 nu	LF nu	HF nu
SCT score	.249	.362	.341	.402*	-.059	.050

Note. RMSSD = root mean square of successive RR interval differences; pNN50 = percentage of successive RR intervals that differ by more than 50 ms; SD1 nu = Poincaré Plot standard deviation perpendicular to the line of identity in normalized units; SD2 nu = Poincaré plot standard deviation along the line of identity in normalized units; LF = low-frequency HRV in normalized units; HF = high-frequency HRV in normalized units.

*p < .05.

Table 5

Intercorrelations Between Resting HRV Measures and Behavioral Rating Scale Scores in Multiple Regression (*n* = 30)

Variable	SWAN ADHD Score	SCT symptom score	Resting-RMSSD	Resting-pNN50	Resting-SD1 nu	Resting-SD2 nu	Resting-HF nu	Resting-LF nu
SWAN ADHD score								
SCT symptom score	.292							
Resting-RMSSD	-.206	.084						

Resting-pNN50	-.247	.196	.895**.				
Resting-SD1 nu	-.244	.211	.938**	.867**			
Resting-SD2 nu	-.121	.368*	.703**	.640**	.765**		
Resting-HF nu	.005	.024	-.502**	-.267	-.469**	-.542**	
Resting-LF nu	.014	.006	-.014	-.150	-.104	.286	-.569**

Note. RMSSD = root mean square of successive RR interval differences; pNN50 = percentage of successive RR intervals that differ by more than 50 ms; SD1 nu = Poincaré plot standard deviation perpendicular to the line of identity in normalized units; SD2 nu = Poincaré plot standard deviation along the line of identity in normalized units; LF nu = low-frequency HRV in normalized units; HF nu = high-frequency HRV in normalized units.

*$p < .05$. **$p < .01$.

Table 6

Regression Model of Resting HRV Measures as Predictors of SCT symptoms (*n* = 30)

Variable	Unstandarized B	Coefficient Std. Error	Standardized Coefficients Beta	*t*	Sig.	R	R^2	Adjusted R^2	R^2 Change
Step 1									
SWAN ADHD score	.193	.119	.292	1.613	.118	.292	.085	.052	.085
Step 2									
SWAN ADHD score	.225	.111	.341	2.032	.052	.500	.250	.194	.165*
Resting - SD2 nu	1.148	.471	.409	2.436	.022				

Note. SD2 nu = Poincaré plot standard deviation along the line of identity in a normalized unit.
*p <.05.

3.2.4 Use of changes in HRV measures to predict SCT Symptoms.

The intercorrelations between the changes in HRV measures and behavioural rating scale scores were shown in the Table 7. Stepwise regression was repeated for predicting participants' SCT score with the changes in the HRV measures. Similarly, SWAN ADHD score was first entered into the model (Step 1), to be followed by SWAN ADHD score, changes in RMSSD, pNN50, SD1 nu, SD2 nu, LF nu, and HF nu entered with a stepwise method (Table 8). SWAN ADHD score alone was not found to be a significant predictor (Table 8). There were three significant predictors for the SCT score. By controlling SWAN ADHD symptoms, the Change in SD2 nu and the Change in pNN50 were significant predictors in the regression models (Steps 2 and 3). The Change in SD2 nu alone explained 14.8% of the variance of the SCT scores (F (2, 27) = 4.098, p<.05). Adding the Change in pNN50 to the model accounted for 13.8% more of the variance of the SCT score (F (3,26) = 5.117, p<.01). The Change in SD2 nu was a stronger predictor than Change pNN50 on the SCT score.

Table 7

Intercorrelations between multiple regression variables (Change in HRV measures and Behavioural Rating Scales) (n = 30)

	SWAN ADHD Score	SCT symptom score	Change - RMSSD	Change – pNN50	Change – SD1 nu	Change- SD2 nu	Change – HF nu	Change – LF nu
SWAN ADHD score								
SCT symptom score	.292							
Change-RMSSD	.026	.246						
Change – pNN50	-.096	.317	.737**					
Change – SD1 nu	-.054	.310	.910**	.786**				
Change - SD2 nu	-.245	.301	.183	-.038	.158			
Change – HF nu	.116	.081	.305	.424	.417	-.491**		
Change – LF nu	-.094	-.083	-.454*	-.596**	-.590**	.38	-.822**	

Note. RMSSD = root mean square of successive RR interval differences.; pNN50 = percentage of successive RR intervals that differ by more than 50 milliseconds; SD1 nu = Poincaré Plot standard deviation perpendicular to the line of identity in a normalized unit; SD2 nu = Poincaré plot standard deviation along the line of identity in a normalized unit; LF nu = low-frequency HRV in a normalized unit, HF nu = high-frequency HRV in a normalized unit. *p <.05, **p<.01

Table 8
Regression Model of Change in HRV Measures as Predictors of SCT symptoms (n = 30)

Variable	Unstandarized B	Coefficient Std. Error	Standardized Coefficients Beta	*t*	Sig.	R	R^2	Adjusted R^2	R^2 Change
Step 1									
SWAN ADHD score	.193	.119	.292	1.613	.118	.292	.085	.052	.085
Step 2									
SWAN ADHD score	.257	.115	.389	2.236	.034	.483	.233	.176	.148*
Change – SD2 nu	1.621	.710	.397	2.281	.031				
Step 3									
SWAN ADHD score	.285	.107	.431	2.669	.013	.609	.371	.299	.138*
Change-SD2 nu	1.721	.657	.421	2.621	.014				
Change – pNN50	.339	.142	.374	2.392	.024				

Note. SD2 nu = Poincaré plot standard deviation along the line of identity in a normalized unit.
*p <.05.

3.3 Discussion

This was the first study to examine the potential association of SCT symptoms with the Arousal/Regulatory Systems proposed in the RDoC framework (NIMH, 2016). It is important to understand these associations for multiple reasons. Firstly, as RDoC is basically a dimensional approach, viewing SCT through RDoC would allow us to understand how variations in the RDoC constructs might affect SCT symptoms levels. Secondly, using RDoC constructs to evaluate SCT may allow us to understand SCT beyond its behavioural manifestations and could

direct researchers and clinician's attention towards the neurophysiological basis (e.g., HRV) of SCT symptoms. The results of these evaluations may enable the development of a more comprehensive model of SCT and clarify the commonalities and differences between SCT and other psychopathologies, such as ADHD and affective disorders (Becker & Willcutt, 2018).

The results of the current study indicated a relationship between the arousal state and SCT symptoms. Specifically, ANS readiness, as reflected by the HRV in the resting condition, was found to associate with the SCT symptoms. Moreover, ANS regulation, as reflected by the magnitude of change in the HRV from the resting to warning signal condition, was also found to associate with the SCT symptoms. Lastly, both ANS readiness and ANS regulation were found to significantly predict the SCT symptoms after controlling the ADHD symptoms.

3.3.1 ANS readiness and SCT symptoms.

The conceptual framework of the current study suggested that ANS readiness, as reflected by the HRV during the resting condition, would associate with SCT symptoms. The results of the present study supported this hypothesis. Resting ANS measures of SD2 nu was found to positively correlate with SCT symptoms. SD2 nu has been suggested to reflect sympathetic activity in the ANS system (Castaldo, Montesinos, Melillo, James & Pecchia, 2019; De Vito et al., 2002; Rahman, Habel & Contrada, 2018; Tulppo et al., 1996). Higher SD2 nu was associated with lower sympathetic activity. These results suggested that participants who had higher level of SCT symptoms showed lower sympathetic activity in the resting condition. Therefore, it is likely that higher level of SCT symptoms is related to under-arousal in the brain of the participants (Barkley, 2013a; Becker & Willcutt, 2018). This explained why individuals with SCT symptoms often appear to be apathy, slow in completing tasks and lack of motivation. Such significant correlations found between the SD2 nu and SCT symptoms would not be

confounded by the ADHD inattention symptoms of the participants because the ADHD symptoms were statistically controlled in the analysis.

The LC plays a major role in modulating arousal (Aston-Jones & Cohen, 2005) and cardiovascular response (Wood & Valentino, 2017). Increase in LC activity inhibits parasympathetic cardiac vagal neurons in the brainstem, thus reducing parasympathetic activity to the heart (Wang et al., 2014). Conversely, decrease in LC activity lowers inhibition of parasympathetic cardiac vagal neurons in the brainstem which subsequently decreases sympathetic activity to the heart. Results of the present study showed that more severe symptoms were associated with lower sympathetic activity (resting SD2 nu as the strongest predictor). Therefore, the current results were consistent with the notion that under-arousal was a possible deficit associated with SCT symptoms (Barkley, 2013a; Becker & Willcutt, 2018). In fact, preliminary results of a drug trial reported atomoxetine, a norepinephrine reuptake inhibitor, significantly improved SCT symptoms (Wietecha et al., 2013). Result of the atomoxetine trial further supports arousal level can partly explain severity of the SCT symptoms. In sum, the current results suggested that lower ANS readiness, because of the lower brain arousal, may explain the increase in difficulties experienced by children with SCT symptoms. The current results also support the notion that SCT can be understood in terms of Arousal/ Regulatory Systems construct in the RDoC framework.

3.3.2 ANS regulation and SCT symptoms.

The results of the current study also revealed a link between SCT symptoms and heightened arousal in the participants. Changes in the magnitude of SD2 nu from the resting to the warning signal condition were positively associated with SCT symptoms. In addition to this, changes in pNN50 (reflecting PNS activity), as well as changes in SD2 nu (reflecting SNS activity), were both found to be significant predictors of SCT symptoms after controlling for ADHD symptoms. In the present study, participants may have experienced a simultaneous increase in sympathetic activity and decrease in parasympathetic activity when exposed to "stressful" stimulus under the warning signal condition. Previous studies have attributed such an increase in sympathetic activity, and such as decrease in parasympathetic activity to an increase in LC activity and consequently the frequency of inhibitory postsynaptic currents in the cardiac vagal neurons (Wang, et al., 2014). The participants with more severe SCT symptoms were more likely to exhibit greater pNN50 changes and SD2 nu changes upon exposure to the "stressful" stimulus, which may reflect a higher level of arousal in the brain. In other words, the current results supported the notion that SCT symptoms may be related to hyper-arousal during the exposure to stressful event in the real life. This may further suggest that SCT symptoms can be understood not only in Arousal/Regulatory Systems of RDoC but also can be related to Negative Valence Systems.

The results of the subsequent study conducted by Becker & McQuade (2020) also supported the results of the current study. They examined the respiratory sinus arrhythmia (RSA) and skin conductance level (SCL) in standardized peer rejection and impossible puzzle tasks of 61 children aged 8-12. In their results, they have found that SCT symptoms were not associated with RSA reactivity (which reflects parasympathetic activity) in both tasks whereas higher SCT symptoms were significantly associated with SCL reactivity in the peer rejection task only. The

authors concluded that SCT symptoms among children were related to sympathetic nervous system reactivity during stress-induced tasks when ADHD symptoms were controlled. Becker & McQuade (2020)'s results were consistent with the results of the present study which both found a linkage between SCT symptoms and hyper-arousal during the stressful events.

It has been speculated that SCT symptoms, particularly those related to withdrawal, may be attributed to a state of hyper-arousal (Becker & Willcutt, 2018). The results of the current study supported the hypothesized association between increased arousal and an exacerbation of SCT symptoms. The withdrawal behaviours exhibited by individuals with SCT may be caused by an increase of arousal in response to environmental stressful events. It is possible that the unpredictability in the social events may trigger higher arousal in children with SCT, like the unpredictability of the warning signals in the current study. In other words, SCT symptoms seems not only to be associate with dysfunction in the Arousal/Regulatory Systems of RDoC, but also in the Negative Valence Systems of RDoC.

Although the results of present study provide a neurophysiological support to the involvement of Arousal/ Regulatory Systems and Negative Valence Systems in the symptoms of SCT, further research on how these systems relate to the neuropsychological deficits commonly seen in SCT is needed. It is also important to investigate how these neurophysiological and neuropsychological deficits may explain the behavioural difficulties such as social difficulties in individuals with SCT.

Chapter 4

Study II: Relationship Between Arousal Regulation and Attention Deficits among Children with High SCT Symptoms

Remarks: Part of the Study II has been published in a peer review journal:

Yung T. W. K. & Lai, C. Y. Y. (2022). Abnormal physiological responses towards sensory stimulus are related to the attention deficits in children with SCT. Frontiers in Neuroscience, 16.

The results of the Study I have reflected that high SCT symptoms were associated with lower arousal resting state reflected by HRV measures. Moreover, the results of the Study I, along with the results of Becker & McQuade's study (2020) both reflected that people with high SCT symptoms would have heightened arousal in response to challenges (such as pure tone auditory stimulus or social stress). Although these results may provide a support that abnormal arousal preparatory state and regulation were two neurophysiological processes which may be related to SCT symptoms, it still could not explain how these processes are related to the sustained attention deficits commonly manifested in individuals with high SCT symptoms. Therefore, Study II (as reported in this section) was conducted to examine the relationship between arousal regulation reflected by cortical activities, ANS activities and sustained attention difficulties among individuals with high SCT symptoms.

Based on Thayer's neurovisceral integration model (Thayer & Lane, 2000; Thayer et al., 2009), cortical activities, ANS functions and cognitive functions are interrelated processes. Specifically, PFC functions and ANS functions are two interrelated processes which support our

attention and executive functions to deal with real life challenges. However, no previous study has examined the linkage between cortical activities, ANS functions and attention difficulties in children with high SCT symptoms. Therefore, it is unclear whether the abnormalities in arousal state and regulation reflected by ANS measures and cortical activities could explain the attention difficulties among these children. The aim of the Study II was to examine the contribution of abnormal neurophysiological function (reflected by abnormal cortical activities and ANS measures) to sustained attention difficulties in children with SCT. It is expected that both abnormalities in cortical activities and ANS activities during sensory stimulation condition would be significantly associated with attention difficulties among children with SCT.

4.1 Method

4.1.1 Participants.

The participants involved in this study were required to meet the following inclusion criteria: (a) aged 6–12 years and (b) a full-scale IQ score >80. Potential participants who met the following criteria were excluded: (a) any psychiatric diagnosis, including ADHD, oppositional defiant disorder, conduct disorder, or dyslexia; (b) a T-score >85 in the Chinese version of the Strength and Weaknesses of ADHD Symptoms and Normal Behavior scale (SWAN; Swanson et al., 2012); (c) a T-score >70 in any subscale of the Child Behavior Checklist (CBCL) (Chinese version) (Achenbach, 2001); (d) any uncorrected visual or auditory problems; and (e) a history of diabetes or cardiac and/or respiratory problems. Children with an ADHD diagnosis or elevated symptoms of ADHD were excluded because these symptoms would have confounded the neurophysiological measures used in the study (i.e., HRV measures). Those with other psychiatric disorders (e.g., childhood anxiety or oppositional defiant disorder/conduct disorder)

were excluded because these disorders have also been found to be associated with different patterns of HRV (Rozenman, Sturm, McCracken, & Piacentini, 2017; Schoorl, Rign, De Wied, Van Goozen & Swaab., 2016).

Eighty-eight primary school students were the participants of the current study. They were recruited via posters sent to primary schools and parent chat groups. Some of them were also the participants of the Study I and Study III. Among the participants, 41 children (mean age = 111.22 months, standard deviation [*SD*] = 19.03; 47.1% female) were categorized as the High SCT group using median split method based on the SCT scale scores (Penny et al., 2009). In contrast. 47 children (mean age = 109.23 months, *SD* = 18.04; 46.8% female) were classified as the Low SCT group. There was a significant difference in the SCT scores between High SCT group (Mean score = 34.34; SD = 7.34) and the Low SCT group (Mean score = 17.47, SD = 4.6).

4.1.2 Procedure and experimental setup.

In the research study, the parents of the participants were provided with a research package containing information about the study and a consent form. Before any data collection took place, written informed consent was obtained from all participants' parents. The researcher contacted the parents to gather basic demographic information such as the participants' names, dates of birth, and genders, as well as the medical history of their children.

All participants were invited to attend a testing session at the university laboratory, which lasted for approximately 2-3 hours. During the testing session, breaks were provided between assessments to ensure the comfort and well-being of the participants. The testing session involved the administration of neuropsychological tests and neurophysiological measures, which will be described in detail in section 4.1.3 of the research study.

While the children were undergoing testing in the laboratory, the parents were asked to fill in rating scales. These rating scales will also be described in detail in section 4.1.3 of the research study. The parents were given the rating scales to complete in the waiting room while their children were being tested.

Participants received the neuropsychological testing in a room without any visual or auditory distractions. Short breaks were offered to the participants between tests. As HRV measurement would be easily affected by the condition of the testing room such as illumination and temperature, the conditions of the experiment laboratory room were set as the following during all the neurophysiological measurements: (a) illumination level was set to 10 lux; (b) room temperature was set to 23 to 25 degree Celsius; and (c) background noise level at 40 to 45 dB. Before the HRV measurements, all participants were reminded not to do the following: (a) intake of caffeinated drinks before the testing; (b) engaged in any rigorous activities 24 hours before the testing; and (c) receiving any treatment or medication that could affect ANS activity as all these events may affect the validity of the HRV measurement.

A Warning Signal paradigm was applied in the current study. This experimental paradigm was adapted from Gomez, Lai, Chan, and Tsang (2018) and Lai (2013). Both HRV and EEG were measured continuously across two conditions: resting and warning signal. During the resting condition, each participant was shown a silent animated video for 200 seconds. Subsequently, the monitor screen turned blank, and the participant was exposed to a block of warning signal condition which is comprised of 10 trials of a 4kHz pure tone at 85dB. The

duration of each trial was 3 seconds. A pseudorandomized interval of 10-15 seconds was set to avoid adaptation to the stimulus.

4.1.3 Measuring instruments.

In this study, the researchers administered both neuropsychological tests and neurophysiological measures to the participants. All participants were invited to complete the neuropsychological measures first. The specific neuropsychological tests used in the study was described in the following paragraphs. After the participants finished the neuropsychological measures, they were then asked to complete the neurophysiological measures. This approach helps to standardize the testing process and minimize potential confounding factors that could arise from completing the measures in a different order.

4.1.3.1 Neuropsychological tests.

- *SWAN—Chinese version.* SWAN is a rating scale used by teachers and parents to assess ADHD symptoms (Swanson et al., 2012). The Chinese-translated version of the scale was utilized and validated for children in Hong Kong (Education Bureau of HKSAR, 2010). The scale consists of 18 items that evaluate a child's control of their attention, impulses, and activity. These items are divided into two subscales, with nine items each, focusing on inattention and hyperactivity/impulsivity. Total scores and subscale scores are calculated by summing the raw item scores and can be expressed as T-scores. higher scores indicate a lower presence of ADHD symptoms. For this study, only the total SWAN scores were utilized. The parent and teacher versions of SWAN have demonstrated excellent internal consistency (alpha > .9) and good discriminant validity (AUC > .8) for both total and subscale scores (Education Bureau of HKSAR, 2010).

- *SCT Scale (Penny et al., 2009).* The 14-item parent and teacher scale is utilized to assess symptoms of Sluggish Cognitive Tempo (SCT) in children. Each item is rated on a 7-point scale, ranging from 0 ("not at all") to 6 ("very much"). Consistent with previous research conducted by Becker, Garner, Tamm, Antonini, and Espstein (2019) and Holdaway and Becker (2018), the present study selected 10 items from the scale instead of using the full scale. These 10 items demonstrated consistent loadings on the SCT factor but not the ADHD inattention factor, as reported by Becker et al. (2016). This selection of items formed a cohesive 10-item construct that aligned with the characteristics of the participants and the study's hypotheses. The internal consistency of the original 14-item SCT scale, as measured by both parent (alpha > .8) and teacher ratings (alpha > .9), was found to be high according to Penny et al. (2009). In the present study, the 10-item version also exhibited a high level of internal consistency, with a Cronbach's alpha of .898.
- *Cued Continued Performance Test (CCPT; Nash et al., 2013).* In the present study, the Continuous Performance Test (CCPT) was utilized to assess the participants' sustained attention ability. The CCPT required the subjects to press a response button when target stimuli appeared on a computer screen while refraining from responding when non-target stimuli appeared. The stimuli consisted of letters presented at the center of the computer screen, with each letter displayed for 200 milliseconds, followed by an inter-stimulus interval of 1,650 milliseconds. The presentation order of the stimuli was pseudo-randomized. The target stimuli were a paired sequence of stimuli, with the letter "O" presented first, followed by the letter "X." In the sequence of non-target stimuli, the letter "O" was presented first, followed by letters other than "X." The stimulus set consisted of two blocks, each comprising 200 trials. After completing the first block, the subjects were given a 1-minute break to

prevent mental fatigue. Within each block, there were 40 "O letter" stimuli, 20 target stimuli, 20 non-target stimuli, and 120 distractor letters (letters other than "O" or "X").

Several measures were derived from each block of the CCPT. These measures included:

1. Target hits: The number of correct responses to the target stimuli (i.e., pressing the response button when the "X" followed the "O").

- 2. Omission errors: The number of instances in which the participant failed to respond to the target stimuli.

3. Commission errors: The number of instances in which the participant incorrectly responded to non-target or distractor stimuli.

4. Response latency toward the target: The time taken by the participant to respond to the target stimuli.

To analyze the data, the final measures used in the study were obtained by subtracting the value of each measure from block 1 from the value of the same measure in block 2. For example, the final measure of omission errors was calculated as the number of omission errors in block 2 minus the number of omission errors in block 1.

- The rationale behind this calculation was to assess performance deterioration over time, which was assumed to reflect sustained attention (Wåhlstedt & Bohlin, 2010).

4.1.3.2 Neurophysiological measures.

- *ANS measures.* In the study, the researchers employed HRV as a method to quantify ANS activity. HRV is used to assess the SNS and PNS activities across different experimental conditions, namely the resting condition and the warning signal condition. To measure HRV,

the researchers used Polar H2 Heart Rate Monitors and the BIOPAC MP260 system (Biopac System, Goleta, CA, USA). These tools have been recognized as valid instruments for HRV measurement in previous studies (de Rooij et al., 2013).

- *EEG measures.* In the study, EEG frequency measures were employed to quantify cortical activities during the resting condition and warning signal condition. During the experiment, electrodes and transducers were applied to the participants and connected to BIOPAC MP 360 system to record EEG signals. EEG was recorded from electrode at Cz and a linked earlobe reference was used. To ensure accurate recording of the EEG signals, BIOPAC EEG amplifier was set to a bandpass filter between 0.1Hz and 100Hz. This filter allowed the recording of EEG signals with a specific frequency range, filtering out unwanted noise and artifacts outside this range. A sampling frequency of 1000Hz was used.

4.1.4 Signal Processing.

4.1.4.1 HRV signal.

The raw HRV data was initially processed using aHRV software (Nevrokard, Slovenia) to convert it into tachograms. The tachograms were visually inspected to identify any ectopic beats, movement artifacts, or abnormal noise signals. Afterward, the data was divided into specific time events based on the experimental paradigm. Any values that fell 20% below or above the mean of the preceding 25 beats were considered artifacts during short-term recording and were corrected through interpolation. Data with a correction rate exceeding 3% compared to the total normalized HRV data samples were discarded, following the recommendations of the Task Force of the European Society of Cardiology and North American Society of Pacing and Electrophysiology (1996).

HRV is a measure of the variation in the time intervals between consecutive heartbeats (Shaffer & Ginsberg, 2017). In the current study, non-linear measurement of HRV were employed. Non-linear measurement of HRV assess the unpredictability of a time series which arises from the complex interplay of the sympathovagal mechanism that regulate the HRV (Shaffer & Ginsberg, 2017). Within non-linear HRV measurement, two commonly used indices are SD1 and SD2 of Poincaré Plot. SD1 represents the standard deviation perpendicular the line of identity in the Poincaré Plot and is suggested to reflect short term variability of HRV, primarily reflecting PNS activity. On the other hand, SD2 represents the standard deviation along the line of identity in the Poincaré Plot and is suggested to reflect long term variability of HRV (Brennan, Palaniswami & Kamen, 2001; Guzik et al., 2007; Shaffer & Ginsberg, 2017; Tulppo et al., 1996). Previous research have indicated that SD2 is negatively associated with sympathetic influence on the heart (Goit & Ansari, 2016; Negrao, Bipath, van der Westhuizen & Viljoen, 2011; Rahman, Habel & Contrada, 2018; Sharma, Makharia, Ahuja, Dwivedi & Deepak, 2009). Recent studies have also suggested that changes in SD2 may be primarily mediated by parasympathetic influence (Rahman, Habel, & Contrada, 2018).

4.1.4.2 EEG signal.

The EEG raw signal was processed by Biopac Acknowledge 5.0 Software. EEG raw signal at Cz was first filtered using Infinite Impulse Response (IIR) band pass filter (low cut off = 0.5 Hz and high cut off = 44 Hz) and was generated into following standard EEG bands: Delta (0.5Hz to 4 Hz), theta (4 Hz to 8 Hz), alpha (8 Hz to 13 Hz), beta (13 Hz to 30 Hz) and gamma (30Hz to 44 Hz). The power spectral density function was used to estimate the power spectrum of each 3-second epoch using a Welch periodogram estimation method. The mean power of all epochs was averaged and was used to represent the power of each EEG brand in two

experimental conditions. In the current study, measure of theta power was calculated for each participant and was used to reflect the attention control of the participants in previous studies (van Son, Blasio, Fogarty, Angelidis, Barry & Putman, 2019; van Son, Rover, Blasio, van der Does, Barry & Putman, 2019).

4.2 Results

4.2.1 Bivariate associations between EEG variables and the CCPT measures.

Bivariate correlation analysis was conducted to examine the correlations between EEG variables: Resting EEG Theta power, Resting EEG Alpha power, EEG Theta power (Warning Minus Resting)[5] and EEG Alpha power (Warning Minus Resting) [6]and CCPT measures (CCPT Omission[7], CCPT Commission [8]and CCPT Response Time[9]). The mean and standard deviation of EEG measures and CCPT measures in the High SCT group and the Low SCT group was shown in the Table 9. In the High SCT group, CCPT Omission was found to have significant positive relationship with EEG Theta power (Warning minus Resting) with r=.495 and p<.05 and EEG Alpha power (Warning minus Resting) with r=.461 and p<.05 (Table 10). In the Low SCT group, no significant correlation was found between the EEG measures and CCPT measures.

[5] EEG Theta power (Warning Minus Resting) was calculated by subtracting the EEG Theta power in the Warning Signal condition from EEG Theta power in the Resting condition).
[6] EEG Alpha power (Warning Minus Resting) was calculated by subtracting the EEG Alpha power in the Warning Signal condition from EEG Alpha power in the Resting condition).
[7] CCPT Omission was calculated by subtracting the number of omission errors in the block 2 of the CCPT from the number of omission errors in the block 1 of the CCPT.
[8] CCPT Commission was calculated by subtracting the number of commission errors in the block 2 of the CCPT from the number of commission errors in the block 1 of the CCPT.
[9] CCPT Response Time was calculated by subtracting the average response time of the correct response in the block 2 of the CCPT from the average response time of the correct response in the block 1.

Table 9

Mean and Standard Deviation of EEG measures and CCPT measures in the High SCT and Low SCT groups

	High SCT group (n = 41)	Low SCT group (n = 47)
	M (*SD*)	*M* (*SD*)
CCPT Omission	1.13 (2.59)	.91 (2.09)
CCPT Commission	2.15 (27.64)	1.46 (9.29)
CCPT Response time (MS)	34.46 (158.34)	54.19 (103.53)
Resting EEG Theta	.000048 (.000056)	.000026 (.000012)
Resting EEG Alpha	.000025 (.000023)	.000015 (.000007)
EEG Theta (Warning minus Resting)	.000023 (.0001)	.00000041 (.0000057)
EEG Alpha (Warning minus Resting)	.0000097(.000041)	.00000087 (.0000032)

Note. CCPT = Cued continued performance test; SCT = Sluggish cognitive tempo; *M* = Mean; *SD* = Standard deviation, CCPT Omission = number of omission errors in block 2 minus block 1, CCPT Commission = number of commission errors in block 2 minus block 1, CCPT Response time (in milli-second) = average response time of correct response in block 2 minus block 1, Resting EEG Theta = EEG Theta power in resting condition, Resting EEG Alpha = EEG Alpha power in resting condition, EEG Theta (Warning minus Resting) = EEG Theta power in the warning condition minus EEG Theta power in the resting condition, EEG Alpha (Warning minus Resting) = EEG Alpha power in the warning condition minus EEG Alpha power in the resting condition

Table 10

Correlation Coefficients of CCPT Measures with the EEG measures in the High SCT group (n = 41)

	CCPT measures		
	Omission	Commission	Response Time (MS)
Resting EEG Theta	.287	.035	-.139
Resting EEG Alpha	.197	.023	-.063
EEG Theta (Warning Minus Resting)	.495*	-.131	.011
EEG Alpha (Warning Minus Resting)	.461*	-.112	-.003

Note. CCPT = Cued continued performance test; CBCL = Child behavior checklist; SCT = Sluggish cognitive tempo; CCPT Omission = number of omission errors in block 2 minus block 1, CCPT Commission = number of commission errors in block 2 minus block 1, CCPT Response time = average response time (in milli-second) of correct response in block 2 minus block 1, Resting EEG Theta = EEG Theta power in resting condition, Resting EEG Alpha = EEG Alpha power in resting condition, EEG Theta (Warning minus Resting) = EEG Theta power in the warning condition minus EEG Theta power in the resting condition, EEG Alpha (Warning minus Resting) = EEG Alpha power in the warning condition minus EEG Alpha power in the resting condition* $p < .05$.

4.2.2 Examining the associations between EEG Variables and the CCPT Omission after controlling ADHD symptoms.

A regression analysis was performed to examine the associations between the EEG variables and the CCPT Omission after entering the SWAN ADHD score into the model to control for ADHD symptoms (Step 1). EEG Theta power (Warning minus Resting) was then entered to the model (Step 2). Finally, EEG Alpha power (Warning minus Resting) was entered

into the model (Step 3) to explain the variance of the CCPT Omission. In the High SCT group, the SWAN ADHD score did not contribute significantly to the regression model to explain the CCPT Omission [$F(1,20) = .703$, $p > .05$] (Table 10). EEG Theta power (Warning minus Resting) was found to be the only significant factor to explain the variance of CCPT Omission [$F(2,19) = 4.085$, $p < .05$] (Table 11). This factor explained 30.1% of the variance in CCPT Omission (Table 12).

4.2.3 Bivariate Associations Between HRV variables and the CCPT measures.

Bivariate correlation analysis was conducted to examine the correlations between HRV variables (SD1 nu Resting, SD2 nu Resting, SD1 nu Warning minus Resting[10] and SD2 nu Warning minus Resting[11]) and CCPT measures (Omission errors, Commission errors and Reaction Latency) in both the High SCT and Low SCT group. The means and standard deviations of the CCPT measures and the HRV variables of both groups are shown in Table 12. In the High SCT group, CCPT Commission was found to be significantly and negatively associated with Resting SD1 nu ($r = -.429$, $p < .01$) and Resting SD2 nu ($r = -.340$, $p < .05$), and positively associated with SD1 nu (Warning minus Resting) ($r = .625$, $p < .01$)(Table 13). In the Low SCT group, no significant correlation was found between HRV variables and the CCPT measures.

[10] SD1 nu Warning minus Resting was calculated by subtracting the SD1 nu value in warning signal condition from the SD1 nu value in resting condition

[11] SD2 nu Warning minus Resting was calculated by subtracting the SD2 nu value in warning signal condition from the SD2 nu value in resting condition

Table 11

Regression Model of the EEG Measures as the Predictors of the CCPT Omissions in the High SCT group

Variable	Unstandardized B	Coefficient standard error	Standardized coefficient beta	*t*	Sig.	*R*	R^2	Adjusted R^2	R^2 change
Step 1									
SWAN ADHD score	.028	.033	.184	.838	.412	.184	.034	-.014	.034
Step 2									
SWAN ADHD score	.017	.029	.109	.565	.579	.548	.301	.227	.267*
EEG Theta (Warning minus Resting)	10652	3956	.522	2.692	.014				
Step 3									
SWAN ADHD score	.018	.029	.117	.615	.546	.601	.361	.254	.060
EEG Theta (Warning Minus Resting)	-22538	25801	-1.1	-.874	.394				
EEG Alpha (Warning Minus Resting)	86708	66634	1.643	1.3	.210				

Note. CCPT = Cued continued performance test; SCT = Sluggish cognitive tempo; ADHD = Attention-deficit hyperactivity disorder; SWAN = the Strength and Weaknesses of ADHD Symptoms

Table 12

Mean and Standard Deviation of HRV measures and CCPT measures in the High SCT and Low SCT groups

	High SCT group	Low SCT group
	M (*SD*)	*M* (*SD*)
CCPT Omission	1.13 (2.59)	.91 (2.09)
CCPT Commission	2.15 (27.64)	1.46 (9.29)
CCPT Response time (MS)	34.46 (158.34)	54.19 (103.53)
Resting SD1 nu	6.12 (2.07)	5.81 (1.99)
Resting SD2 nu	10.77 (3.03)	9.33 (2.39)
SD1 nu (Warning minus Resting)	- .25 (1.43)	.22 (1.04)
SD2 nu (Warning minus Resting)	.87 (3.13)	1.76 (2.09)

Note. CCPT = Cued continued performance test; SCT = Sluggish cognitive tempo; *M* = Mean; *SD* = Standard deviation, CCPT Omission = number of omission errors in block 2 minus block 1, CCPT Commission = number of commission errors in block 2 minus block 1, CCPT Response time = average response time of correct response (in milli-second) in block 2 minus block 1, Resting SD1 nu = SD1 nu in resting condition, Resting SD2 nu = SD2 nu in resting condition, SD1 nu (Warning minus Resting) = SD1 nu in the warning condition minus SD1 nu in the resting condition, SD2 nu (Warning minus Resting) = SD2 nu in the warning condition minus SD2 nu in the resting condition

Table 13

Correlation Coefficients of the CCPT Measures with the HRV in the High SCT group

	CCPT measures		
	Omission	Commission	Response Time (MS)
Resting SD1 nu	-.132	-.429**	.195
Resting SD2 nu	-.046	-.340*	.277
SD1 nu (Warning	.202	.625**	-.08

Minus Resting)			
SD2 nu (Warning Minus Resting)	-.031	.083	.01

Note. CCPT = Cued continued performance test; CBCL = Child behavior checklist; SCT = Sluggish cognitive tempo; CCPT Omission = number of omission errors in block 2 minus block 1, CCPT Commission = number of commission errors in block 2 minus block 1, CCPT Response time = average response time (in milli-second) of correct response in block 2 minus block 1, Resting SD1 nu = SD1 nu in resting condition, Resting SD2 nu = SD2 nu in resting condition, SD1 nu (Warning minus Resting) = SD1 nu in the warning condition minus SD1 nu in the resting condition, SD2 nu (Warning minus Resting) = SD2 nu in the warning condition minus SD2 nu in the resting condition

* $p < .05$, ** $p < .01$.

4.2.4 Examining the associations between HRV variables and the CCPT commission after controlling ADHD symptoms.

A stepwise regression analysis was performed to examine the associations between the CCPT Commission and the HRV variables after entering the SWAN ADHD score into the model to control for ADHD symptoms (Step 1). SD1 nu (Warning minus Resting) was then entered to the model (Step 2). Finally, Resting SD1 nu and Resting SD2 nu were entered into the model (Step 3) to explain the variance of the CCPT Commission.

In the High SCT group, the SWAN ADHD score did not contribute significantly to the regression model to explain the CCPT Commission [$F(1,37) = .101$, $p > .05$] (Table 13). The SD1 nu (Warning minus Resting) was found to be a significant factor in explaining the variance of the CCPT Commission (Table 14). This factor explained 39.4% of the variance in CCPT Commission [$F(2, 36) = 11.72$, $p < .05$].

Table 14

Regression Model of the ANS Measures as the Predictors of the CCPT Commissions in the High SCT group

Variable	Unstandardized B	Coefficient standard error	Standardized coefficient beta	*t*	Sig.	*R*	R^2	Adjusted R^2	R^2 change
Step 1									
SWAN ADHD score	.10	.315	.052	.318	.75	.052	.003	-.024	.003
Step 2									
SWAN ADHD score	−.118	.253	−.061	−.466	.644	.628	.394	.361	.392**
SD1 nu (Warning minus Resting)	12.32	2.554	.636	4.824	.000				
Step 3									
SWAN ADHD score	-.195	.249	-.102	-.783	.439	.668	.446	.398	.080
SD1 nu (Warning Minus Resting)	11.503	2.519	.594	4.567	.000				
Resting SD2 nu	-.215	1.191	-.236	-1.8	.080				

Note. CCPT = Cued continued performance test; SCT = Sluggish cognitive tempo; ADHD =

Attention-deficit hyperactivity disorder; SWAN = the Strength and Weaknesses of ADHD Symptoms and Normal Behavior scale; Commission = CCPT Commission errors. *$p < .05$, **$p < .01$.

4.3 Discussion

The aim of the current study was to investigate the relationship between cortical/ANS activities and attention difficulties in children with high SCT symptoms. In the current study, attention difficulties among children in the High SCT group were found to be significantly associated with cortical/ANS abnormalities. Specifically, the study revealed that Theta power (Warning minus Resting) was significantly associated with CCPT Omission after controlling ADHD symptoms. Additionally, SD1 nu (Warning minus Resting) was significantly associated with CCPT Commission, after controlling ADHD symptoms. CCPT Omission errors typically reflect deficits in sustained attention, while CCPT Commission reflected deficits in inhibition. These two neuropsychological processes have been previously linked with SCT symptoms, even after controlling for ADHD symptoms (Baytunca et al., 2018; Creque & Willcutt, 2021; Wahlstedt & Bohlin, 2010; Willcutt et al., 2014). The novelty of the current study lies in its exploration of the underlying neurophysiological factors associated with the deficits in sustained attention and inhibition in children with high SCT symptoms. Previous research has not extensively investigated these factors. Therefore, the present study's findings provide valuable evidence regarding the neurophysiological underpinnings associated with deficits in sustained attention and inhibition in children with high SCT symptoms.

4.3.1 The Association between the theta power during warning signal task and ccpt omission errors in high SCT group.

The present study found that higher magnitude of theta signals during warning signal

condition was associated with higher omission errors in CCPT. Theta wave are known to be generated by the anterior cingulate cortex (ACC) and was often associated with the neural processes involved in conflict monitoring and resolution (Cavanagh, Cohen & Allen, 2009; Eschmann, Bader & Mecklinger, 2018; Nigbur, Ivanova & Sturmer, 2011). Previous research has found that mid-frontal theta power increases in the conditions of novelty, conflict, punishment, and error (Cavanagh, Zambrano-Vazquez & Allen, 2012). Theta signals originating from the cingulate cortex have been associated with active avoidance of potentially aversive outcomes (Cavanagh & Shackman, 2015). In the current study, participants were presented with a series of unexpected and high pitch monotone sounds during the warning signal condition. This research paradigm created a situation for the participants characterized by uncertainty (i.e., unexpected auditory stimulus[12]) and goal conflicts (wanted to escape from the aversive stimulus vs had to remain on their seat during the experiment). The challenge posed by this situation may have activated the anterior cingulate cortex leading to enhanced theta wave activities.

According to Gray's reinforcement sensitivity theory (2000), Behavioural Inhibition System (BIS) is a brain system that activates responses of inhibition and avoidance when aversive consequences are expected. Research has shown that Theta power is a significant neurophysiological factor in distinguishing individuals with high and low sensitivity to the BIS (Moore, Mills, Marshman & Corr, 2012). Individuals with higher sensitivity to BIS tended to exhibit higher theta signal during goal-conflict task (Moore, Mills, Marshman & Corr, 2012). BIS has also been found to be significantly and positively associated with SCT symptoms using behavioural rating scale (Becker et al., 2013; Becker et al., 2018). However, no previous study has provided neurophysiological evidence to support this association. Therefore, the present

[12] The stimulus was unexpected to the participants because the intervals between the stimulus were pseudorandomized

study aimed to provide the first neurophysiological evidence supporting the link between hyper-sensitivity to BIS and SCT symptomology. Specifically, the results of the current study suggested that omission error, which are a common difficulty in sustained attention in SCT, were related to hyper-sensitivity to the BIS. High levels of Anxiety has been found to be associated with high sensitivity to BIS. Therefore, it is possible that higher level of state anxiety, often associated with the BIS hypersensitivity, may be related to their difficulty in attention. According to the Attention Control Theory (ACT), anxiety may increase the influence of stimulus-driven attentional systems and decrease the influence of goal directed attention system in individuals (Eysenck, Derakshan, Santos & Calvo, 2007). When the goal-directed attention system fails to override the stimulus-driven attentional systems, individuals tend to direct their attentional resources towards salient and conspicuous stimulus in order to detect threat-related information (Eysenck et al., 2007). As a result, fewer attentional resource are directed to process goal-related information or stimulus leading to negative effects on task performance. In the current study, individuals with high SCT, possibly due to their high sensitivity to BIS, may experience more anxiety, which direct their attention towards the salient non-target (e.g., any letters) stimulus during the CCPT. Consequently, they may fail to direct attentional resources towards inconspicuous target stimulus (e.g., X and then O), resulting in omission errors.

The results of the current study provide new evidence to support the argument that individuals with high SCT symptoms are not universally “sluggish” in their processing speed. Previous studies have yielded mixed fndings regarding processing speed in individuals with high SCT symptoms. Some studies have found significantly slower processing speed in individuals with high SCT symptoms than typical individuals (Tamm et al., 2018; Willcutt et al., 2014), while other studies have not found significant differences (Bauermeister et al., 2012; Skirbekk et

al., 2011). Additionally, Kofler et al. (2019) found no significant associations between cognitively modeled information processing speed (drift rate) and SCT symptoms, suggesting that SCT symptoms are not related to general processing speed. Instead, Kofler et al. (2019) found a significant association between faster inhibition speed and parent-reported SCT symptoms. They interpreted this finding as evidence that children with high SCT symptoms are behaviourally over-inhibited and SCT symptoms are related to increased BIS sensitivity (Kofler et al., 2019). The results of the current study provided further neurophysiological evidence to support this notion. The current study's findings indicate that increased BIS sensitivity, reflected in higher theta wave activity during a sensory challenge situation, may negatively affect children with high SCT symptoms in allocating their attentional resources towards non salient but relevant information in the task. Therefore, it is likely that increased BIS sensitivity may affect these children's inhibition abilities in the similar manner. For example, anxiety may increase the influence of the stimulus-driven attentional system, leading individuals to be more attentive towards the salient signal (e.g. an auditory signal indicating to stop) in the stop signal task, thereby enhancing their inhibition speed. With this tendency, individuals with high SCT symptoms tends may be oversensitive to salient but irrelevant environmental information while being slow to respond to inconspicuous but relevant information in real life. In summary, children with high SCT symptoms do not appear to respond slowly to all information in real life. They tend to respond slowly to the target information if it is threat-related and/or if there are competing distractions that are threat-related in nature.

4.3.2 The association between HRV and CCPT commission errors in High SCT group.

The current study has found a significant relationship between SD1 nu (Warning minus

Resting) and CCPT Commission errors. SD1 nu has been suggested to reflect parasympathetic activity, which is involved in heart rate decelaration durng stressful events, a process know as freezing. Freezing is thought to facilitate appropriate responses by allowing for further information gathering (Livermore et al., 2021). Heart rate deceleration in heart rate during response preparation has been found to be related to facilitation of perceptual decisions (Ribeiro & Castelo-Branco, 2019). Individuals with higher levels of state anxiety tend to have higher freezing reaction, such as bradycardia (a decrease in heart rate), when exposed to angry faces (Roelofs, Hagenaars & Stins, 2010). SCT symptoms were often associated with higher levels of anxiety. Therefore, it is speculated that Higher CCPT commission errors may be related to a higher propensity of freezing in children with high SCT symptoms.

Freezing during a stressful event was associated with higher commission erros on the CCPT in children with high SCT symptoms possibly because freezing is often linked to altered perceptual sensitivity. Studies have shown that Heart rate deceleration, which is characteristics of freezing, is associated with improved detection of low-spatial frequency (LSF)[13] cues but at the expense of high spatial frequency (HSF)[14] detection (Lojowska, Gladwin, Hermans & Roelofs, 2015). Increase in the sensitivity towards LSF may promote individuals to detect coarse threat-relevant features of an object, such as its presence or location, rather than focusing on the the details of its visual presentation (Bocanegra & Zeelenberg, 2011). In the context of children with high SCT symptoms, it is possible that due to their BIS sensitivity, they tend to rely more on stimulus-driven attention system to detect salient threat-related information in their environment, rather than prioritizing the underlying goals. Consequently, when perfomring the CCPT, these children may be more prone to make response whenever they see the letter “O” , which could

[13] Low Spatial Frequency (LSF) refers to coarse visual features (Lojowska et al., 2015)
[14] High Spatial Frequency (HSF) refers to fine grained visual details (Lojowska et al., 2015)

lead to more commission errors. The findings of the current study support the idea that children with high SCT symptoms have a greater tendency to make attentional errors, such as omissions and commissions, due to their hyper-sensitivity towards salient threat-related information.

Barkley (2013b) found that children with SCT symptoms were more likely to have lower parent education, lower income, and a greater likelihood of having a parent out of work due to disability compared to children with ADHD. However, no previous research has been conducted to explain the underlying reasons for this linkage. The present study may provide a possible explanation of this association. The results of the present study suggested that freezing reactions, which involve an increase of parasympathetic activity during warning signal condition, are related to the attentional errors (specifically, commission errors) in children with high SCT symptoms. Previous research has shown that individuals with adverse previous experience, such as trauma, tend to exhibit stronger freezing reaction in response to stressful stimulus (Hagenaars, Stins & Roelofs, 2012; Niermann, Smeekens, Figner, Riksen-Walraven & Roelofs, 2015). It is possible that the social adversities associated with SCT, such as lower parent education, lower income, and parental unemployment due to disability, may exacerbate the freezing response in these children. This heighted freezing response could contribute to more attentional problems and subsequently negatively impact their real-life functioning. Future study should further examine the relationship between their family socio-economical status and the response to anxiety-provoking situation in children with high SCT symptoms.

The current understanding of why children with high SCT symptoms have a higher tendency to experience daydreaming in their daily lives is still unclear. However, the results of the present study may provide a possible explanation and a direction for further research. According to the study, the daydreaming tendencies in children with high SCT symptoms could

be attributed to their heightened sensitivity towards threat-related information in their environment. This increased sensitivity may lead to more freezing-like behaviours, which bear similarities to the behavioural manifestation of day-dreaming and mind-wandering. Such freezing-like behaviour may impact their ability to respond effectively to event in the real life. For example, children with high SCT symptoms may exhibit a tendency to divert their attention towards salient stress-related information, while potentially neglecting inconspicuous yet important goal related information in their environment. As a result, they may struggle to generate appropriate responses to the demands of real life events. This explanation aligns with previous research showing that individuals are more likely to make commission errors when they experience stress-induced mind-wandering (Smallwood, Fitzgerald, Miles & Philips, 2009).

Chapter 5
Study III: The association of social difficulties (social problems and withdrawn behaviour) with sustained attention deficits among children with SCT

Remarks: The part of the study has been published in a peer review journal. The contents of this chapter were mostly extracted from the published paper resulted from this study.

Yung, T. W. K., Lai, C. Y. Y., Chan, J. Y. C., Ng, S. S. M., & Chan, C. C. H. (2021). Examining the role of attention deficits in the social problems and withdrawn behaviour of children with sluggish cognitive tempo symptoms, Frontiers in Psychiatry, 12.

In this Chapter, the social difficulties include social problems and withdrawn behaviour. Social problems refer to two core issues: social rejection and difficulties in initiating and maintaining social relationships with peers (Bierman & Welsh, 2000). Social withdrawal, social isolation and low initiative in social situations were frequently found to be linked with SCT symptoms (Becker, Garner, Tamm, Antonini & Epstein, 2017; Marshall, Evans, Eiraldi, Becker & Power, 2014). However, no previous study has examined the possible underlying neuropsychological mechanism causing the social problems among individuals with SCT. Such results do not only help us to understand the nature of social problems in children with SCT but also the nature of social problem in other developmental disorders such as ADHD and autism spectrum disorder. Among different neuropsychological mechanisms, sustained attention deficit has been frequently found to be related to SCT. However, its relationship with the social problems commonly seen in individuals with SCT has been rarely examined in the previous studies because there is lack of a comprehensive model to explain the problems encountered by the individuals with SCT. The present study aimed to examine the relationships of sustained attention deficit, social problems and withdrawn behaviour in school-aged children with high SCT symptoms. Specifically, it sought to characterize the possible associations of sustained attention with social problems and withdrawn behaviour among children with SCT by exploring

the specific parameters of these attention measures which contribute to social problems and withdrawn behaviour of children with SCT. In the current study, sustained attention was conceptualized to cause difficulties for children with SCT to be alert to the social information during the social process. Therefore, it was hypothesized that sustained attention measures would be significantly associated with the severity of social problems and withdrawn behaviour measured by the parent rating scale among children with high SCT symptoms.

5.1 Method

5.1.1 Participants.

The participants involved in this study were required to meet the following inclusion criteria: (a) aged 6–12 years and (b) a full- scale IQ score >80. Potential participants who met any of the following criteria were excluded: (a) any psychiatric diagnosis, including Autism, oppositional defiant disorder, conduct disorder; (b) a T-score >85 in the Chinese version of the Strength and Weaknesses of ADHD Symptoms and Normal Behavior scale (SWAN; Education Bureau of HKSAR, 2010; Swanson et al., 2012). Those with other psychiatric disorders (e.g., ADHD, childhood autism or oppositional defiant disorder/conduct disorder) were excluded because these disorders have been found to be associated with different neuropsychological deficits. In other words, these conditions could have confounded the relationship between the attention deficits and social problems. Researchers gave a research package (information on the nature and purpose of the study and a written consent form) and explained the research to parents who expressed an interest in joining the study. The informed consent forms were signed prior to the collection of data.

Eighty-eight primary school students in Hong Kong were the participants in the current study. There were recruited via posters sent to primary schools and parent chat groups. Among

them, 40 children (mean age = 114.08 months, SD = 18.81; 52.5% female) were grouped into the High SCT group while 48 children were grouped into the Low SCT group (mean age = 108.92 months, standard deviation [SD] = 20.74; 45.8% female) using median split method on the SCT rating scale score. Some of the participants of the current study were also the participants of the Study I and Study II.

5.1.2 Procedure and experimental setup.

Each participant was then asked to attend one 1.5-hour testing session conducted in a laboratory free from visual or auditory distractions. Breaks were offered before or during the tests. The procedures of Study III were similar to Study II, except measuring instruments.

5.1.3 Measuring instruments.

Each participant underwent the following neuropsychological tests:

- Wechsler Intelligence Scale for Children, Fourth Edition (Hong Kong) short-form (WISC-IV; Wechsler, 2010).

This is a short version of the WISC-IV, a formal intelligence scale. It comprises four subscales: similarities, matrix reasoning, coding, and digit span. The raw scores for these four subscales are combined to give a total raw score and subsequently transformed into a full-scale IQ score.

- Child Behavior Checklist for Ages 6–18 (CBCL/6-18) (Achenbach, 2001).

The CBCL/6-18 is an assessment tool designed for parents to rate the emotional and behavioural problems of children between the ages of 6 and 18. Each item on the scale is rated by the respondent using a 3 point scale, where 0 represents “not true”, 1 indicates “somewhat or sometimes true”, and 2 signifies “very true or often true”. The CBCL consists of eight subscales including withdrawn behaviour, anxiety/depression, somatic complaints, social problems, thought problems, attention problems, rule-breaking behaviour, and aggressive behaviour. The

total raw score for each scale is then converted into a standardized score. Previous study has shown that the CBCL exhibits good to excellent test-retest reliability (intra-class correlation coefficient: .66–.87) and good discriminant validity (Leung et al., 2006). • SWAN—Chinese version.

SWAN is a parent and teacher rating scale used to screen for ADHD symptoms (Swanson et al., 2012) The Chinese-translated version used in this study has been validated for use with children in Hong Kong (Education Bureau of HKSAR, 2010). The scale comprises 18 items that measure a child's control of their attention, impulses, and activity. The items are divided into two subscales of nine items each, which address inattention and hyperactivity/impulsivity, respectively. The total and subscale scores are generated by summing the raw item scores, which can be expressed as T-scores. A higher score indicates fewer ADHD symptoms. In this study, only the total SWAN scores were used. All of the total and subscale scores for both the parent and teacher versions of SWAN have been found to yield a very good internal consistency (Cronbach's alpha > .9) (Education Bureau of HKSAR, 2010) and good discriminant validity (AUC > .8) (Education Bureau of HKSAR, 2010).

- SCT Scale (Penny et al., 2009).

This 14-item parent and teacher scale is used to measure SCT symptoms in children. Each item is rated on a 7-point scale (range: 0 = not at all to 6 = very much). As with those previous researches using this measure (Becker et al., 2017; Holdaway & Becker, 2018), 10 items were selected for use instead of the full scale in the present study. These 10 items were found to yield consistent loadings on the SCT factor but not the ADHD inattention factor (Becker et al., 2016). This unified 10-item construct was consistent with the participants' characteristics and the hypotheses of the study. The internal consistency of the 14-item SCT is high when measured by

both parent (Cronbach'salpha > .8) and teacher ratings (alpha > .9) (Penny et al., 2009). Additionally, the 10-item version yielded a high level of internal consistency in the present study (Cronbach's alpha = .898).

- Cued Continued Performance Test (CCPT) (Nash, Schiller, Gianotti, Baumgartner & Knoch, 2013).

CCPT was used to measure the performance of sustained attention ability in the present study. Subjects were required to press the response button when the target stimuli appeared on the computer screen while withheld to respond when the non-target stimuli appeared. Stimuli were letters which were presented at the center of the computer screen (one letter at a time for 200ms and the inter-stimulus interval was 1650 ms) in a pseudo-randomized order. Target stimuli were a paired sequence of stimuli in which the letter O was first presented and then followed by the letter X. Non-target stimuli were the letter O followed by non-X letters. The stimulus set consisted of two blocks of 200 trials and subjects were asked to take a 1-minute break after the first block to avoid mental fatigue. In each block, 40 were "O letter" stimuli, 20 were target stimuli and 20 were non-stimuli. The remaining 120 stimuli were distractor letters (letters other than O or an X without a preceding O). The measures generated from each block of the tests were the number of target hit (X with a preceding O), omission error (no response towards target), commission error (response to non-target and distractor stimulus) and response latency towards target. The final measures used in the analysis of the current study were calculated by deducting the value of each measure in block 1 from the value of each measure in block 2 (i.e. the final measure of Omission Error = number of Omission Errors in block 2 minus the number of Omission Errors in block 1). The rationale behind such calculation was to obtain a

measurement of performance deteriorations over time which was assumed to reflect sustained attention (Wåhlstedt & Bohlin, 2010).

5.1.4 Data analysis.

MANOVA was used to examine the behavioral difference (reflected by the CBCL) between High SCT group and the Low SCT group. Eight subscale scores (Withdrawn, Somatic Complaints, Anxious/Depressed, Social Problems, Thought Problems, Attention Problems, Delinquent Behaviour and Aggressive Behaviour) of CBCL were used as dependent variables. After that, bivariate correlation analysis was conducted to examine the correlations between CBCL Social Problem Subscale/Withdrawn Subscale score and CCPT scores (Correct responses, Omission Errors, Commission Errors and Response Time). CCPT scores were found to have significant associations with CBCL Social Problem Subscale score or/and CBCL Withdrawn Subscale score and then CCPT scores were put into the regression analysis as independent variables. All of these analyses were conducted using SPSS 23.0 (IBM, U.S.A.), and the significance level was set at .05.

5.2 Results

5.2.1 Behavioural difference between group with High SCT and Low SCT group.

One-way MANOVA was conducted with SCT group status (High SCT vs Low SCT group) as independent variables and CBCL Subscale scores (Withdrawn, Somatic Complaints, Anxious/Depressed, Social Problems, Thought Problems, Attention Problems, Delinquent Behavior and Aggressive Behavior) as dependent variables. Higher score in the CBCL subscale score represents more clinical problems in daily life.

Significant differences were found on CBCL subscale scores between High SCT group and Low SCT group, $F (8, 75) = 3.617$, $p < .05$; Wilk's Lambda = .72, partial eta squared = .28. After Bonferroni correction ($p = 0.05/8 = 0.00625$), High SCT group was found to have significantly higher scores than the Low SCT group on Withdrawn subscale ($F (1, 82) = 16.83$, $p < .006$; Partial Eta Squared = .17), Anxious/Depressed subscale ($F (1, 82) = 10.71$, $p < .006$; Partial Eta Squared = .12), Social Problems subscale score ($F (1, 82) = 18.17$, $p < .006$; Partial Eta Squared = .18) and Attention Problems subscale score ($F (1, 82) = 14.56$, $p < .006$; Partial Eta Squared = .15) (See Table 15). These results suggested that High SCT group had more problems in withdrawn behavior, anxiety/depression, attention and social problems than the Low SCT group.

Table 15. High SCT group and the Low SCT group's mean and standard deviation on CBCL subscale scores

	High SCT group (n = 40)	Low SCT group (n = 48)	*F*	*p*	partial Eta Squared
	Mean (SD)	Mean (SD)			
Withdrawn	3.63 (3.267)	1.33 (1.79)	16.829	<.001	.170
Somatic Complaints	1.47 (1.751)	1.15 (1.813)	.675	.414	.008
Anxious/Depressed	4.68 (3.655)	2.24 (3.192)	10.709	.002	.116
Social Problems	3.82 (2.103)	2.00 (1.801)	18.166	<.001	.181
Thought Problems	.84 (1.151)	.37 (.741)	5.165	.026	.059
Attention Problems	5.79 (2.961)	3.43 (2.689)	14.564	<.001	.151
Delinquent Behavior	2.50 (1.885)	1.50 (1.847)	5.987	.017	.068
Aggressive Behavior	8.03 (6.441)	6.15 (5.432)	2.094	.152	.025

Table 16. High SCT group and the Low SCT group's mean and standard deviation on CCPT measures

	SCT group (n= 40)	Control group (n=48)
	Mean (SD)	Mean (SD)
Correct Response	-.4872 (2.316)	- .9149 (2.04)
Omission	.9487 (2.743)	.9149(2.041)
Commission	-1.615 (25.31)	1.702 (10.24)
Response Time	48.85 (116.76)	53.68 (96.83)

Table 17

Correlation Coefficients between CCPT Measures and CBCL Withdrawn subscale score and Social Problem subscale score in the High SCT group (n = 40)

	CCPT measures			
	Correct	Omission	Commission	Response Time (MS)
Withdrawn	.04	.54**	.41*	.04
Social Problem	-.11	.43**	.17	.14

Note. Withdrawn = CBCL Withdrawn subscale score; Social Problem = CBCL Social Problem subscale score; Correct = CCPT correct response, Omission = CCPT omission errors; Commission = CCPT commission errors; Response Time = CCPT response time in milli-second

* $p < .05$., ** $p < .01$

Table 18

Correlation Coefficients between CCPT Measures and CBCL Withdrawn subscale score and Social Problem subscale score in the Low SCT group (n = 48)

	CCPT measures			
	Correct	Omission	Commission	Response Time
Withdrawn	.04	-.04	.41**	-.17
Social Problem	.07	-.07	.34	-.26

Note. Withdrawn = CBCL Withdrawn subscale score; Social Problem = CBCL Social Problem subscale score; Correct = CCPT correct response, Omission = CCPT omission errors; Commission = CCPT commission errors; Response Time = CCPT response time

* $p < .05$., ** $p < .01$

5.2.2 Bivariate associations of sustained attention measures (CCPT) with CBCL Social Problems and CBCL Withdrawn Behaviour subscale scores.

Bivariate correlation analysis was used to test the associations of the sustained attention measures with the subjects' CBCL Social Problems and Withdrawn subscale scores in both the SCT and the Control group. The means and standard deviations of the CCPT measures, Social Problem subscale and the Withdrawn subscale scores of both groups were shown in the Table 16. In the High SCT group, significant correlations were found between Withdrawn subscale score and CCPT Omission, Withdrawn subscale score and CCPT Commission as well as Social Problem subscale score and CCPT Omission (Table 17). In the Low SCT group, significant correlation was found between Withdrawn Behavior subscale score and CCPT Commission (r=.41, p<.01). (Table 18)

Table 19
Regression Model of CCPT Measures as Predictors of CBCL Withdrawn subscale score in the High SCT group (n = 40)

Variable	Unstandardized B	Coefficient Standard Error	Standardized Coefficient Beta	*t*	Sig.	R	R^2	Adjusted R^2	R^2 Change
Step 1									
SWAN ADHD score	-.059	.049	-.193	-1.19	.24	.193	.037	.011	.037
Step 2									
SWAN ADHD score	-.022	.044	-.070	-.488	.628	.543	.295	.256	.258**
Omission	.608	.167	.522	3.63	.001				

Note. Omission = CCPT Omission errors
*p < .05. **p <.01

5.2.3 Use of CCPT measures to explain CBCL Social Problems subscale and CBCL Withdrawn Behaviour subscale scores.

Stepwise regression was conducted to examine the association of CCPT measures with CBCL Withdrawn and Social Problem subscale scores after entering the Swan ADHD score into the model to control for ADHD symptoms (Step 1). Subsequently, the CCPT measures (Omissions, Commissions) were entered using the stepwise method (entry probability = .05; removal probability = .10) (Step 2) to explain the variance of the CBCL Withdrawn subscale score and the CBCL Social Problem subscale score in both groups.

In the High SCT group, the SWAN ADHD score did not contribute significantly to the regression model to explain the CBCL Withdrawn subscale score [$F(1,37) = 1.43$, $p > .05$] (Table 19) and to explain the CBCL Social Problem subscale score [$F(1,37) = .44$, $p>.05$] (Table 20). The stepwise analysis identified only the CCPT Omission as a significant independent variable in the regression models to explain CBCL Withdrawn subscale score and CBCL Social Problem subscale score. The CCPT Omission measure explained 25.8% of the variance in the CBCL Withdrawn subscale score [$F(1,36) = 13.17$, $p < .01$] and 17.5% of the variance in the CBCL Social Problem subscale score [$F(1,36) = 7.75$, $p < .01$].

In the Low SCT group, the SWAN ADHD score also did not contribute significantly to the regression model to explain the CBCL Withdrawn Behaviour subscale score but contributed significantly to the regression model to explain the CBCL Social Problems subscale score. CCPT Commission was found to be the significant independent variable that could explain the CBCL Withdrawn subscale score (Table 21). It explained 15.3% of the variance of the CBCL Withdrawn subscale score [$F(1,44) = 8.2$, $p < .01$]. CCPT Commission score was found to be the significant independent variable which could explain the CBCL Social Problem subscale score

(Table 22), but the CCPT Commission only explained 8.7% variance of the CBCL Social Problem subscale score [$F(1,44) = 5.56$, $p < .05$].

Table 20

Regression Model of CCPT Measures as Predictors of CBCL Social Problem subscale score in the High SCT group (n = 40)

Variable	Unstandardized B	Coefficient Standard Error	Standardized Coefficient Beta	*t*	Sig.	R	R^2	Adjusted R^2	R^2 Change
Step 1									
SWAN ADHD score	-.022	.033	-.108	-.664	.511	.108	.012	-.015	.012
Step 2									
SWAN ADHD score	-.002	.031	-.008	-.050	.960	.432	.187	.142	.175**
Omissions	.326	.117	.430	2.784	.009				

Note. Omissions = CCPT omission errors

*$p < .05$. **$p<.01$

Table 21

Regression Model of CCPT Measures as Predictors of CBCL Withdrawn subscale score in the Low SCT group (n = 48)

Variable	Unstandardized B	Coefficient Standard Error	Standardized Coefficient Beta	*t*	Sig.	R	R^2	Adjusted R^2	R^2 Change
Step 1									
SWAN ADHD score	-.023	.021	-.161	-1.095	.279	.161	.026	.004	.026
Step 2									
SWAN ADHD score	-.018	.020	-.122	-.889	.379	.423	.179	.142	.153**
Commission	.068	.024	.393	2.865	.006				

Note. Omission = CCPT Omission errors

*p < .05. **p <.0

Table 22

Regression Model of CCPT Measures as Predictors of CBCL Social Problem subscale score in the Low SCT group (n = 48)

Variable	Unstandardized B	Coefficient Standard Error	Standardized Coefficient Beta	*t*	Sig.	R	R^2	Adjusted R^2	R^2 Change
Step 1									
SWAN ADHD score	-.069	.019	-.475	-3.63	.001	.475	.226	.209	.226
Step 2									
SWAN ADHD score	-.065	.018	-.446	-3.55	.001	.559	.313	.282	.087*
Commissions	.051	.022	.296	2.357	.023				

Note. Omissions = CCPT omission errors

*p < .05. **p<.01

5.3 Discussion

The current study was to examine the relationships between sustained attention, social problems and withdrawn behaviour among children with high SCT. The results support our hypothesis that sustained attention, as measured by the CCPT omission errors, was identified as a significant variable in explaining the social problem and withdrawn behaviour in children with high SCT symptoms after controlling for ADHD symptoms. Therefore, the results of the current study support the linkage between sustained attention difficulties, social problems and withdrawn behaviour among children with high SCT symptoms.

5.3.1 Behavioural difference between children with SCT and their healthy peers

The results of the current study indicate that children in the High SCT group had significantly more problems in withdrawn behavior, anxiety/depression, attention and social problems than those children in the Control group. This is consistent with the previous research (Becker, Luebbe, Fite, Stoppelbein & Greening, 2014; McBurnett, Villodas, Burns, Hinshaw, Beaulieu & Pfiffner, 2014), which found that SCT symptoms were associated with social problems, anxiety, depression, and withdrawn behavior in U.S. children. The results of the current study further support that these impairments were evident in children with SCT.

5.3.2 Sustained attention difficulties and social issues in children with high SCT symptoms.

Previous research had showed that SCT symptoms were more related to sustained attention difficulties than to executive function deficits (Baytunca et al., 2018; Wahlstedt & Bohlin, 2010; Willcutt et al., 2014). However, no research has been done to examine the linkage between such attention difficulties and the unique social difficulties (social problems and withdrawn behavior) in children with SCT. The results of this study suggest that, even after the

statistical control of ADHD symptoms, omission errors in CCPT were found to be a significant factor to explain social problems and withdrawn behavior in the High SCT group. In the Low SCT group, social problems and withdrawn behavior could be significantly explained by the commission errors in CCPT. Therefore, the social problems and withdrawn behavior in children with SCT were more related to their sustained attention difficulties while the social problems and withdrawn behaviour were more related to impulsivity in children with typical development.

Severity of SCT symptoms was found to be associated with neurophysiological states of arousal (Yung, Lai, Chan, Ng & Chan, 2020) (reported in the Study I of this thesis), which in turn may cause sustained attention deficit among these children (Petersen & Posner, 2012). Their sustained attention deficit may pose difficulties for these children to remain vigilant during social conversation and to receive important social cues during the social encounters (Andrade et al., 2009; Mikami et al., 2007). The results of the study II which found that Theta power (reflected high sensitivity to BIS) was associated with more omission errors in children with SCT symptoms. Therefore, it is possible that children with SCT symptoms, when they are under stress in social encounters, tend to allocate their attentional resources to look for salient and potential threatening information in the social environment. Subsequently, they assign relatively less resources on crucial but non-salient cues embedded in social interaction and make less appropriate social responses in social situations.

To summarize, the current study (Study III) is the first to identify the neuro-psychological correlates of social problems and withdrawn behavior among children with high SCT symptoms. Social problems and withdrawn behavior have been regarded as hallmark features of children with high SCT symptoms. However, not much is known about the underlying neuropsychological factors which contributed to these clinical features of SCT. The results of the

present study established a linkage between sustained attention difficulty (reflected by the omission errors) and social difficulties (social problems and withdrawn behavior).

Coupled with the results of the Study I and Study II of the current thesis, abnormalities in Arousal/Regulation Systems and Negative Valence systems were shown to contribute to the sustained attention deficits in children with SCT. Furthermore, the results of Study III provide evidence to show that the sustained attention deficits (a component of Cognitive System in RDoC) predicts clinical problems (social difficulties) among individuals with high SCT symptoms.

Chapter 6 Discussion and conclusion

6.1 The multifaceted nature of SCT

6.1.1 Using RDoC to understand the nature of SCT.

Traditionally, SCT was seen as a construct of ADHD and was often seen as part of inattentive symptoms of ADHD. However, there is increasing evidence to support the notion that SCT is a disorder distinct from ADHD (Becker et al., 2016; Garner, et al., 2014; Lahey et al., 1988; Lee et al., 2015; Willcutt et al., 2014). Although we generally understand SCT as a separate condition from other psychopathology, its underlying nature of this condition is still largely unknown. To understand its nature, we should employ a psychopathological model which enable us to understand the relationship between SCT behavioural symptoms and different biological systems which could be studied using neuroscientific methods. RDoC[15] is a case in point. By understanding SCT through RDoC framework, we may be able to identify dysfunctions in single or multiple biological systems which may lead to the behavioural symptoms of SCT.

It is widely accepted that mental disorders are often caused by multiple etiology. There may be different pathways involving different brain mechanisms which may be involved in the development of SCT symptoms. However, previous research in SCT often focused on purely cognitive domain such as attention and executive deficits. Less attention was focused on the possible neural mechanisms underlying the clinical presentation of SCT. As a results, it would be very difficult for clinicians to employ appropriate treatment directed at the specific underlying neural mechanisms which causes SCT symptoms. The thesis attempts to understand SCT in a multi-dimensional approach through three studies as reported in Chapters 3, 4 and 5. The

[15] The relationship between four RDoC systems and SCT were examined in the current thesis: arousal/regulation system (Study 1), negative valence system and cognitive system (study 2), cognitive systems and social systems (study 3)

findings revealed that there were relationships between those biological systems defined by the RDoC framework and the behavioural dysfunctions in SCT.

In this chapter, it will firstly discuss how different biological systems namely Negative Valence Systems, Arousal/Regulation Systems and Cognitive Systems are related to the SCT symptomology. Secondly, it will also discuss how dysfunctions in these systems may be related to social difficulties and emotional disturbance commonly seen in SCT. Thirdly, it will discuss the significance of the present study in terms of its impact on understanding SCT and on how we should view mental disorders in general. Lastly, limitations of the present study will be discussed and future research directs will be suggested.

6.1.2 Arousal/Regulatory Systems and SCT.

In RDoC, arousal has been defined as a continuum of sensitivity of the organism to external and internal stimuli (NIMH, 2016). Petersen & Posner (2012) also suggested that arousal and alertness is closely related. Norepinephrine (NE) is the main neuromodulator in the human alerting system and the locus coeruleus (LC) was found to be the main source of NE (Aston-Jones & Cohen, 2005). Previous evidence supports the two-way pathway between LC and ANS (Samuels & Szabadi, 2008; Wang et al., 2014; Wood & Valentino, 2017). Changes in the arousal in the brain will lead to changes in the ANS system. Therefore, measuring changes in the ANS can measure changes in the brain arousal system in human. Becker & Willcutt (2018) has suggested that SCT may be associated with both under-arousal and hyper-arousal state because SCT is often associated with daytime sleepiness and depression. The results of the Study I in this thesis provided the first evidence to support the assertion made by Becker & Willcutt (2018). It was found that lower ANS readiness was associated with higher SCT symptoms. This supported that under-arousal may be related to SCT symptoms. In addition to this, the current

study found that higher arousal in Warning Signal condition compared to Resting condition was associated with higher SCT symptoms. This supported that SCT symptoms may be related to hyper-arousal state during the exposure to stressful event in the real life. The results of the current study supported the involvement of arousal regulatory system in the development of SCT symptoms.

The results of the Study I may also provide an explanation on the linkage between SCT and ADHD. SCT has often been found to be associated with ADHD. This may be because ADHD and SCT are both associated with abnormality in arousal state and regulation. Low brain arousal state and deficits in arousal regulation have been found to be associated with ADHD symptoms in adults (Strauß, Ulke, Paucke, Huang, Mauche, Sander, Stark & Hegerl, 2018). The results of the Study 1 may explain why SCT symptoms were often observed in children with ADHD.

6.1.3 Negative Valence Systems, Cognitive Systems and SCT.

Response to anxiety provoking events is one of the constructs under the Negative Valence Systems while attention is the construct under Cognitive Systems. Studying the relationship between these two mental processes across two different biological systems is important in understanding the nature of SCT. Anxiety was frequently shown to have impairing effect on cognitive performance. Hyperarousal, which is often associated with anxiety, produced high levels of NE which impair PFC dependent functions such as attention and working memory. Based on the results of the Study I of this thesis, children with higher SCT symptoms were found to have higher arousal during Warning Signal condition. Therefore, it is speculated that these children are likely to suffer from cognitive performance impairment caused by anxiety. In the Study II of this thesis, it is hypothesized that physiological responses such as HRV and EEG

during Warning Signal condition may associate with more errors in sustained attention task. The results of the Study II support this hypothesis. Specifically, higher power of theta wave in Warning Signal condition compared to Resting condition was found to be significant predictor of CCPT Omission errors. Individuals with higher sensitivity towards BIS tended to have higher magnitude of theta wave during goal-conflict task (Moore et al., 2012). High anxiety level was often found to be associated with BIS hypersensitivity. Such higher level of state anxiety may cause attention difficulties in individuals with SCT. Specifically, individuals with high SCT, due to their high sensitivity to BIS, may experience more anxiety which direct their attention towards the salient non-target during attention task and subsequently they failed to direct attention resources towards inconspicuous target stimulus in the task.

In the Study II, higher propensity of freezing in term of bradycardia was found to be a significant predictor of CCPT Commission errors in children with high SCT symptoms. These children, due to their BIS sensitivity, tends to employ stimulus-driven attention system to detect salient threat-related information instead of the inconspicuous goal of the task. As a result, they may be more prone to make commission errors. Therefore, the attention problems exhibited by individuals with SCT may not only be related to their under-arousal, but also due to their abnormal response towards anxiety.

6.2 Understanding Social Difficulties in SCT through their deficits in RDoC Constructs

Study III found that children with high SCT symptoms had significantly more withdrawn behaviour and social problem than those children with low SCT symptoms. This is consistent with the findings of the previous research (Becker et al., 2017; Becker, et al., 2014; Marshall, et al., 2014; McBurnett, et al., 2014). Social problems and withdrawn behaviour are two hallmark clinical features associated with SCT but it is still not clear why these two behavioural

difficulties develop in children with SCT. There is no previous study to examine the underlying neuropsychological and neurophysiological mechanism which explains the social problem and withdrawn behaviour exhibited by the individuals with SCT. Study III found that sustained attention, as measured by the CCPT omission errors was significantly associated with the social problems and withdrawn behaviour in children with high SCT symptoms after controlling for ADHD symptoms. Therefore, results of the Study III found the linkage between sustained attention difficulties, social problems and withdrawn behaviour among children with SCT symptoms.

Low arousal level in the resting state was found to be associated with SCT symptoms, as indicated by the results of the Study I. Low arousal state may be one of the factors causing the sustained attention deficits in SCT because sustained attention required optimum level of arousal (Petersen & Posner, 2012). Sustained attention deficit may negatively affect these children's ability to remain vigilant during social conversation and to receive important social cues during the social interaction (Andrade et al., 2009).

High sensitivity to BIS was found to be associated with more omission errors in children with high SCT symptoms in the Study II. Under the stress in social encounters, they tend to allocate their attentional resources to look for salient and potential threatening information in the social environment. Subsequently, they assign relatively less resources on detecting crucial but non-salient cures embedded in social interactions and thus make less appropriate social responses in social situations. This explains why children with high SCT symptoms may make fewer social responses and failed to attend to subtle social cues in Mikami et al's study (2007).

6.3 Understanding Emotional Disturbances in SCT through their Deficits in RDoC Constructs

The results of the Study III indicated that children with high SCT symptoms had significantly more anxiety and depression problems than those children with less SCT symptoms. This is consistent with the previous research which found that SCT symptoms were associated with internalizing symptoms such as anxiety and depression (Bauermeister et al., 2012; Becker & Langberg, 2012; Penny et al., 2009). The results of the Study II indicated that higher power of theta signals during Warning Signal condition than Resting condition was associated with higher omission errors in CCPT. Theta power has been found to be the significant indicator in discriminating with high/low sensitivity to Behavioural Inhibition System (BIS) (Moore, Mills, Marshman & Corr, 2012). The BIS activates anxiety and arousal, as well as inhibition and avoidance behaviour which are core symptoms in both SCT and Anxiety Disorders. The results of the Study I also found that SCT symptoms are associated with heightened arousal during warning signal condition.

Study I and Study II both provides novel neurophysiological evidence to support the results of the Becker et al.'s study (2018) which found SCT was uniquely associated with high BIS and Neuroticism using personality scales. Individuals with high SCT symptoms may direct their attentional resources towards the potential negative valence information in the environment which may cause more anxiety. Enhanced anxiety may prompt them more towards anxiety provoking information which further exacerbate their anxiety level. This assertion is consistent with the results of Becker, Webb & Dvorsky's study (2021) which has found that SCT symptoms and internalizing symptoms may exacerbate each other over time.

SCT symptoms were often found to be associated with depression symptoms. However, no previous research has explained the linkage between SCT symptoms and depression symptoms. The results of the Study I, which found the hyperarousal tendency in children

associated with SCT symptoms, may provide explanation to the linkage between SCT symptoms and depression. Hyperactivity in the central noradrenergic system, particularly in LC, was often found in individuals with depression (Gold et al., 2005; Itoi and Sugimoto, 2010; West et al., 2010). High noradrenergic activities are often associated with behavioural over-inhibition which is a core symptom of depression (Stone et al., 2011). Hyperarousal state is often associated with the tendency to withdraw or avoid social interactions and external stimulation which are typical symptoms of SCT and Depression. Through RDoC, we could identify the commonalities between SCT and other psychopathologies such as anxiety and depression. This can help clinicians to provide precise clinical management for individuals with these mixed symptoms.

6.4 Significance of the Current Study

Firstly, the current study was the first study to examine the relationships between SCT symptoms and the arousal/regulatory system in children. The results were also the first evidence supporting that SCT symptoms are associated with both hypo-arousal state and hyper-arousal state. As SCT symptoms are associated with abnormal arousal regulatory functions, it is not surprising that SCT symptoms are often found to be related to ADHD, Anxiety and Depression.

Secondly, the results of the current study provide a new perspective to conceptualize SCT. Previous research have been focused on the cognitive deficits in individuals with SCT. However, there are growing number of researchers who suggested that psychopathology should be conceptualized into different biologically based constructs. One of the models applied this concept was Research Domain Criteria (RDoC) initiated by the National Institute of Mental Health. It proposes that mental disorders should be studied in terms of different biological constructs such as Negative Valence Systems, Cognitive Systems, Positive Valence Systems, Social Processes and Arousal/Regulatory Systems using different unit of analysis (e.g.,

neuropsychological data, neurophysiological data and genetics). The current study could be seen as one of the initiatives to conceptualize SCT as a condition caused by different dysfunctions across different biological constructs such as Cognitive Systems, Negative Valence Systems and Arousal/regulatory Systems. By doing so, we will be able to have a thorough understanding of this condition and to formulate appropriate treatment based on their deficits in these systems.

Thirdly, the results of the current study linked up physiological dysfunction with behavioural difficulties in explaining the nature of SCT. Such research method not only can help us to understanding the deficits of SCT at the physiological and behavioural levels, but also help us to understand the relationship between these two levels. With these research findings, we will be able to formulate a neuroscientific model of SCT which can inform us on the clinical management of this disorder. Fourthly, the current study identified hypersensitivity towards stressful situation as the mechanism related to the attention problems in SCT. Therefore, it provides a scientific basis to research new treatment on SCT. For example, anxiolytic drugs may be a plausible medication treatment for SCT. In fact, previous research has shown that atomoxetine, which is an NE reuptake inhibitor and is frequently used as treatment for depression and anxiety, could significantly improve the SCT symptoms in patients.

6.5 Limitations of the Current Study and Future Research Direction

One of the limitations of the current study was that the findings were correlational in nature. It could not provide an empirically evidence on the causal relationship between BIS sensitivity, anxiety and attention difficulties in children with SCT. Future study should compare the group difference between the High SCT group and the Low SCT group in the neurophysiological variables such as such as theta power and HRV in the attentional control task

during high vs low stress condition. Through manipulating the group status (SCT vs Control) and the stress level (High vs Low Stress), we will be able to provide direct evidence to support SCT as the cause of the abnormal physiological changes and behavioural response during high stress situation and to confirm the role of emotional regulation deficits in SCT symptomology.

Moreover, the current studies have the small sample size. Although it may undermine the significance of the current study, the results of the current study provided initial evidence that the attention difficulties exhibited by children with high SCT symptoms was associated with their abnormal neurophysiological responses towards challenge/stressful stimulus. It may shift the focus of the future research in SCT from purely cognitive domains such as attention and executive functions towards emotional state and regulation domains. By doing so, we will have a more comprehensive understanding of the nature of the SCT symptoms.

Although the results of the current study suggest a link between sustained attention and social problems in children with SCT, it is not clear their attention difficulties were related to which aspects of their social problem (e.g., initiation to communication or peer rejection or) or which stage of social information processing (e.g., encoding or response selection). Future studies should further investigate how the above-mentioned attention deficits are related to different aspects of social problems and social information processing in children with SCT. One possible approach is to measure the electroencephalography (EEG) of the individuals with SCT while they are performing a simulated social task e.g., social rejection task or simulated chat room task. Examination of the power of the individual EEG frequency bands may clarify the attentional and emotional states of these individuals in different social situations during the task. Such Evidence may confirm the causal link between arousal regulation, attention deficits and social problems in these individuals.

6.6 Conclusion

In the current thesis, low arousal state during resting condition and hyperarousal during sensory challenge condition were found to be significantly associated with SCT symptoms. Higher theta power during sensory challenge condition, reflecting increased BIS sensitivity, was found to be significantly associated with omission errors in the CCPT. Omission errors were also found to be significantly associated with social problems and withdrawn behaviour in children with SCT. All these evidence supported the notion that SCT symptoms and its associated problems such as social problems could be explained by the abnormalities in the Arousal/Regulation Systems, Negative Valence Systems and Cognitive Systems delineated in the RDoC.

SCT should not only be conceptualized as a condition resulted from cognitive deficits such as sustained attention deficits. Instead, SCT should be conceptualized as a condition characterized by multiple deficits in different biological systems such as Cognitive Systems, Negative Valence Systems and Arousal regulatory System. Without understanding such multiple facet of this condition, we will hardly be able to understand the nature of this condition and to devise effective treatment for it.

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