A COMPARISON OF TWO MODELS OF ADHD:

STATE REGULATION VERSUS DELAY AVERSION

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CONTENTS

CHAPTER 1

GENERAL INTRODUCTION

ABSTRACT

Attention-Deficit/Hyperactivity Disorder (ADHD) is a lifespan disorder that causes significant problems in social and academic life. In this chapter, we first give information about the general characteristics of ADHD and briefly explain the genetic, environmental and neurobiological factors implicated in the aetiology. We discuss the neuropsychological theories of ADHD with focusing on State Regulation and Delay Aversion models. We then explain the objective of the dissertation, which is to compare the State Regulation and Delay Aversion Models. Finally, we provide a summary of the chapters.

WHAT IS ADHD?

Attention Deficit/Hyperactivity Disorder (ADHD) is characterized by persistent and pervasive inattention and/or hyperactivity and impulsivity (DSM-IV-TR, American Psychiatric Association, 2000). The worldwide prevalence of ADHD is estimated to be around 5.29% making it one of the most prevalent psychiatric disorders (Polanczyk, De Lima, Horta, Biederman, & Rohde, 2007). ADHD causes significant disability in social and academic life. It is a major burden to individuals, families, clinical services and communities (Pelham, Foster, & Robb, 2007). In the long term, it increases the risk of delinquency, academic failure, job insecurity, substance use disorder and motor accidents (Harpin, 2005; Kessler et al., 2005).

Numerous studies conducted to understand the aetiology of ADHD indicate that it is a complex and heterogeneous disorder in which several genetic, environmental and neurobiological factors might be involved (see Nigg, 2005 for a review). The heritability of ADHD is estimated to be 76% making it one of the most heritable psychiatric disorders (Faraone et al., 2005). The most commonly implicated genes in the pathophysiology are those encoding dopamine receptor subtypes (D4 and D5), enzymes involved in monoamine synthesis (dopamine hydroxylase), proteins involved in the structure of synapses (SNAP-25), and proteins involved in serotonergic transport (Faraone & Mick, 2010). Although there is evidence for that certain variants of these genes increase the risk of ADHD, a meta-analysis of genetic studies showed that none of the known risk variants was significantly associated with the disorder suggesting that the contribution of individual genes to the aetiology must be small or other variants are involved (Neale et al., 2010).

Environmental factors are also likely to be involved in the aetiology of ADHD. To date several pre and perinatal factors, childhood infections, and nutritional deficiencies have been implicated in the aetiology with strongest evidence being for maternal smoking and low birth weight (Cortese, 2012). However, it is questionable whether the link between these risk factors and ADHD is causal (Thapar, Cooper, Eyre, & Langley, 2013). Besides these environmental effects, the interaction between environmental and genetic factors also seems to be important in the aetiology of ADHD. For instance, it has been shown that environmental factors might increase the risk due to genetic factors by affecting the expression of genes (Pennington et al., 2009). Such interactions have been

found between genes involved in dopaminergic and seratonergic transport and prenatal and perinatal risk factors (Nigg, Nikolas, & Burt, 2010).

The research exploring the neurobiology of ADHD revealed that multiple types of deficits in the brain structure, function and chemistry might play a role in pathogenesis. Neuroimaging studies have shown altered structure and function in prefrontal areas involved in response inhibition, working memory, response organization, sustained attention as well as their connections with striatum, cerebellum and parietal areas (Arnsten & Rubia, 2012), impaired suppression of default mode brain network (Liddle et al., 2011) and altered sensitivity to rewards in nucleus accumbens and, orbitofrontal cortex (Scheres et al., 2007 and Cubillo et al, 2012). The most commonly implicated neurotransmitter in the pathology is dopamine. In vivo imaging studies with positron emission tomography (PET) showed that a reduction of dopamine in reward pathways was associated with symptoms of inattention and motivational deficits (Volkow et al., 2009 and 2011). In addition, the efficacy of noradrenergic medications such as modafinil and atomoxetine in treatment suggests that noradrenergic deficits might also be involved (del Campo, Chamberlein, Sahakian, & Robbins, 2011).

NEUROPSYCHOLOGICAL DEFICITS IN ADHD

Earlier accounts postulated that the symptoms of ADHD arise due to deficits in executive functions involving response inhibition (Barkley, 1997). The disinhibition account of ADHD is based on the general observation that the children with ADHD have a problem with inhibiting or withholding their responses in socially inappropriate settings and it is supported by the evidence from experimental studies which showed that children with ADHD perform worse than typically developing children in tasks tapping inhibitory functions (Oosterlaan, Logan, & Sergeant, 1998). In addition to inhibition, the neuropsychological deficits in ADHD have been found to involve other executive domains such as sustained attention, planning, set shifting and working memory (Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005) suggesting a more global deficit in executive control.

Despite the strong evidence, the role of executive function deficits in ADHD has been questioned for a number of reasons. First, the meta-analyses have shown that the

effect sizes for group differences in executive functions are much smaller than the effect sizes for ADHD symptoms suggesting that the symptoms cannot be explained only with executive deficits (Willcutt et al., 2005). Second, only a subgroup of children with ADHD has executive deficits suggesting the pathophysiological heterogeneity within the disorder (Nigg, 2005). Third, children with ADHD have information processing deficits even in tasks which require little or no executive processing (Rommelse et al., 2007). Taken together, these observations suggest that executive functions deficits are neither necessary nor sufficient to make a diagnosis of ADHD (Willcutt et al., 2005) and basic processing deficits are likely to be involved in ADHD in addition to the executive deficits.

Fixed or context-dependent deficits?

It is known that the executive functions are not static processes but rather fluctuate from state to state. For instance, research in the 60s and 70s has shown that human information processing capacity is affected non-specifically from energetic resources such as arousal, activation and effort (Pribram & McGuinness, 1975). Arousal refers to phasic alertness for environmental stimuli and it affects the processing of the input. On the other hand, activation describes the tonic readiness to make a motor response. The arousal and activation are affected from a number of external and internal factors, such as availability of environmental stimulation, stress, sleep-wake cycle, noise, and, medications. (Sanders, 1983). Effort is a top-down process, which describes the cognitive capacities allocated to a particular task and the amount of effort allocation is determined by the motivational salience of the task. Arousal, activation and effort have been integrated into a basic information processing framework by Sanders resulting in the Cognitive-Energetic model (CEM) of information processing (1983). According to this model the basic steps in processing of a stimulus are encoding, feature extraction, response selection and response execution (see Figure 1). These basic steps are affected from the levels of arousal and activation. In suboptimal conditions, which induce over/under- arousal/activation, the effort can be employed as a compensatory mechanism to regulate the level of arousal and activation.
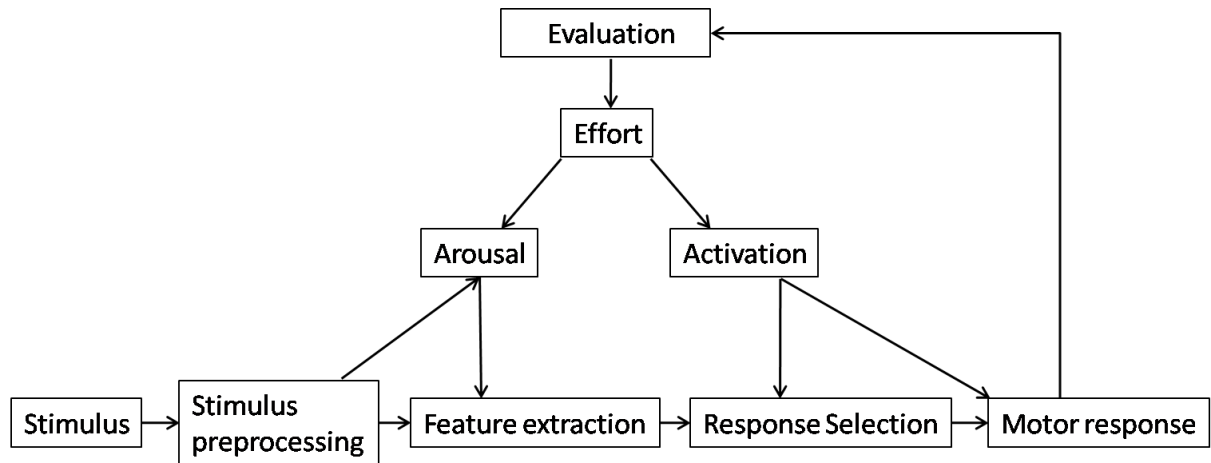
Figure 1. Cognitive Energetic Model of Sanders (1983).

The **State Regulation Deficit** (SRD) model was built on the CEM. It postulates that the children with ADHD have a problem with regulating their energetic state (arousal, activation, and effort) when challenged to do in suboptimal conditions (Sergeant, 2005; van der Meere, Börger, & Wiersema, 2010). This model has been supported by evidence from studies which used event rate (ER) manipulation. The ER implies the presentation rate of stimuli in a task, which is determined by the inter-stimulus interval (ISI) and it affects the level of motor activation (Sanders, 1983; Sergeant, 2005). The studies that compared the performance of children with and without ADHD at different ERs have shown that the children with ADHD are differentially sensitive to ER manipulation in tasks tapping different cognitive functions (Chee, Logan, Schachar, Lindsay, & Wachsmuth, 1989; Conte, Kinsbourne, Swanson, Zirk, & Samuels, 1986; Scheres, Oosterlaan, & Sergeant, 2001; van der Meere, Stemerdink, & Gunning, 1995). The SR deficits at suboptimal ER conditions were also confirmed with electrophysiological studies, which showed that the children with ADHD have a problem with regulating the level of allocated effort (Wiersema, van der Meere, Antrop, & Roeyers, 2006; Wiersema, van der Meere, Roeyers, Van Coster, & Baeyens, 2006). According to the SRD model, a fast ER produces over-activation and a slow ER produces under-activation producing an inverted U pattern of performance curve for all individuals. As the children with ADHD have a deficit in regulating their level of activation, this inverted U pattern will be accentuated for them. This prediction of the SRD model could not be tested by previous studies which used only two ERs.

The **Delay Aversion** (DAv) model explains the context dependent nature of neuropsychological deficits in ADHD from a motivational perspective. This model postulates that the core deficit in ADHD is at the dopaminergic reward processing pathways and that the signalling of future rewards in these pathways is impaired (Sonuga-Barke, Wiersema, Van der Meere, & Roeyers, 2010). This deficit has two main manifestations: First, children with ADHD prefer the immediately available rewards to the delayed ones producing impulsive drive for immediate rewards (IDIR). Second, when delay is imposed externally such as during a long and boring task, they display negative responses, become overactive and inattentive resulting in poor task performance. This model is supported by evidence from several studies. For instance, it has been shown that the children with ADHD have an increased preference for small sooner (SS) over large later (LL) rewards (Antrop et al., 2006; Bitsakou, Psychogiou, Thompson, & Sonuga-Barke, 2009; Kuntsi, Oosterlaan, & Stevenson, 2001; Marco et al., 2009; Sonuga-Barke, Taylor, Sembi, & Smith, 1992; but see also Bidwell, Willcutt, Defries, & Pennington, 2007; Scheres et al., 2006; Sjöwall, Roth, Lindqvist, & Thorell, 2012 for negative results). For non-choice settings, it has been shown that children with ADHD have inappropriate responses to unexpected delays and delay predicting cues (Bitsakou, Antrop, Wiersema, & Sonuga-Barke, 2006; Sonuga-Barke, Houwer, Ruiter, Ajzenstzen, & Holland, 2004) and show more activity during the delay periods (Antrop, Roeyers, Oost, & Buysse, 2000).

There have also been other models which tried to explain the symptoms of ADHD from a motivational point. The dynamic development theory (DDT) postulates that ADHD arises due to a hypofunctioning dopaminergic system. This deficit affects prefrontal circuits resulting in poor attention capacity and alters reinforcement/extinction processes producing impulsive choice and disinhibition (Sagvolden, Johansen, Aase, & Russell, 2005). According to dopamine transport deficit (DTD) model, the anticipatory firing of dopaminergic neurons for reward predicting cues is dysfunctional in ADHD, which results in altered reinforcement/extinction processes. Due to this deficit, individuals with ADHD have problems with regulating their behaviour according to environmental reinforcements (Tripp & Wickens, 2009).

OBJECTIVES OF THE DISSERTATION

The main objective of this dissertation is to compare two models (SRD and the DAv), which predict that the performance deficits in ADHD change from state to state. The aim of this comparison is to explore which model is more successful in explaining the context-dependent nature of neuropsychological deficits in ADHD. Another important question that needs to be answered is "Do the two models point to the same kind of neuropsychological deficit or do they describe different type of pathologies?

ER sensitivity is accepted as the primary manifestation of the SR deficits. According to the SRD model, fast and slow ERs produce over- and under-activation, respectively in ADHD children. On the other hand, the DAv model postulates that the effects of ER are due to increased delay between stimuli at slow ERs (Sonuga-Barke et al., 2010). Therefore the models make different predictions for the effects of ER. The SRD model predicts deficits at both fast and slow ERs, while the DAv predicts that only slow ERs would cause performance deficits. We performed a meta-analysis of ER effects and also conducted our own ER study to compare the models for their predictions.

As mentioned above, the SRD model postulates that the performance deficits in ADHD are at basic energetic levels and it predicts that the executive dysfunctions could be explained by basic deficits related to arousal and activation. According to the model, the performance deficits should be independent of the level of executive demands. To test this prediction, we disentangled the basic processing deficits from higher order deficits by analysing performance both in a task that require basic perceptual decision making and another task with executive demands.

Another important prediction of the SRD model is about the effects of ER on performance. According to the model, the ER sensitivity in ADHD can be explained by a deficit in regulating the motor activation: children with ADHD become over-activated at fast ERs and under-activated at slow ERs (see Sergeant, 2005; van der Meere, 2002 and van der Meere, 2010 for reviews). We aimed to test this hypothesis by segregating the effects of ER on different information processing steps and exploring the effects of ER on motor processes.

The SRD and DAv models also make different predictions for impulsive choice in ADHD. For instance, according to the DAv model, the SS reward preference in ADHD is due to the aversive nature of delay. On the other hand, the SRD model postulates that

children with ADHD choose SS option to reach an optimally stimulating environment (Sonuga-Barke et al., 2010). Therefore the SRD model predicts that providing neutral stimulation during delay would decrease SS preference, while the DAv model does not make any prediction. In the final chapter, we used these predictions to compare the models.

OVERVIEW OF THE CHAPTERS

Chapter 2. A Meta-Analytic Study of Event Rate Effects on Go/No-Go Performance in ADHD

In this chapter, a meta-analytic synthesis of results from several studies that used a Go/No-Go task to compare the performance of children with and without ADHD is presented. The SRD and DAv models were compared for their predictions about the effect of ER on ADHD-related deficits.

According to the SRD model, both very fast and very slow ERs should cause performance deficits in ADHD with producing an inverted U pattern of deficits. On the other hand, according to the DAv model, this deficit in adapting to a changing ER is due to increased perception of time passage at slow ER conditions (Sonuga-Barke et al., 2010). Therefore the DAv model predicts greatest deficits at slow ERs producing a linear pattern. These differential predictions can be used to compare the two models.

Chapter 3. Event rate effects on variability in ADHD

The study presented in Chapter 1 had certain limitations due to the nature of the data available from previous studies. First, most of the previous studies included only two ERs and when they included three ERs, they did not cover the very fast and very slow presentation rates. Therefore, the number of ERs was not enough to test the quadratic relationship between ER and performance by the SRD model. Second, most of the previous studies only reported a non-specific measure of variability (standard deviation of reaction time-SDRT) which cannot separate the variability into specific components, namely Gaussian variability and variability due to extreme responses

(Tamm et al., 2012). To address these limitations a new study was designed in which four levels of ER covering both very fast and very slow presentation rates were included. The non-specific variability was disentangled into specific components using ex-Gaussian model. The SRD model predicts that children with ADHD will have lower performance at very fast and very slow presentation rates producing an inverted U pattern of deficits. On the other hand the DAv model predicts performance deficits only at very slow presentation rates.

Chapter 4. Executive and non-executive deficits in ADHD: A diffusion model analysis

In Chapter 4, the contribution of basic processing deficits to executive deficits in ADHD is explored. We analyzed the performance of children with and without ADHD with a simple two choice perceptual decision task and a task that requires conflict control.

Although several studies have reported that ADHD is associated with deficits in executive function domains (Willcutt et al., 2005), there is also evidence for that the individuals with ADHD have performance deficits in tasks that require little or no executive processing and executive deficits can be explained by deficits at basic processing level (Rommelse et al., 2007; Van De Voorde, Roeyers, Verté, & Wiersema, 2010). These studies suggest that the performance deficits in executive tasks may not be due to deficits in executive functions but can be explained by basic deficits at the level of feature extraction, motor execution and speed-accuracy trade-off (SATO). These basic information processing steps cannot be disentangled with the conventional performance measures such as mean reaction time (MRT) and accuracy. However sophisticated RT models such as the Ratcliff Diffusion model (DM) provides an alternative by estimating separate parameters for each processing step (Voss, Rothermund, & Voss, 2004).

Chapter 5. Effects of event rate on ADHD information processing: The role of motor preparation

In this chapter a reanalysis of data from Chapter 3 is presented. The aim of the analysis is to test a prediction from the SRD model. The model postulates that children with ADHD cannot regulate the level of motor activation according to the non-optimal

ER conditions (Sergeant, 2005; van der Meere, 2002). Therefore, the model predicts that ER would primarily affect the motor preparation level and children with ADHD would be more sensitive to these effects due to a deficit at this level. Classical performance measures do not allow disentangling of different elements of information processing such as such as speed of information accumulation, speed-accuracy trade-off and motor preparation/execution. However the sophisticated models such as DM might help to identify the contribution of different steps in information processing to ER-related deficits in ADHD.

Chapter 6. Effects of environmental stimulation on impulsive choice in ADHD: A "pink noise" study

In this study a recent extension to the SRD model has been tested: Impulsive decision making in ADHD can be alleviated with increasing the arousal level via environmental stimulation (Sonuga-Barke et al., 2010). The children with and without ADHD completed tasks that measure impulsive choice. For arousal modification, pink noise, which is known to increase arousal level and improve performance in children with ADHD (Sanders, 1983; Söderlund, Sikström, & Smart, 2007), was used.

To date, several studies have shown that the children with ADHD have a preference for SS over LL rewards (Antrop et al., 2006; Bitsakou et al., 2009; Kuntsi et al., 2001; Marco et al., 2009; Sonuga-Barke et al., 1992), which is called impulsive drive for the immediate reward (IDIR). The DAv model explains this phenomenon with abnormalities in dopaminergic pathways which result in impaired signalling of future rewards (Sonuga-Barke et al., 2010). The SRD model explains the IDIR from a different perspective: The children with ADHD have a problem with regulating their arousal and activation. In under-aroused or activated states, they act on their environment to increase the level of arousal and activation resulting in hyperactivity and impulsive decision making. Therefore the preference for SS can be thought as a secondary adaptation to compensate for under-arousal or activation (Sonuga-Barke et al., 2010). From that point, the SRD makes the prediction that manipulations of arousal level during delay period might alleviate IDIR or SS preference. On the other hand, the DAv model predicts that the children with ADHD would have higher SS prefrence under both neutral and noise conditions.

Chapter 7. General Discussion

In the last chapter, first a general overview of the empirical chapters will be presented with summarizing the predictions made and the results. After the overview, we will interpret the findings by recapitulating the goals of the thesis. Next, we will describe the potential limitations of the studies. The clinical and methodological implications of the work presented in this thesis will be discussed and objectives for future research will be suggested. In the last section, we will present the final conclusions.

It is important to note that the chapters of the dissertation are actually papers that are already published, under review or submitted for publication. Therefore each chapter is a self-contained manuscript and there can be considerable overlap between chapters.

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CHAPTER 2

A META-ANALYTIC STUDY OF EVENT RATE EFFECTS ON GO/NO-GO PERFORMANCE IN ADHD[1]

ABSTRACT

Background: According to the State Regulation Deficit (SRD) model event rate (ER) is an important determinant of performance of children with Attention-Deficit/Hyperactivity Disorder (ADHD). Fast ER is predicted to create over-activation and produce errors of commission while slow ER is thought to create under-activation marked by slow and variable reaction times (RT) and errors of omission. **Method**: To test these predictions, we conducted a systematic search of the literature to identify all reports of comparisons of ADHD and control individuals' performance on Go/No-Go tasks published between 2000 and 2011. In one analysis we included all trials with at least two event rates and calculated the difference between ER conditions. In a second analysis, we used meta-regression to test for the moderating role of ER on ADHD vs. control differences seen across Go/No-Go studies. **Results**: There was a significant and disproportionate slowing of reaction time in ADHD relative to controls on trials with slow event rates in both meta-analyses. For commission errors, the effect sizes were larger on trials with fast event rates. No ER effects were seen for RT variability. There were also general effects of ADHD on performance for all variables which persisted after effects of ER were taken in account. **Conclusions**: The results provide support for the SRD model of ADHD by showing the differential effects of fast and slow ER. The lack of an effect of ER on RT variability suggests that this behavioral characteristic may not be a marker of cognitive energetic effects in ADHD.

INTRODUCTION

Attention-Deficit/Hyperactivity Disorder (ADHD) is a life-span disorder which causes significant academic, social and behavioral problems. In principle identifying the neuropsychological deficits in ADHD could stimulate therapeutic innovation by helping to identify new targets for novel treatments (Sonuga-Barke & Halperin, 2010). Identifying which deficits are implicated in ADHD is complicated by a number of factors. First, children with ADHD, as a group, perform poorly on a wide range of laboratory tasks even when they are designed to tap very different neuropsychological processes (Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005). Indeed, it is increasingly clear that there is substantial pathophysiologic heterogeneity in the ADHD population in terms of the specific patterns of deficits implicated – some individuals display one type of neuropsychological profile while others show a different one (Willcutt et al., 2005). For instance, while once thought of as the core deficit in ADHD, executive function deficits are reported in only a subset of individuals (Nigg, Willcutt, Doyle, & Sonuga-Barke, 2005).

Second, there is accumulating evidence for the context-dependent nature of deficits when they do occur - performance of an individual subject may vary from setting to setting as a function of the motivational and energetic state that they engender (Sonuga-Barke, Wiersema, van der Meere, & Roeyers, 2010). For instance, performance on a wide range of cognitive tasks is affected in non-specific ways by the rate at which stimuli are presented (i.e., event rate (ER)), which is determined by inter-stimulus interval (ISI) (Sergeant, 2005; van der Meere, 2002). These ER effects have been observed on tasks of different sorts including go/no-go (van der Meere, Stemerdink, & Gunning, 1995), stop signal (Scheres, Oosterlaan, & Sergeant, 2001), vigilance (Chee, Schachar, Lindsay, & Wachsmuth, 1989) and associative learning (Conte, Kinsbourne, Swanson, Zirk, & Samuels, 1986) tasks. Such task non-specific ER effects have been explained in different ways. The most often invoked explanation is based on the cognitive energetic model of Sanders (1983). This extends the basic information processing framework by integrating concepts such as effort, arousal and activation so that task performance is influenced not only by cognitive capacities but also by environmentally-determined levels of activation and arousal and the extent to which variations in these can be managed to ensure optimal performance. The model predicts

an inverted-U shaped curve relating cognitive energetic factors to performance with both over and under activation (linked to fast and slow ERs) having potentially adverse effects if not effectively managed (Sergeant, 2005). The state regulation deficit (SRD) model of ADHD, builds on this perspective. It postulates that children with ADHD have problems with effectively allocating their effort to properly regulate activation states (van der Meere, Börger, & Wiersema, 2010). Because cognitive energetic processes are general rather than task specific, the SRD predicts that ADHD children's performance across a range of different tasks tapping a diversity of executive and non-executive processes will be adversely affected by either speeding up or slowing down the ER. More specifically the model predicts a pattern of ADHD-related under-activation and slow inattentive responding under slow ER, and fast impulsive responding, produced by over-activation under fast ER conditions.

An alternative explanation of ER effects on performance is provided by Delay Aversion model (Sonuga-Barke et al., 2010, Sonuga-Barke, Taylor, Sembi, & Smith, 1992). According to this model individuals with ADHD act on their environment to escape or avoid delay. In fixed delay situations this is said to be achieved by reallocating attention to more interesting stimuli that make time pass more quickly. Thus the DAv model predicts a pattern of task disengagement on longer trials with slower ER and longer inter-stimulus intervals (i.e., greater delay). As such it differs from the SRD model by predicting that performance of ADHD individuals will deteriorate in a linear fashion with longer intervals resulting in lower performance (i.e., adverse effects on slow but not fast ER trials).

To test predictions of the SRD model of ADHD we conducted a systematic review and meta-analyses of the effects of ER on performance on Go/No-Go (GNG) tasks. Our strategy was to focus on one task in order to optimize homogeneity. The GNG task was chosen as it has been used frequently with ADHD populations. In the GNG task participants are presented consecutively with a series of *Go* stimuli to which they have to make a simple choice response and then occasionally with an alternative *No-Go* stimulus to which they have to withhold their response. The task is well suited for testing the SRD model as it allows the estimation of variables in a range of performance domains: mean reaction time (MRT), errors of commission (EOC), errors of omission (EOO) and response time variability (measured by standard deviation of reaction time-SDRT). While the SRD model predicts general energetic, rather than cognitive process-

specific effects, it makes some specific predictions with regard to different GNG performance parameters: Compared to controls, ADHD children are predicted to experience over-activation in the fast ERs and under-activated in the slow ERs (Sergeant, 2005; van der Meere, 2002). This over-activation will produce more impulsive EOC during fast ERs. On the other hand, under-activation during slow ERs will produce slower and more variable MRT and a greater number of errors of omission (EOO) typical of inattentive performance. Two types of meta-analyses were performed to test these predictions. First, we estimated the differential impact of ER on ADHD vs. control performance as a function of different ERs presented within the same studies. We then attempted to replicate these within-study effects by using meta-regression techniques to test the extent to which ER levels in different studies explained the between study heterogeneity of ADHD vs. control performance differences.

METHOD

Search strategy

We searched Medline databases for studies published between January 2000 and December 2011. For this purpose, we used combinations of the term ADHD with the following keywords (using AND): reaction time, accuracy, continuous performance test, Go/No-Go, inhibition, event rate and inter-stimulus interval. Records were then screened for initial eligibility on the basis of titles and abstracts. Potential records were then screened on the basis of full-text articles. At this stage we removed studies where GNG paradigms had less than 50% Go trials. There was no age restriction and studies conducted with adolescent or adult participants were also included. Studies which used a highly variable range of ISI (variability >1sec) and did not report the results for each ISI were excluded. Self-paced and cued tasks were also excluded. In order to maximize homogeneity, tasks with additional stimuli (e.g., cue or feedback) were excluded from analysis as these would provide extra stimulation for subjects and the "real" ISI is therefore difficult to determine.

Coding, calculation and synthesis of the effect sizes

We undertook two analyses. Both analyses employed comprehensive Meta-Analysis software (version 2.2.057, Biostat Inc., NJ, USA). In both analyses the outcome variables were the MRT, EOC and SDRT. Too few studies (N=5) reported inattentive errors of omission in the slow ER and so this outcome, which would provide a more direct assessment of inattentive errors, was not included in the analysis. When summary statistics were not reported, effect size (ES) was extracted from test statistics (e.g., t values, means and p values) using the appropriate formula. The other extracted variables were mean age of each group, ISI used, the percentage of males in the ADHD and the control group, percentage of Go and No-Go trials in the task, number of trials, co-morbidity and the medication status. ER (i.e., inter-stimulus interval) was defined as the time interval between the onsets of two consecutive stimuli.

The first analysis was restricted to those studies where ER was manipulated as a within-subject variable (i.e., had trials with two or more ER levels). We used these data to estimate the differential effect of ER on ADHD vs. control performance for the variables MRT, EOC and SDRT. The method proposed by Borenstein et al. (2009) was employed to compare different outcomes or time-points within a study. First, the standard mean difference (SMD) between the groups at each ES is calculated using the recommended formula - *mean of the ADHD group minus the mean of the control group divided by the pooled standard deviation*. Second, the ES for differential effect of ER on ADHD vs. control performance is calculated by subtracting the SMD of the group difference at SMD^{fast} from that at SMD^{slow} and then variance of this synthetic ES was calculated using the formula $V=V1+V2-2r\sqrt{V1}\sqrt{V2}$, where V is the variance of the synthetic ES, V1 and V2 are the variance for the effect sizes for the two outcomes and r is the correlation between the outcomes. This is equivalent to calculating the ES for the group x event rate interaction and so we will refer to it as $ES^{group \times event\ rate}$. The ES^{fast}, ES^{slow} and $ES^{group \times event\ rate}$ calculated for each study were then combined using a random effects model to give overall ES estimates. One difficulty with this method is that it requires that the within-subject correlations between performance under the different conditions are known and these are often not reported. To deal with this issue we ran a sensitivity analysis based on the correlation in other studies to estimate a range of effect sizes and p values.

The second analysis adopted a different approach in order to utilize all GNG studies meeting our entry criteria even where only one ER was employed. First, we calculated the SMD for ADHD vs. control effects for each outcome in each individual study using the same formula as in the first analysis. The SMDs were then combined across studies using the random effects method. The Q and I^2 statistics were calculated as an estimate of between-study heterogeneity in SMD. We then performed a meta-regression to examine the independent effect of ER (as well as a number of other factors such as the difference between the percentage of the males within groups and age of the ADHD group) in predicting between study variation in ADHD vs. control SMDs on our three dependent variables. For the regression analysis, a random effects regression model was used assuming a heterogeneous distribution of effect sizes for the studies sharing the same predicted value. One difficulty with such a regression analysis is that more studies have used a fast or a moderate ER than a slow one. Thus there are fewer studies in the slow ER range which reduces our power to accurately estimate the effects of ER on performance. In order to address this point we maximized the number of studies with a slow ER by choosing data for the slowest ER condition when studies had more than one ER condition. We also conducted sensitivity analyses to explore whether the observed effects were dependent on the small numbers of studies with unusual age and gender composition. The first was related to age – and involved excluding all studies with a mean age above 11 (N=8). The rationale for choosing the age of 11 was to exclude studies conducted with adolescent populations and to explore whether the regression results were driven by effects in these samples of older participants. The second related to gender composition of samples; we excluded studies (N=7) with high difference for male percentage (>20) between clinical and control groups. In other sensitivity analyses we excluded studies (N=2) with a small number of trials (<50) and with fewer than 60% Go trials (N=3) to explore whether the regression results depended on confounding effects of studies with fewer number trials or lower percentage of Go trials.

RESULTS

Figure 1 gives the PRISMA flow chart for the identification of studies according to our inclusion criteria. The number of studies excluded for each exclusion criterion are also summarized in the figure. A total of 30 studies met the entry criteria. Of those, 19 studies had just one ER level and 11 studies manipulated ER as a within-subject variable. In each case ER was manipulated by block – with different ERs presented in *separate test blocks* (see Table 1 and 2 for study details and summary statistics).
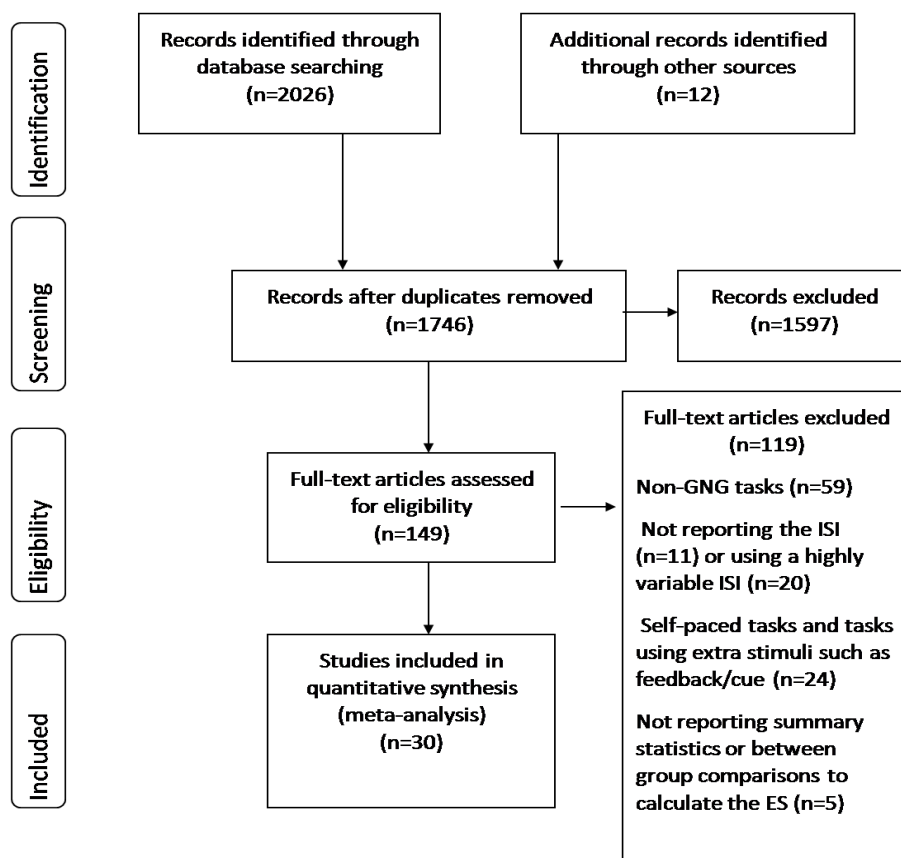

Figure 1. Prisma diagram for the flow of information through different phases of the review.

Table 1. Characteristics of the included studies

Study	ISI (sec)	Age[a]	%Male[b] ADHD	%Male Cont.	No. Trial[c]	%Go[d]	Diagnosis[e]	IQ[f]	MS[g]
Berlin et al. 2000	5.5	8.3	100	100	100	75	C/HI(ODD+ TS)	>70	off
Bistakou et al. 2008	1.5	14.8	81	58	100	75	C(ODD)	>70	>48
Bistakou et al. 2008	1.5	10.5[h]	83	76	100	75	C(ODD)	>70	>48
Borger & van der Meere 2000	2.3 6.3	10.1	100	100	300 100	80	-	-	off
Desman et al. 2008	3	10.3	100	100	40	50	C (CD)	>80	>24
Epstein et al. 2011	1.5 5.5	8.1	72	66	120 120	90	C/A (ODD+CD)	>80	off
Groom et al. 2008	2.25	15.6	93	42	304	80	C	>70	>24
Hervey et al. 2006	1.25 4.25	10.7	77	77	120 120	90	C/A/HI (ODD+CD)	-	off
Johnson et al. 2007	1.4	11.4	84	72	225	88	C/A/HI (ODD+CD)	>70	>24
Kerns et al. 2001	1	9.4	76	76	150	50	C	>70	>24
Klein et al. 2006	2.5	10.5	86	82	300	85	C/A/HI(CD)	-	>12
Koschack et al. 2003	2	11	91	60	50	50	C(CD)	>80	>24
Kooistra et al. 2009	1.5 7	9.3	66	51	210 60	75	C/A	-	>24
Kuntsi et al. 2009	1.3 8.3	8.8	91	48	462 72	80	-	>70	off
McNally et al. 2010	1.8	10.5	59	59	217	75	C/A/HI (ODD)	>85	>24
O'Brein et al. 2010	1.8	10.2	53	53	~267	75	C/A/HI (ODD)	>80	>24

Study									
Raymaekers et al. 2007	2 8	9.6	62	71	300 75	75	C/IA (ODD+CD)	>85	>20
Rovet & Hepworth 2001	1.2 4.2	9.8	70	47	40 40	90	-	>75	>24
Rubia et al. 2007	1.6	11.1	93	88	190	74	C	>75	>24
Ryan et al. 2010	1.5	10.9	80	50	216	75	C/A/HI (ODD)	>70	>24
Uebel et al. 2010	1.3 8.3	11.3	91	72	462 72	80	C	-	>48
van der Meere et al. 2009	2.15 6.15	8	59	47	300 100	80	C/HI	-	>36
Van de Voorde et al. 2010a	2.3	10.6	83	58	600	80	C/A/HI (ODD)	>80	>24
Van de Voorde et al. 2010b	1.9	10.2	61	62	600	60	C/A (ODD)	>80	>24
Vaurio et al. 2009	2.6	10.9	60	48	217	75	C/A/HI (ODD)	>80	>24
Wada et al. 2000	2	9	100	100	~169	77.5	C/A/HI	>90	off
Wiersema et al. 2009	1.3	29.3	56	57	~508	75	-	>80	>48
Wiersema et al. 2006a	2.3 8.3	10.3	64	67	287 80	75	C(CD+ODD)	-	>24
Wiersema et al. 2006b	2.3 8.3	32.1	100	100	287 80	75	-	>80	>48
Wodka et al. 2007	1.8	11.6	62	52	217	75	C/A/HI (ODD)	>85	>18
Yang et al. 2011	1.5	8.4	90	89	200	80	CD+ODD	>75	off

^a Mean age of the ADHD group.

^b % of males in the ADHD group.

^c Number of trials for each event rate condition. When the total trial number was not
given, an approximate value was calculated from the task duration and event rate.

^d % of Go trials requiring a motor response.

^e Diagnosis according to DSM criteria (C, Combined; A, Inattentive; HI, Hyperactive-
Impulsive; CD, Conduct Disorder; ODD, Oppositional Defiant Disorder; TS, Tourette
syndrome).

^f Lower cutoff for IQ.

^g Medicational status (hours refrained from drug; off, no medication).

^h The study included two independent subgroups based on age.

Estimating the differential effect of ER using within-subject study data

Eleven studies provided data for the calculation of both SMD^{slow} and SMD^{fast} for
MRT and EOC. Ten studies reported sufficient data for an analysis of SDRT. Based on the
four studies from which we obtained the correlation coefficient (see Table 3), we
imputed correlations ranging from 0.6-0.8, 0.4-0.7 and 0.6-0.8 for MRT, EOC and SDRT
analyses respectively for the seven studies with unreported correlation. The mean fast
ER was 1.8 sec (1.25-2.3 sec) and the mean slow ER was 6.9 sec (4.25-8.3 sec). For *MRT*,
groups differed significantly at both slow and fast ER (SMD^{slow}=0.56; CIs 0.36 to 0.76;
SMD^{fast} = 0.33; CIs 0.13 to 0.53). The forest plots for both analyses are given in Figure 2.
$ES^{group \times event\ rate}$ was significant (ES between 0.22 and 0.26, p value between 0.004 and
0.003) with bigger SMDs between ADHD and control participants on slower ERs
demonstrating a disproportionate slowing of RT in the ADHD group on those trials. For
EOC, again the groups differed significantly at both slow and fast ERs (SMD^{slow}=0.37; CIs
0.18 to 0.57; SMD^{fast} = 0.57; CIs 0.37 to 0.76) (See Figure 3 for forest plots). $ES^{group \times event}$
^{rate} was significant (ES btw -0.17 and -0.18, p value btw 0.006 and 0.001) with bigger
SMDs between ADHD and control participants on fast ER trials. For *SDRT,* the groups
differed significantly at both slow and fast ER (SMD^{slow}=0.75; CIs 0.48 to 1.03;
SMD^{fast}=0.85; CIs 0.63 to 1.08) (See Figure 4 for forest plots). $ES^{group \times event\ rate}$ was not
significant (p value btw 0.03 and 0.11).

Table 2. Summary statistics[a] of the included studies

Study	n	MRT	EOC	SDRT
Berlin et al. 2000	21 ADHD		13.71(5.76)	
	42 NC		11.04 (5.22)	
Bistakou et al. 2008	54 ADHD	378 (108)	43.73 (20)	197 (169)
	29 NC	359 (64)	28.2 (19)	118 (118)
	23 ADHD	324 (123)	36.55(20)	150 (174)
	21 NC	314 (75)	33.54|(17)	58 (19)
Borger & van der Meere 2000 (fast)	27 ADHD	504 (109)	37.81(18.95)	174.70 (55.78)
	22 NC	428 (91)	39.77(19.1)	149.41 (36.77)
Borger & van der Meere 2000 (slow)	27 ADHD	652 (118)	31.63 (22.81)	243.52 (124.1)
	22 NC	526 (118)	38.95 (23.06)	
				166.59 (74.18)
Desman et al. 2008	19 ADHD	466.54(70.28)	3.11 (2.21)	96.39 (36.2)
	19 NC	495.37 (122.63)	2.21 (2.1)	97 (44.75)
Epstein et al. 2011 (fast)	104 ADHD	463 (101)	10.9 (7.1)	205.6 (82.7)
	47 NC	416 (105)	5.96 (7.07)	151.8 (82.4)
Epstein et al. 2011 (slow)	104 ADHD	801 (357)	11.23 (8.6)	452 (264)
	47 NC	649 (393)	5.6 (8.9)	298 (267)
Groom et al. 2008	27 ADHD	312.61(16.48)		
	36 NC	313.3 (20.64)		
Hervey et al. 2006 (fast)	65 ADHD	381 (58)	66.54 (18.78)	155 (36)
	65 NC	365 (50)	60.9 (22.63)	126 (36)
Hervey et al. 2006 (slow)	65 ADHD	530 (123)	67.05 (22.02)	340 (196)
	65 NC	466 (94)	64.23 (23.12)	211 (166)
Johnson et al. 2007	63 ADHD	456 (89)	3.75 (2.5)	
	29 NC	467 (114)	2.3 (1.6)	
Kerns et al. 2001	21 ADHD		t^{b}=1.52	
	21 NC			
Klein et al. 2006	57 ADHD	427.2 (80.9)	19.5 (7.7)	174 (74.4)
	53 HC	389.4 (53.9)	17.5 (7.4)	115 (43.2)
Koschack et al. 2003	35 ADHD	467 (94)	6.2 (5.2)	
	35 NC	492 (91)	5.2 (5.0)	
Kooistra et al. 2009 (fast)	47 ADHD	446.13 (51.7)	24.26 (7.44)	129.91 (19.35)
	39 NC	434.83 (54.03)	23.32 (8.49)	115.17 (17.88)

Kooistra et al. 2009 (slow)	47 ADHD	514.35 (68.6)	5.65 (2.71)	132.43 (31.61)
	39 NC	686.1 (74.98)	5.18 (3.1)	118.74 (23.65)
Kuntsi et al. 2009 (fast)	58 ADHD	434.44 (71.95)	61.8 (14.48)	202.33 (69.04)
	1098 NC	420.86 (62.52)	50.86 (16.36)	159.64 (56.89)
Kuntsi et al. 2009 (slow)	58 ADHD	616.13 (179.49)	64.36 (20.8)	311.04 (232.44)
	1098 NC	584.38 (129.02)	54.52 (23.12)	219.26 (143.83)
McNally et al. 2010	56 ADHD		39.4[d]	0.39[c,d]
	45 NC		33	0.32
O'Brein et al. 2010	56 ADHD		43(19)	0.37 (0.17)[c]
	90 NC		35 (19)	0.31 (0.15)
Raymaekers et al. 2007 (fast)	24 ADHD	565.18 (106.12)	15.66 (9.3)	198.78 (53.72)
	28 NC	518.89 (82.87)	9.17 (7.8)	144.81 (48.1)
Raymaekers et al. 2007 (slow)	24 ADHD	755.76 (211.49)	2.95 (2.44)	262.79 (292.5)
	28 NC	665.72 (108.16)	2.0 (2.58)	158.24 (89.25)
Rovet & Hepworth 2001 (fast)	41 ADHD	358.0 (81.3)	61.3 (24.7)	
	68 NC	363 (67.1)	49.5 (25)	
Rovet & Hepworth 2001 (slow)	41 ADHD	514.7 (131.3)	67.0 (21.2)	
	68 NC	457.3 (96.2)	58.2 (28.9)	
Rubia et al. 2007	32 ADHD		28 (14)	
	34 NC		19 (15)	
Ryan et al. 2010	25 ADHD	464.15 (177.52)	29 (22)	0.35 (0.13)[c]
	14 NC	463.98 (132.9)	24 (19)	0.23 (0.07)
Uebel et al. 2010 (fast)	205 ADHD	430 (114.48)	50.3 (24.72)	183 (114.54)
	53 NC	387 (72.8)	34.8 (18.92)	110 (72.8)
Uebel et al. 2010 (slow)	205 ADHD	651 (286.35)	49.6 (34.61)	292 (272.03)
	53 NC	569 (182)	31.3 (26.21)	162 (174.72)
van der Meere et al. 2009 (fast)	26 ADHD	614.62 (98.48)	60.05 (18.6)	331.46 (80.01)
	60 NC	511.75 (83.92)	38.05 (16.15)	188.22 (63.78)
van der Meere et al. 2009 (slow)	26 ADHD	965.85 (332.5)	58.45 (22.07)	819.88 (433.68)
	60 NC	644.62 (137.64)	32.25 (22.15)	224.08 (102.16)
Van de Voorde et al. 2010a	40 ADHD	497.32 (91.99)	38.77 (18.2)	174.12 (50.5)
	19 NC	518.7 (98.9)	17.9 (10.9)	151.3 (51.2)

Van de Voorde et al. 2010b	31 ADHD	517.6 (81.2)	35.13 (12.76)	179 (33.2)
	16 NC	512.2 (72.2)	23.4 (9.1)	156.8 (33.7)
Vaurio et al. 2009	57 ADHD	401.55 (85.02)	38 (20)	0.35 (0.13)[c]
	83 NC	395.62 (109.47)	29 (19)	0.28 (0.12)[c]
Wada et al. 2000	17 ADHD	523.76 (181.91)	33.41 (19.11)	221.41 (103.29)
	19 NC	416.47 (79.92)	16.56 (9.85)	109.31 (49.11)
Wiersema et al. 2009	23 ADHD	419 (45)	13 (6)	96.5 (19.8)
	19 NC	406 (41)	11 (6.3)	88.2 (24)
Wiersema et al. 2006a (fast)	22 ADHD	535 (97)	37 (21)	193 (45)
	15 NC	570 (88)	21 (15)	150 (39)
Wiersema et al. 2006a (slow)	22 ADHD	645 (116)	20 (14)	227 (81)
	15 NC	607 (118)	20 (19)	168 (86)
Wiersema et al. 2006b (fast)	19 ADHD	432 (45)	10.9 (7.1)	110 (39)
	19 NC	435(52)	6.8 (5.7)	91 (17)
Wiersema et al. 2006b (slow)	19 ADHD	510 (67)	7.4 (5.7)	121 (33)
	19 NC	467 (65)	5.4 (6.3)	102 (31)
Wodka et al. 2007	58 ADHD	392.2 (63.9)	36.3 (20.3)	0.33 (0.14)[c]
	84 NC	405.1 (109.6)	27.9 (18.4)	0.28 (0.13)[c]
Yang et al. 2011	100 ADHD	451.86 (136.72)	13.49(5.56)	
	100 NC	448.38 (127.45)	12.08 (5.18)	

MRT, mean reaction time (msec); EOC, percent errors of commissions; SDRT, standard deviation of reaction time; ADHD, attention-deficit/hyperactivity disorder; NC, normal control.

[a] Mean and (SD).

[b] t test statistic.

[c] Coefficient of variability.

[d] Effect size is calculated from mean and p value.

Table 3. Correlations between event rates.

Study	MRT	EOC	SDRT
Borger & van der Meere, 2000	0.76	0.59	0.77
Kooistra et al., 2010	0.81	0.48	0.64
Raymaekers et al., 2007	0.70	0.6	0.65
van der Meere et al., 2009	0.69	0.72	0.75

MRT, mean reaction time (msec); EOC, percent errors of commissions;

SDRT, standard deviation of reaction time.

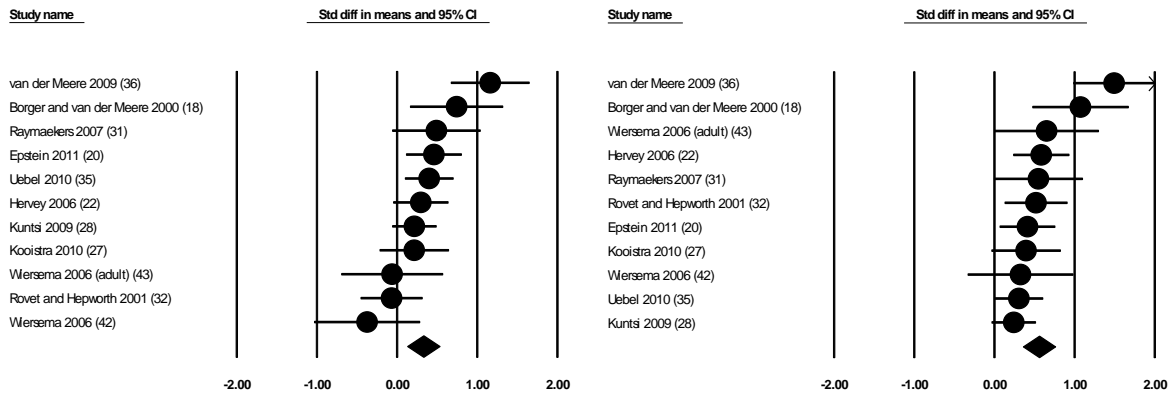**Figure 2.** Forest plots of effect sizes for mean reaction time at fast (left) and slow event rate (right) conditions of the within-subject studies
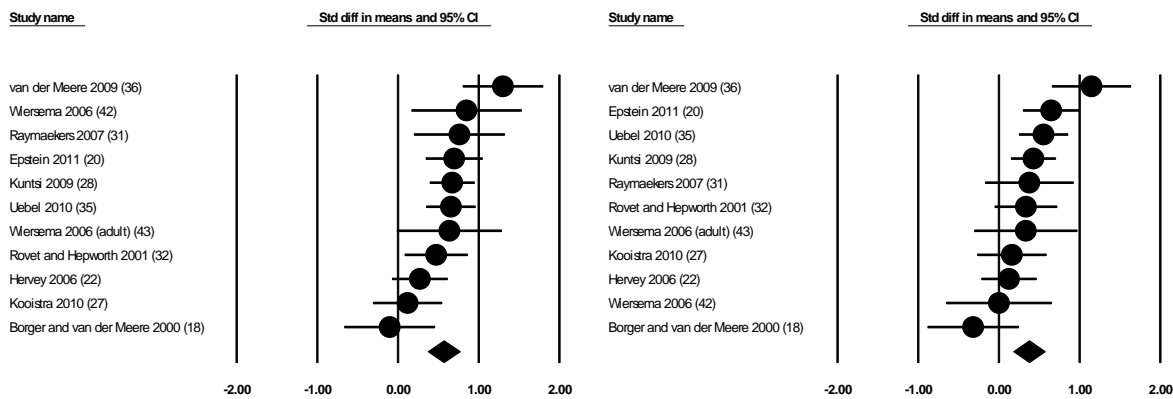

Figure 3. Forest plots of effect sizes for commission errors at fast (left) and slow event rate (right) conditions of the within-subject studies.
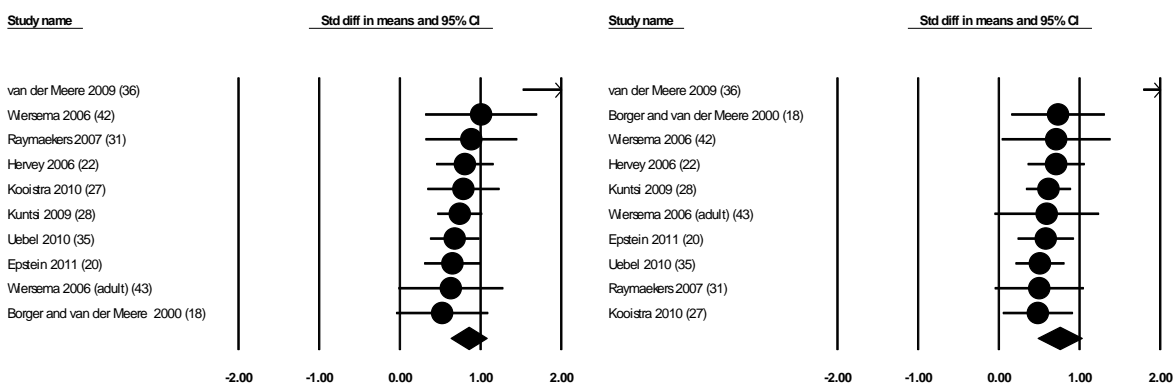

Figure 4. Forest plots of effect sizes for reaction time variability at fast (left) and slow event rate (right) conditions of the within-subject studies.

Estimating the differential effect of ER using between study data

Twenty-five *studies* contributed to the MRT, 29 to the EOC and 22 to the SDRT analysis. One study contributed two independent data sets to each analysis: one comparing a pediatric ADHD group and the other an adolescent group along with separate age matched control groups (Bitsakou, Psychogiou, Thompson, & Sonuga-Barke, 2008). There was a significant between group effect overall - slower MRT was seen for ADHD samples (SMD= 0.28 (95% CIs 0.14 to 0.43). There was significant between-study heterogeneity (Q(25)=67.15, p<0.001, I^2=62.77). Variation in SMD between studies was significantly predicted by ER (z=2.88, p=0.004) and age (ES decreasing with increasing age, z=-2.43, p=0.02). However heterogeneity was still significant after including ER and age in the model (Q(24)=52.91, p=0.001; Q(20)=56.93, p<0.001 respectively). Figure 5 plots the MRT SMD as a function of ER. There was a significant overall group difference for EOC (SMD= 0.44, 95% CIs 0.34 to 0.54). There was also significant heterogeneity (Q(29)=46.07, p=0.02, I^2=37.05). ER and age did not account for a significant proportion of the between-group SMD variance between studies (z=-0.65 p=0.51, z=-0.61, p=0.54 respectively). For SDRT, the group effect (SMD=0.66; 95% CIs 0.51 to 0.81) was highly significant. The between-study ES heterogeneity was also significant (Q(22)=54.07, p<0.001, I^2=59.32). ER was not a predictor of between-group SMDs (z=0.4, p=0.69) However there was an inverse relationship between age and SMDs (z=-2.29, p=0.02).
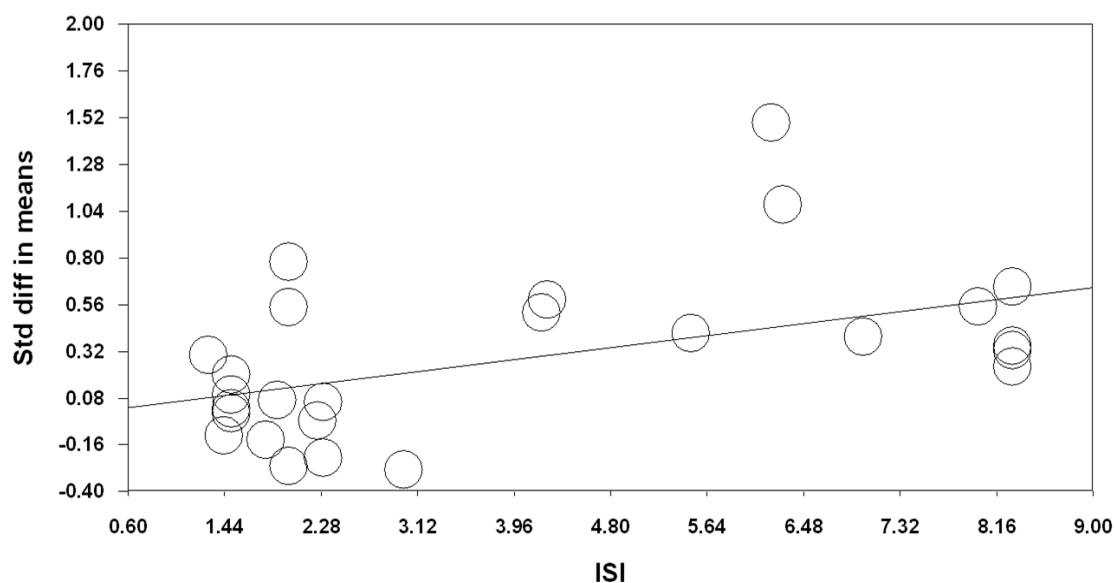
Figure 5. Scatter plot for regression of ISI (inter-stimulus interval) on effect size for mean reaction time.

Sensitivity analyses

For MRT, restricting analyses to studies with participants under the age of 11 years and to studies with a small difference in gender composition had no effect on the results (z=2.14, p=0.03; z=2.5, p=0.01 respectively). For EOC the same restrictions did not change the results either (for age restriction z=-0.92 p=0.35; for gender restriction z=-0.4, p=0.68). The sensitivity analyses for number of trials and % of Go trials were also not significant for none of the variables

DISCUSSION

Consistent with the predictions of the SRD model, GNG performance in ADHD was differentially affected by ER. First, both analyses found an impact of ER on the SMD between ADHD and control participants for MRT in the predicted direction: There was a disproportionate slowing of ADHD responding with reducing ERs. From an SRD perspective this effect is regarded as being due to under-activation in people with ADHD brought about by a failure to adjust their activation level according to the demands of long and boring tasks (Sergeant, 2005; van der Meere, 2002). The second prediction – of a disproportionate increase in EOCs under fast ER condition in ADHD relative to controls

– was also supported by the within-subject analysis. However, this effect was weaker than for the MRT and the slope, although in the right direction, was not significant in the between-study meta-regression. This might be explained by the greater power in within-subject analysis due to taking into account the correlation between measurements. From the SRD perspective this increase in impulsive errors is due to the failure to moderate an over-activated state induced by the fast ERs (Sergeant, 2000; Sergeant, 2005; van der Meere, 2002). Slower responding in slow ERs and more errors in the fast ERs is also consistent with a possible role altered response strategy in ADHD. A complete speed-accuracy trade-off (SATO) analysis requires access to trial-by-trial data which was not available in our case but future studies could examine contribution of these factors to the state regulation deficits. However, a provisional analysis of SATO based on averaged data for each study found no relationship between error rates and MRT.

Despite these positive findings implicating the effect of ER in ADHD performance, it is also clear that ER is not the sole determinant of ADHD-related deficits on GNG tasks. Both analyses found strong effects of group not accounted for only by ER: ADHD children had longer MRTs and made more EOCs on both high and low ER trials. This conclusion is supported by the meta-regression analysis of between-subject design studies where ER accounted for only a proportion of the between-study heterogeneity. Across all variables, a substantial proportion of the ADHD group differences were not due to ER manipulations. Thus the current results are in line with previous research which found that although motivational and energetic factors, such as reward, can have substantial effect on ADHD performance, they rarely fully alleviate deficits – this could be due either to a common partial response or alternatively normalization in only a sub-group of individuals with ADHD (Epstein et al., 2011, Kuntsi, Wood, van der Meere, & Asherson, 2009). If this latter case were true it would provide further evidence of neuropsychological heterogeneity in ADHD.

The negative result for SDRT is also worthy of further discussion given that response variability has been suggested to be a particularly important marker of state regulation problems in ADHD in the past (Leth-Steensen, Elbaz, & Douglas, 2000). There are at least two possible explanations for the lack of an ADHD-specific effect of ER on this outcome. First, SDRT may not be a sufficiently sensitive measure of the energetic processes. For instance, increased variability in ADHD could be related to a number of different putative cognitive processes (Epstein et al., 2011) such as motor timing (Rubia,

2001), top-down executive control (Bellgrove, Hester, & Garavan, 2004), impaired suppression of default mode network (Sonuga-Barke & Castellanos, 2007) and attentional lapses (Leth-Steensen et al., 2000). Second, it has been suggested that response variability represents a non-specific finding which is seen in multiple types of disorders (Kuntsi et al., 2009). In this view SDRT, although associated with ADHD, may not be related to ADHD-specific processes but be a more general marker of psychopathology (Geurts et al., 2008). However, this objection may also hold for MRT and EOCs. Thus, exploring the specificity of these outcomes for ER effects and finding more specific measures of state regulation deficits could be the aim of future studies.

Can other models explain the ER effects in the data? The Delay aversion model (DAv) (Sonuga-Barke et al., 2010, Sonuga-Barke et al., 1992) also makes predictions with regard to ER effects. In this model ADHD behavior is motivated by the escape or avoidance of delay. When there are options with different delay outcomes, individuals with ADHD will choose the least delayed option all else being equal – producing impulsive choice (Marco et al., 2009). When no choice exists and delay is to some extent imposed (as is the case in the GNG paradigms included in the current meta-analysis), then individuals with ADHD are predicted to engage in patterns of off-task inattentive behaviors that have been shown to reduce the subjective experience of delay. The performance corollary of such behavior are higher errors of omission and long and variable RTs when the length of delay between stimuli increases. From a different point of view, one might argue that slower RT and higher variability in ADHD on slow ER trials are due to attentional lapses (Leth-Steensen et al., 2000) linked to increased interference from the so-called default mode brain network (Sonuga-Barke & Castellanos, 2007). The finding of longer RTs on slow ER trials is consistent with both of these models. However, neither DAv nor default mode network model make specific predictions about EOC and certainly would not predict a disproportionate increase of EOC on fast ER trials as found in the current study. Thus, these models do not offer a parsimonious explanations of ER effects seen in this study. At the same time ADHD is not a neuropsychologically homogeneous condition. Therefore it is quite possible that the association between ER and performance is multi-factorially determined with different patterns of deficits linked to SRD, DAv and the default mode interference, leading to problems attending on slow ER trials. The large SMD between ADHD and controls for the MRT effects compared to the EOC effects would be consistent with this.

While interpreting these results one needs to take into account of a number of limitations of the current analysis. First, the aim was to identify the effect of ER on performance and a number of studies have been excluded as they did not report ER explicitly or used a highly variable presentation rate. Therefore the summary effect sizes calculated do not represent all the studies published and should be evaluated carefully. Second, while between study variance can be explained partially by ER and age other factors such as task setup, instructions, severity of ADHD symptoms, diagnostic criteria and scales are likely to be important. The analysis of such factors is not within the scope of this study given the limited information available in specific papers relating to these factors. Although we could not analyze the specific factors that may cause this heterogeneity we took account of it by using a random effects model which assumes that the true effect size varies from study to study.

There is potentially a number of clinical implications of the results. First, they may help us design more appropriate ways of delivering information in the classroom: the slower the information is presented, the more sluggish the ADHD children may become. On the other hand, a fast teaching style and presentation of abundant stimuli may induce an over-activated impulsive response style. Therefore the content of the lecture and the environment could be adapted to tailor the stimulation level to an optimal level. This may require increased use of information and communication technology to promote active and personalized learning. Second, it may be possible to train individuals with ADHD to cope with a broader range of ER settings through methods like neurofeedback and cognitive training that can improve management of their energetic resources. Third, they can highlight the potential of targeting brain systems related to energetic factors – for instance noradrenaline pathways originating in the locus ceruleus (LC) is likely to be the main neurochemical system involved in regulating the arousal state (Ashton-Jones, Rajkowski, & Cohen, 1999). The interplay between the LC and cerebral cortex mediates adaptation to the changing environmental conditions such as changing ER. A methodological implication of our findings relates to choosing the optimal GNG task design for the future studies. Given the apparent context dependent nature of task performance in ADHD – studies of cognitive test performance in ADHD should, as a matter of course, include a range of ERs that cover the full range of the values explored here. We would recommend at least a fast condition (ISI $\leq$ 2 sec) to

capture errors of commission and a slow condition (ISI $\geq 6 \, sec$) to induce low and variable inattentive responses.

In summary, the SRD model provides the most parsimonious explanation of the differential ER effects on the GNG performance of ADHD and control participants – more EOC on fast ER trials and longer RTs on slow ER trials. However, the finding that group differences exist over and above those related to ER and the possibility that other deficits could account for these differences highlight the neuropsychological heterogeneity in ADHD. Therefore, future studies should aim to develop theories of ADHD which could better explain this sort of neuropsychological heterogeneity by modeling the presence of different deficits in different individuals in the ADHD population (Fair, Bathula, Nikolas, & Nigg, 2012).

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EVENT RATE EFFECTS ON VARIABILITY IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER

ABSTACT

Background: There are a number of competing models of increased reaction time variability (RTvar) in Attention-Deficit/Hyperactivity Disorder (ADHD). Event rate (ER) manipulation during task performance provides a way to test between these accounts. For instance, the State Regulation Deficit model predicts an "inverted U" ER-RTvar relationship with higher RTvar on both fast and slow ER trials; while the Delay Aversion model predicts a linear ER-RTvar relationship with higher RTvar on slow ER trials only. In this study we tested these predictions by employing an ex-Gaussian decomposition of RTvar into *sigma* (Gaussian variability) and *tau* (variability due to slow responses). **Method**: Twenty-nine controls and 25 children with ADHD (age range: 8-12 years) completed a simple computer-based Go/No-Go task under four different ER conditions (1, 2, 4 and 8 sec). **Results**: For *sigma* children with ADHD showed an accentuated "inverted U" pattern of ER-RTvar with significant group differences only at the slowest and fastest ERs. *Tau* was significantly greater for ADHD, but this effect was unaffected by ER. **Conclusions**: Our results provide compelling evidence for state regulation deficits in ADHD by showing that children with ADHD have an increased *sigma* on fast and slow ERs. These results were not predicted by the Delay Aversion model. In contrast, *tau* was not affected by ER suggesting that this parameter may not be sensitive to state regulation problems.

INTRODUCTION

Attention-Deficit/Hyperactivity Disorder (ADHD) is a prevalent childhood disorder which often persists into adulthood. It is characterized by symptoms of inattention and/or hyperactivity-impulsivity which lead to substantial social and academic impairment (DSM-IV-TR, American Psychiatric Association, 2000). ADHD is associated with deficits on tasks tapping a wide range of specific cognitive processes such as response inhibition, planning, vigilance and working memory (see Nigg, 2005; Rubia, 2011; Sonuga-Barke, Sergeant, Nigg, & Willcutt, 2008; Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005 for reviews). At the same time ADHD also seem to be affected by increased levels of intra-individual variability independent of tasks. Studies have consistently reported that reaction time variability (RTvar) is elevated for individuals with ADHD although the neuropsychological basis of this finding is not understood (see Tamm et al., 2012 for a review).

There are a number of competing neuropsychological models of RTvar in ADHD. The Cognitive Energetic model extends the basic information processing framework by integrating energetic concepts such as effort, arousal and activation. This model assumes that task performance is influenced not only by cognitive capacities but also by environmentally-determined levels of arousal/activation and the extent to which variations in these factors can be managed to ensure optimal performance. According to this model RTvar is an important indicator of arousal/activation as it reflects between-trial variation in energetic resources (Sanders, 1983). Building on this, the State Regulation Deficit model suggests that children with ADHD have difficulty in properly regulating their energetic state (arousal/activation) when challenged to do so in sub-optimal settings. This failure leads to abnormally high RTvar. Crucially, the energetic state can be manipulated by changing the rate at which information is presented during tasks leading to sub-optimal states under both fast and slow event rate (ER) conditions (Sergeant, 2005; van der Meere, Börger, & Wiersema, 2010). More specifically, the State Regulation Deficit model predicts that performance of individuals with ADHD would deteriorate at ER extremes (very fast or very slow ERs): Fast ERs lead to over-

arousal/activation which is predicted to result in ADHD-related fast/impulsive errors; while slow ERs lead to under-arousal/activation and produce slow responding marked by RT slowing. Within this account RTvar is implicated in two ways. First, sub-optimal performance under both fast and slow ERs is expected to manifest as greater Gaussian variability reflecting the variable response style at ER extremes. The ER-RTvar relationship for this type of variability is predicted to follow an accentuated "inverted U" function in ADHD. Second, it has been shown that ADHD is associated with increased attentional lapses leading to greater variability due to occasional slow responses (Leth-Steensen, Elbaz, & Douglas, 2000). According to the State Regulation Deficit model these slow responses are expected to increase at slow ERs where more effort for attentional control is needed.

The Delay Aversion hypothesis provides an alternative model of ER effects on ADHD performance (Sonuga-Barke, Wiersema, van der Meere, & Roeyers, 2010). According to this model, individuals with ADHD are motivated to escape or avoid delay. In choice situations this is achieved through impulsive choices (Marco et al, 2009; Sonuga-Barke, Taylor, Sembi, & Smith, 1992). In non-choice settings, where delay cannot be actually reduced, delay aversion is expressed as attempts to modify the perception of the passage of time during the delay so its aversive properties lessen (Sonuga-Barke et al., 2010). The Delay Aversion model postulates that under these conditions individuals with ADHD will act on their environment to either access (through attentional strategies often leading to off-task or "inattentive" behavior) or create (through activity) additional environmental stimulation to alter time perception and that the tendency to do this will increase with the length of the delay to be tolerated. This leads to the prediction that levels of attention and performance should deteriorate linearly as a function of the length of the delay experienced – and while this would be the case for all individuals, the rate of performance decrement would be greater in individuals with ADHD than in controls. Therefore, in contrast to the State Regulation Deficit model the Delay Aversion model predicts a heightened linear ER-RTvar relationship in ADHD with increased RTvar under slow ER conditions – effects that should be related to both Gaussian variability and variability due to occasional slow responses.

To date, several studies have found increased sensitivity to ER changes in the performance of individuals with ADHD on different tasks, such as Go/No-Go (GNG) (van de Meere, Stemerdink, & Gunning, 1995), stop signal (Scheres, Oosterlaan, & Sergeant,

2001), vigilance (Chee, Logan, Schachar, Lindsay, & Wachsmuth, 1989) and associative learning (Conte, Kinsbourne, Swanson, Zirk, & Samuels, 1986) tasks. However, these studies have often not been equipped to test between the different neuropsychological accounts because (i) they do not have a sufficient number of ER levels to give power to model the "inverted U" function predicted by the State Regulation Deficit model and/or (ii) they have used non-specific variability measures such as standard deviation of reaction time (SDRT) and so cannot distinguish effects of Gaussian variability due to slow responses (Castellanos et al, 2005; Metin, Roeyers, Wiersema, van der Meere, & Sonuga-Barke, 2012, Tamm et al., 2012). A recent meta-analysis of GNG studies comparing slow and fast ERs confirmed, that consistent with the State Regulation Deficit model, individuals with ADHD made more impulsive errors on tasks with fast ERs and produced longer RTs on tasks with slow ERs (Metin et al., 2012). However, this meta-analysis did not show any significant effect of ER on SDRT although no attempt was made to model Gaussian variability and variability due to slow responses separately. Due to the non-specific nature of SDRT, it has been suggested that future studies should use more specific variability measures that can disentangle different components of general variability (Tamm et al., 2012). This can be achieved by employing the ex-Gaussian model (Matzke & Wagenmaekers, 2009) which differentiates a number of RT components (*mu*, *sigma*, *tau*) which better describe the RT distribution and in particular its rightward skewed nature. The *mu* and *sigma* parameters correspond to the mean and standard deviation (SD) of the normal component of the RT distribution (with *sigma* equating to Gaussian variability) and they represent the fast component of the RT distributions. The *tau* parameter represents the exponential component of the RTvar and is an estimate of the degree of skewness or the positive tail of the RT distribution (which can be equated to occasional long RTs). Thus, mean RT depends on *mu* and *tau* and SD is decomposed into *sigma* and *tau*.

Previous research with the ex-Gaussian model has shown that individuals with ADHD differ from controls in terms of both *tau* (Buzy, Medoff, Schweitzer, 2009; Epstein et al., 2011; Hervey et al, 2006; Leth-Steensen, et al., 2000; Vaurio, Simmonds, Mostofsky, 2009) and *sigma* (Buzy, et al., 2009; Gooch, Snowling, & Hulme, 2012; Hervey et al, 2006; Vaurio et al., 2009). Two of these studies also used ER manipulations. Hervey et al. (2006) used 1, 2 and 4 sec interstimulus intervals (ISI) and reported that groups differed in all ex-Gaussian parameters (for *mu* control > ADHD and for *sigma* and *tau* ADHD > control) with

the greatest group difference in *tau*. In addition, the group difference in *tau* increased as a function of ER. There was no evidence for the predicted exacerbated "inverted U" function in ADHD with *sigma*. Epstein et al. (2011) used 1, 3 and 5 sec ISIs and found that the ADHD group had greater *tau* and that *tau* increased as ER slowed. The interaction between group and ER for *tau* was significant in only one of the several tasks used. Group differences for *mu* and *sigma* were not significant in this study. Although both *mu* and *sigma* increased as ER slowed, there was no interaction between group and ER. Together these studies provide evidence for both increased *tau* and *sigma* RTvar in ADHD although the effects of ER on different variability components are not entirely consistent and the evidence for an "inverted U" pattern is lacking. This may be because the longest ISI used in these studies was 5 sec which does not produce a very slow ER and/or only three ERs were used which may limit the power for detecting linear or quadratic interactions between group and ER.

In the current study, we analyzed RTvar under four ER level conditions covering very fast to very slow presentation rates (1, 2, 4 and 8 sec). This gave sufficient degrees of freedom to effectively model the quadratic function as predicted by the State Regulation Deficit model on RTvar. We also employed an ex-Gaussian decomposition of RT distributions to allow us to distinguish RTvar associated with occasional long RTs in slow ER conditions (*tau*) and Gaussian RTvar in slow and fast ER conditions (*sigma*). Our aim was to test the predictions of two different models. The State Regulation Deficit model predicts increased *sigma* at both fast and slow ERs while the Delay Aversion model predicts increased Gausian RTvar exclusively at slow ER conditions. For *tau* the predictions of increased RTvar on slow ER trials is the same for both models.

METHOD

The study was approved by the Ethics Committee of Ghent University, Faculty of Psychology and Educational Sciences. Written informed consent was taken from all parents and their children participating in the study.

Participants

Twenty-five children with ADHD and 29 controls between the age of 8 to 12 years were tested. The ADHD and the control groups did not differ in age and gender composition. All children were screened for ADHD, oppositional defiant disorder (ODD) and conduct disorder (CD) with the parent version of the Disruptive Behavior Disorder Scale (DBD) (Pelham, Gnagy, Greenslade, & Milch, 1992). The demographic information and the symptom scores on the DBD scale can be found in Table 1. To exclude Autism Spectrum Disorder, the Social Communication Scale (SCQ) (Rutter, Bailey, & Lord, 2003) and the Social Responsiveness Scales (SRS) (Constantino & Gruber, 2005) were administered to both clinical and control groups. However, none of the children were excluded due to clinical scores on these scales.

The children in the control group were recruited from local schools and scout camps. Children with ADHD were recruited from the community and formal diagnosis by a clinician was required. The ADHD, ODD and CD diagnoses were ascertained by a DSM-IV oriented parent interview (disruptive behavior module of the Diagnostic Interview Schedule for Children, DISC-IV) (Shaffer, Fisher, Lucas, Dulcan, & Schwab-Stone, 2000) administered by an experienced clinical psychologist. Fourteen children were classified as ADHD-combined type, 8 children as inattentive type and 3 children as hyperactive-impulsive type. Eight children received an ODD diagnosis and 3 had a CD diagnosis. All children had a total IQ (TIQ) score above 75. TIQ was assessed by the short version of the Wechsler Intelligence Scale for Children – 3rd edition (WISC-III) (Grégoire, 2005). The children in the ADHD group had lower TIQ scores than the controls but this difference did not reach statistical significance ($F(1,52) = 3.35$, $p = 0.07$). The summary statistics for TIQ can be found in Table 1.

Table 1. The characteristics of the ADHD and control group and the scores for comorbid symptoms.

	ADHD (*N* = 25)	Control (*N* = 29)
Age in months[a]	122.4 (19.1)	123.8 (17.7)
Male:Female	16:9	14:15
TIQ[a]	103.6 (13.5)	109.8 (11.2)
HI[ab]	14.78 (1.79)	10.69 (1.05)
IA[abc]	14.76 (1.81)	10.5 (1.18)
ODD[abc]	13.04 (1.95)	10.88 (1.14)
CD[abd]	12.0 (2.02)	10.77 (0.99)

Note: [a] Means and standard deviations (SD), [b] Measured by Disruptive Behavior Disorders Scale, [c] $p<0.0001$, [d] $p < 0.05$, TIQ = total Intelligence Quotient, HI=Hyperactivity/Impulsivity, IA = Inattention, ODD = Oppositional Defiant Disorder, CD = Conduct Disorder.

Experimental Task

All children completed a GNG task programmed using E-prime software (version 2). The stimuli were an upright triangle (Go stimulus) and an inverted triangle (No-Go stimulus). The stimuli were chosen based on a pilot study during which the performance of healthy controls on different tasks was compared across a range of levels of perceptual difficulty. The children were told to respond to every upright triangle and to withhold responding to every inverted triangle. Both speed and accuracy were equally emphasized in the instructions. The order of Go and No-Go stimuli was pseudo-randomized (a No-Go stimulus was always followed by a Go stimulus and maximum four Go stimuli were presented consecutively) with 72% Go and 28% No-Go stimuli. The duration of stimulus presentation was 300 msec. The task was preceded by a 2 minutes practice session. This was followed by 4 blocks of trials presented in a random order; each block had a different

inter-stimulus interval (ISI: ERs of 1, 2, 4 and 8 sec). The children were allowed to have small breaks between the sessions.

The duration of each condition was about 10 minutes in total. The 1 sec condition contained 560 stimuli, the 2 sec condition 280, the 4 sec condition 140 and the 8 sec condition 70. All responses up to 1 sec from stimulus onset were recorded for the fastest condition. For the other conditions, the cutoff for recording was 2 sec.

Procedure

All children completed the GNG task before the IQ test. The children completed the computer testing in a quiet room together with an experimenter sitting outside of their sight. The diagnostic interview of the parents of children with ADHD took place in another room with an experienced clinical psychologist. Seventeen children with ADHD were on stimulant medication. They were asked to discontinue their treatment at least 24 hours before the start of the experiment. All children received 15 euro compensation for participation in the study.

Analysis

All RT analyses were performed on data of correct Go trials. To eliminate the premature anticipated responses, we used a low cutoff of 100 msec. For ex-Gaussian modeling the RTSYS (Heathcote, 1996) program was used. When the ex-Gaussian model does not fit the RT distribution, the program reports the parameter estimates as missing values. In our sample this happened for four subjects (two children with ADHD and two controls). The ex-Gaussian parameters (*mu*, *sigma* and *tau*) were allowed to vary between ER conditions for each subject. As there were fewer responses available in the 8 sec condition and this could potentially affect the reliability of the parameter estimates (Heathcote,1996), we also performed supportive analyses with combining data across participants (Vincent averaging) to confirm the initial results. The statistical analysis was completed using SPSS (version 19.0). For each parameter an univariate repeated-measures ANOVA was performed with ER level (1, 2 , 4 and 8 sec) as the within subject variable and group (ADHD versus controls) as the between subject variable. The specific predictions relating to the nature of the interactions (linear, quadratic, etc.) were tested

using trend analysis and follow-up univariate *F*-tests explored which ERs were responsible for the group differences.

RESULTS

Table 2 reports summary statistics and the results of statistical comparisons for all parameters as a function of group and ER. The analyses of conventional performance measures revealed that the ADHD group had longer RTs than controls and the group difference increased as ER slowed. The groups did not differ in omission and commission errors and the interactions between group and ER were not significant for these variables.

For *mu* there was no group effect. There was an effect of ER: *mu* increased in a linear fashion as a function of increasing ER (Figure 1). The interaction between group and ER approached significance ($F(1,48) = 3$, $p = 0.09$), with the group difference for *mu* increasing as ER slowed. This interaction became significant when 2, 4 and 8 sec conditions were analyzed separately ($F(1,48) = 5.33$, $p = 0.03$). *Sigma* was overall greater in the ADHD group. There was an effect of ER on s*igma* following a significant quadratic trend across ERs (Figure 2). As predicted, there was a significant quadratic interaction between group and ER with group effects seen at the 1 sec ($F(1,48) = 6.28$, $p = 0.02$) and 8 sec ($F(1,48) = 5.02$, $p = 0.03$) conditions, but not in the 2 sec ($F(1,48) = 0.8$, $p = 0.38$) and 4 sec ($F(1,48) = 1.78$, $p = 0.19$) conditions. For *tau*, there was a significant group effect with the ADHD group having greater *tau.* There was an overall increase in *tau* as a function of ER with the slow ERs producing greater *tau*. However, this effect appeared to be driven by reduced *tau* in the 1 sec condition (Figure 3) which probably resulted from the necessary imposition of a high cutoff. The interaction between group and ER was not significant. The results of the Vincent averaged data (Figure 4) confirmed the results of the first analysis with the difference in the *tau* parameter remaining stable across different ERs and the ADHD group showing an accentuated inverted U pattern for *sigma.*
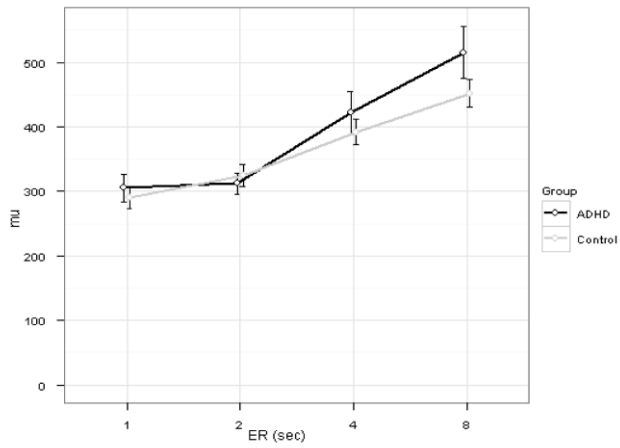
Figure 1. *Mu* parameter for the ADHD and control group in each event rate condition (Error bars: standard error (SE) of the mean).
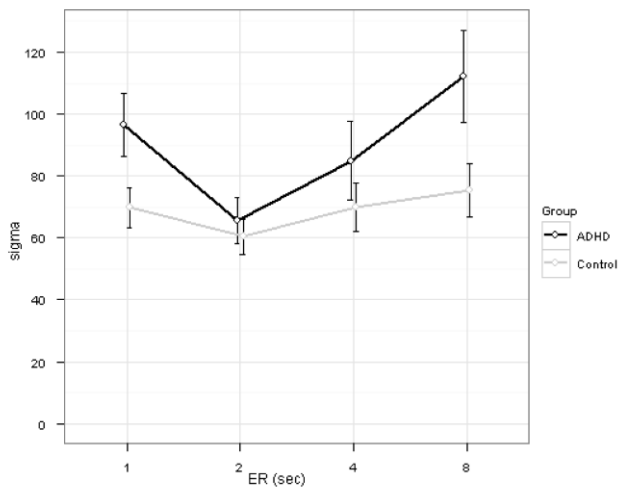

Figure 2. *Sigma* parameter for the ADHD and control group in each event rate condition (Error bars: SE of the mean).
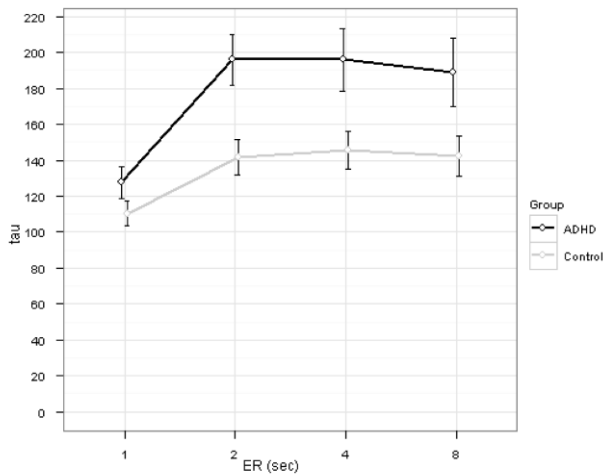
Figure 3. *Tau* parameter for the ADHD and control group in each event rate condition (Error bars: SE of the mean).

Table 2. Means and Standard Deviations (SD) for the variables at each event rate condition.

Variable	Event Rate				ANOVA			ES
	1 sec	2 sec	4 sec	8 sec	Group	ER[b]	Group x ER	
MRT (msec)					$F(1,52)$ 7.35*	$F(1,52)$ 168.93**	$F(1,52)$ 6.06*	0.77
ADHD	438.7 (86.2)	521.0 (111.3)	619.3 (169.6)	715.5 (205.7)				
Control	395.9 (76.5)	456.9 (96.1)	521.0 (125.8)	585.5 (119.9)				
EOC (%)					$F(1,52)$ 2.47	$F(1,52)$ 3.11	$F(1,52)$ 0.03	0.42
ADHD	45.1 (17.0)	43.6 (18.2)	42.5 (25.0)	39.2 (24.6)				
Control	38.2 (14.6)	34.6 (19.3)	33.1 (21.7)	33.4 (23.0)				

EOO (%)					F(1,52)	F(1,52)	F(1,52)	0.53
					3.77	21.62**	1.15	
ADHD	13.4	6.8	5.6	7.8				
	(8.5)	(7.8)	(7.6)	(8.3)				
Control	8.0	4.1	3.6	5.2				
	(9.7)	(4.1)	(5.1)	(7.7)				
SDRT					F(1,52)	F(1,52)	F(1,52)	0.92
					10.47*	34.08**	0.02	
ADHD	167.5	234.4	222.6	234.7				
	(38.4)	(90.9)	(76.0)	(91.5)				
Control	133.2	170.8	170.0	194.0				
	(37.0)	(57.1)	(66.9)	(79.4)				
Mu					F(1,48)	F(1,48)	F(1,48)	0.3
					1.1	113.7**	3.0	
ADHD	305.2	312.1	421.5	515.6				
	(102.8)	(80.6)	(158.5)	(196.6)				
Control	288.7	315.8	382.9	444.2				
	(83.2)	(82.9)	(98.5)	(110.4)				
Sigma					F(1,48)	F(1,48)	F(1,48)	
					4.94*	21.03**	5.5*	0.63
ADHD	96.5	65.7	84.9	112.2				
	(49.4)	(35.6)	(61.3)	(72.0)				
Control	66.9	57.5	65.4	74.7				
	(33.8)	(29.4)	(41.5)	(44.8)				
Tau					F(1,48)	F(1,48)	F(1,48)	
					13.31**	15.5**	1.58	1.04
ADHD	127.7	196.1	196.0	188.9				
	(42.1)	(67.5)	(84.3)	(90.5)				
Control	109.4	141.7	141.8	141.				
	(34.9)	(48.9)	(54.5)	(60.7)				

Note: MRT = Mean Reaction Time, EOC = Errors of Commission, EOO = Errors of Omission, SDRT = Standard Deviation of Reaction Time, ER = Event Rate, effect size (ES) is Cohen's *d* for the group effect, [b]ER and interaction analyses have been performed with the use of appropriate contrasts (linear or quadratic), *$p < 0.05$, **$p < 0.001$.
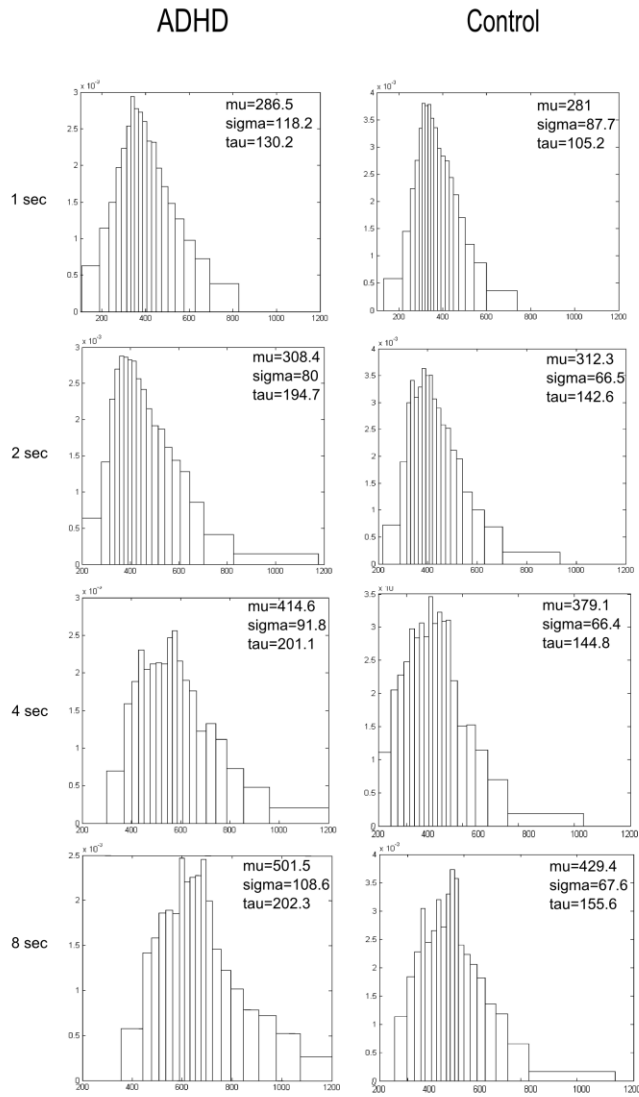
Figure 4. Vincent Histograms for each group at each condition and the estimated model parameters.

DISCUSSION

In this study, we tested the predictions regarding the effects of ER on RTvar in ADHD derived from the State Regulation Deficit and Delay Aversion models, using ex-Gaussian decompositions of RT distributions. ADHD individuals differed from controls on RTvar parameters of the ex-Gaussian model (greater *sigma* and *tau*). The findings suggest that higher RTvar in ADHD is caused by two mechanisms: (i) reaction times which result in higher Gaussian variability; (ii) occasional slow responses which create elongated tails in RT distributions. When the case control differences for each parameter are evaluated together with the ER effects and the predictions made by different models, important conclusions can be drawn about the validity of these models in explaining the elevated variability in ADHD.

For *sigma*, the results were in striking conformity with the predictions of the State Regulation Deficit model. In particular, while for all subjects the effect of ER on *sigma* followed an "inverted U" function, this was accentuated for the ADHD group – with significantly greater *sigma* on the very short and very long ER trials but no difference on the moderate ER trials. This suggests that the ADHD group might have problems with regulating their energetic state at very fast and very slow ERs which lead to a higher variability at these sub-optimal settings. Previous ER studies did not report this effect relating ADHD to *sigma* (Epstein et al., 2011; Hervey et al, 2006). This might be due to the broader range of ERs used in the current study – group effects were only significant at very fast (1 sec) and very slow (8 sec) ERs and previous studies did not cover these ERs.

The *mu* effects were also generally consistent with previous studies – *mu* increases as ER slows. This increase was most pronounced in the ADHD group especially when only 2, 4 and 8 sec conditions were analyzed. This finding is congruent with a general slowing of RTs in ADHD on trials with slower ERs (Metin et al., 2012); however, it also indicates that the RT slowing is prominent after 2 sec.

While our findings regarding *tau* are consistent with previous reports of greater *tau* in ADHD in general, these effects were not affected by ER. This appears counterintuitive from a number of perspectives. First, the *tau* component is often suggested to be a marker of attentional lapses in ADHD which is postulated to be due to impaired regulation of energetic resources (Leth-Steensen et al, 2000). Therefore, one might expect that *tau* will be affected by ER manipulations. However, the assumption that

tau is a good index of attentional lapses is questionable and it has also been argued that the nature of these periodic long RTs in ADHD remains unknown (Epstein et al, 2011). One of the previous ER studies reported that *tau* increased disproportionately as a function of ER in children with ADHD (Hervey et al., 2006). However, this study did not use a filter for slow RTs. In slow ER conditions there is a longer interval between stimuli for collection of RTs. On the other hand, for fast ERs an obligated high cutoff is applied due to the short ISI. This allows collection of outlier RTs exclusively at slow conditions and elongation of the tail of the RT distribution. Given that children with ADHD are more prone to make accidental button presses between stimuli due to hyperactivity, the *tau* parameter may be found to be disproportionately elevated in the ADHD group at slow ER conditions if no high cutoff is applied. In our study, analyzing the data within the 2 sec window, which is expected to contain all stimulus-related button presses in a simple GNG task, showed that the tail of the RT distribution is not affected by ER. Therefore, our results suggest that *tau* may not be a sensitive marker of attentional lapses that arise during slow ERs. Second, it has also been claimed that ADHD performance is negatively affected in a non-task specific way by interference from the default-mode network (DMN) brain areas (Sonuga-Barke & Castellanos, 2007). This interference may result in occasional slow RTs and thereby an increase in *tau*. From the State Regulation point of view, one might expect greater interference in slow ER settings where more effort is needed to suppress the DMN activity. However, it is again not certain whether the *tau* parameter is sensitive or specific enough to illustrate DMN interference. Interestingly, one study reported that DMN suppression deficits in ADHD correlate not only to *tau* but also to *sigma,* suggesting that *tau* is not a specific indicator of these deficits (Fassbender et al., 2009).

The Delay Aversion model predicts greater task disengagement in slow ER conditions which would lead to higher RTvar only on slow ER trials. Therefore, it would predict a linear pattern with variability increasing as ER slows. However, the current results provide little support for the predictions of the Delay Aversion model on ADHD variability. While both models predict greater variability on slow ER trials, our finding of increased *sigma* on fast ER trials is completely counter to the Delay Aversion model predictions and seems to provide a telling test between the models.

Another account proposes that increased RTvar in ADHD is due to altered timing (Toplak, Rucklidge, Hetherington, John, & Tannock, 2003). To date several studies have

confirmed that individuals with ADHD have timing problems (Barkley, Murphy, & Bush, 2001; Rommelse, Oosterlaan, Buitelaar, Faraone, & Sergeant , 2007; Rubia, Halari, Christakou, & Taylor, 2009; Rubia, Noorloos, Smith, Gunning, & Sergeant, 2003; Smith, Taylor, Rogers, Newman, & Rubia, 2002; Sonuga-Barke, Saxton, & Hall, 1998; Toplak et al., 2003). It has been argued that for individuals with ADHD the passage of time is subjectively longer and more intolerable. In addition, they have impulsive timing of motor behavior and decreased temporal foresight which creates a preference of small immediate gains (Rubia et al., 2003). Although, not explicitly stated previously, one might expect ER to have an impact on temporal processing deficits in ADHD. This is because longer intervals will be perceived as more intolerable and will place greater demands on the timing abilities of individuals thereby exacerbating deficits in ADHD. Thus for this model a linear ER-RTvar relationship is predicted with increased RTvar during slow ERs and there is no reason to predict differences between Gaussian and exponential components (van der Meere, Shalev, Börger, & Wiersema, 2009). However, our findings indicate an "inverted U" shaped effect for *sigma* which cannot be explained by the time perception deficit model.

The current study had a number of strengths. First, we used the ex-Gaussian model which successfully describes RT distributions (Matzke & Wagenmaekers, 2009). Second, the task contained sufficient ER levels to model quadratic interactions and the range of ERs was wide enough to cover very fast and very slow ERs. A limitation of the current study could be the lower number of trials in the 8 sec condition. In our study we tried to ensure that the conditions had equal durations to avoid any effect of time-on-task on group differences. Therefore, having more trials in the slowest ER condition would make the task much too long for the children. In a previous study, Vincent averaging was used which allows accurate parameter estimation even when the conditions had fewer trials (Leth-Steensen et al., 2000). We also used the same method and this analysis confirmed the initial analyses.

To summarize, our results show that elevated RTvar in ADHD is caused by both fast and slow RTs and the findings can be best explained by the State Regulation Deficit model which predicts that children with ADHD have problems with adapting their energetic state to changing ER – with both fast and slow ERs creating greater *sigma*. In addition, the groups differed significantly for slow responses represented by the *tau*

parameter which is thought to represent attentional lapses. However, the effect of ER on *tau* was not significant. This finding suggests that the attentional lapses hypothesis may not be a satisfying explanation for greater *tau* in ADHD.

Key Points

- Performance of ADHD children is affected by the rate at which information is presented.
- Inconsistent and variable responding is common in ADHD and a potentially important treatment target.
- Both of these effects have been explained in terms of a State regulation deficit model although previous studies have not been able to show the inverted U function linking event rate to response variability predicted by this model - more variability at both very fast and very slow event rates.
- This study which had four different event rates on reaction time on a response inhibition task found the predicted inverted U function when Gaussian variability (i.e., sigma) but not variability due to slow responses (tau) was considered.
- These results support the State Regulation Deficit model and also highlight the clinical potential of manipulating cognitive energetic variables in the environment as part of the management of ADHD.

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EXECUTIVE AND NON-EXECUTIVE DEFICITS IN ADHD: A DIFFUSION MODEL ANALYSIS[1]

ABSTRACT

Background: Attention-Deficit/Hyperactivity Disorder (ADHD) is associated with performance deficits across a broad range of tasks. While individual tasks are designed to tap specific cognitive functions (e.g., memory, inhibition, planning, etc.) these deficits could also reflect general effects related to either inefficient or impulsive information processing or both. These two components cannot be isolated from each other on the basis of classical analysis in which mean reaction time (RT) and mean accuracy are handled separately. **Method**: Seventy children with a diagnosis of combined type ADHD and 50 healthy controls (between 6 and 17 years) performed two tasks: a simple 2 choice reaction time (2-CRT) task and a conflict control task (CCT) which required higher levels of executive control. RT and errors were analyzed using the Ratcliff Diffusion Model which divides decisional time into separate estimates of information processing efficiency (called drift rate) and speed accuracy trade-off (SATO, called boundary). The model also provides an estimate of general non-decisional time. **Results**: Results were the same for both tasks independent of executive load. ADHD was associated with lower drift rate and less non-decisional time. The groups did not differ in terms of boundary parameter estimates. **Conclusions**: RT and accuracy performance in ADHD appears to

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[1] Based on Metin, B., Roeyers, H., Wiersema, J. R., Van der Meere, J.J., Thompson, M., & Sonuga-Barke, E. (In press).ADHD Performance Reflects Inefficient But Not Impulsive Information Processing: A Diffusion Model Analysis. Neurospychology.

reflect inefficient rather than impulsive information processing; an effect independent of executive function load. The results are consistent with models in which basic information processing deficits make an important contribution to the ADHD cognitive phenotype.

INTRODUCTION

Attention-Deficit/Hyperactivity Disorder (ADHD) is a life span disorder that is characterized by persistent and pervasive hyperactivity, impulsivity and/or inattention together with a significant degree of functional impairment (DSM-IV-TR, American Psychiatric Association, 2000). It has been characterized as an executive function disorder caused by deficits in higher order self-regulatory functions such as inhibitory control, working memory, planning and behavioral flexibility (Barkley, 1997; Doyle, 2006; Halperin & Schulz, 2006). It has been argued that deficits in inhibitory control are at the roots of executive dysfunction in ADHD (Barkley, 1997) – whereby affected individuals have a reduced ability to withhold or suppress inappropriate responses when required to, leading to more errors of commission on laboratory paradigms such as the Stop Signal Task (Oosterlaan, Logan, & Sergeant, 1998), Go/No-Go task (Iaboni, Douglas, & Baker, 1995; Rubia, Smith, & Taylor, 2007; Wodka et al., 2007) and the Continuous Performance Test (Losier, McGrath, & Klein, 1996).

Although there is a large body of evidence showing that ADHD children make more errors (both of commission and omission) than controls on these sorts of tasks (Willcutt et al., 2005) the view that ADHD is primarily a disorder of inhibitory-based executive control has been challenged in at least two ways. First, it now seems clear that only a proportion of ADHD children have deficits on tasks measuring executive dysfunction – for many non-executive deficits play a role in their condition (Nigg, 2005; Sonuga-Barke, Wiersema, van der Meere, & Roeyers, 2010; Willcutt et al., 2005). Second, there is evidence showing that even when ADHD children do perform poorly on executive inhibitory control tasks, these effects may be accounted for by more basic information processing deficits. Indeed, individuals with ADHD do show performance deficits on tasks with very low executive or inhibitory loads (Van De Voorde, Roeyers, Verté, & Wiersema, 2010). Furthermore, when researchers have compared performance deficits under varying conditions of inhibitory control load and those where no such control is required, they have often found little or no evidence for a specific inhibitory control deficit (Rommelse et al., 2007; Van De Voorde et al., 2010). In addition, studies of event-related brain potentials on inhibitory control tasks are consistent with the idea

that poor performance of ADHD children on those tasks are due to early response preparatory rather than later inhibitory components (Banaschewski et al., 2004).

What kind of information processing deficit might be responsible for the increased error rates observed when ADHD children perform these laboratory tasks if not a deficit in higher order executive control? One possibility is that individuals with ADHD are less efficient in the general accumulation of information needed to make response decisions on laboratory tasks and that such deficits occur, by and large, irrespective of task demands (i.e., they have reduced information processing efficiency). A second possibility is that although as efficient as controls they are less willing, or able, to spend time in the information gathering phase before responding – they trade response speed for accuracy. This could be described as an impulsive rather than an inefficient information processing style. On the face of it, despite impulsivity being a core component of the ADHD clinical phenotype, and evidence of impulsive choice on laboratory tasks (Marco et al., 2009; Sonuga-Barke, 1994), existing evidence from RT tasks is against this second account as a general explanation of ADHD task performance deficits. This is because individuals with ADHD tend to be slow-inaccurate, rather than fast-inaccurate responders on fast-paced laboratory information processing tasks (van der Meere, Stemerdink, & Gunning, 1995; Van der Meere, Marzocchi, & De Meo, 2005; see van der Meere, 2002 for a review). Furthermore, Sergeant and Scholten (1985) found no evidence that ADHD children's fast responses could explain their decreased levels of accuracy – there was no evidence of speed accuracy trade-off (SATO).

Analyses to date however, have largely been constrained by the use of traditional models which deal with errors and RT separately and cannot disentangle general estimates of processing efficiency (speed of information take-up) and the impulsive information processing style associated with SATO from each other and from non-decisional components such as stimulus encoding and motor organization. The Ratcliff Diffusion Model (RDM), an empirically validated model of cognitive processes involved in two choice decisions (Ratcliff, 1978; Rattcliff & McKoon, 2008; Voss, Rothermund, & Voss, 2004), offers an alternative to classical RT and error analysis, by providing separate estimates of different components of information processing on the basis of a combined analysis of RTs and errors. It has the potential to allow inferences about the processes implicated in ADHD and in particular allows us to disentangle the role of processing inefficiency and impulsive processing style in ADHD deficits. Crucially, this can be

achieved under single experimental conditions without the need to manipulate tasks parameters or instructions. The RDM assumes that RT is made up of separate decisional and non-decisional components. The non-decisional component (Ter) represents the extra-decisional processes such as encoding and motor execution. It has a standard deviation (st) representing the variability of this parameter. The decision time is the time interval for the noisy information accumulation process (drift), beginning from the starting point (z), to reach the upper or lower boundary. The steepness of the drift (drift rate-v) represents the rate of accumulation of information (i.e., processing efficiency) and shows the quality of the stimulus or the efficiency of information processing. The drift rate and the starting point also have standard deviations (sv and sz). The boundary (a) represents the threshold of accumulated information for a response to be committed reflecting the SATO or the degree of impulsive information processing style. The higher this boundary is set, the longer it will take for the drift vector to hit the upper boundary but the responses will be more accurate. A graphic representation of the RDM parameters can be found in Figure 1. RDM has been widely used in experimental psychology to explore the effects of various factors on task performance such as age (Rattcliff, Thapar, & McKoon, 2004), practice (Dutilh, Vandekerckhove, Tuerlinckx, & Wagenmakers, 2009), task interference (Boywitt & Rummel, 2012), and sleep deprivation (Rattcliff & van Dongen, 2009). It has also demonstrated a beneficial role in understanding clinical disorders (White, Ratcliff, Vasey, & McKoon, 2010).

The RDM was first used to examine ADHD information processing by Mulder et al. (2010). The researchers compared the ability of individuals with ADHD to adjust SATO (i.e., the boundary parameter) by testing them under two different instructional conditions in which either speed or accuracy was emphasized. They used a perceptual decision making task in which they equated the drift rate across participants by adjusting the stimulus difficulty for each subject in order to isolate case-control differences in the boundary parameter. They did not find a group difference in boundary parameter (or drift rate) per se, but they did find that children with ADHD, compared to controls, were less able to adjust their boundary condition to the instructional demands – they had higher boundaries when speed was emphasized but lower boundaries when accuracy was emphasized. Their conclusion was that basic cognitive processes such as perceptual decision making are affected by problems with optimization of SATO which

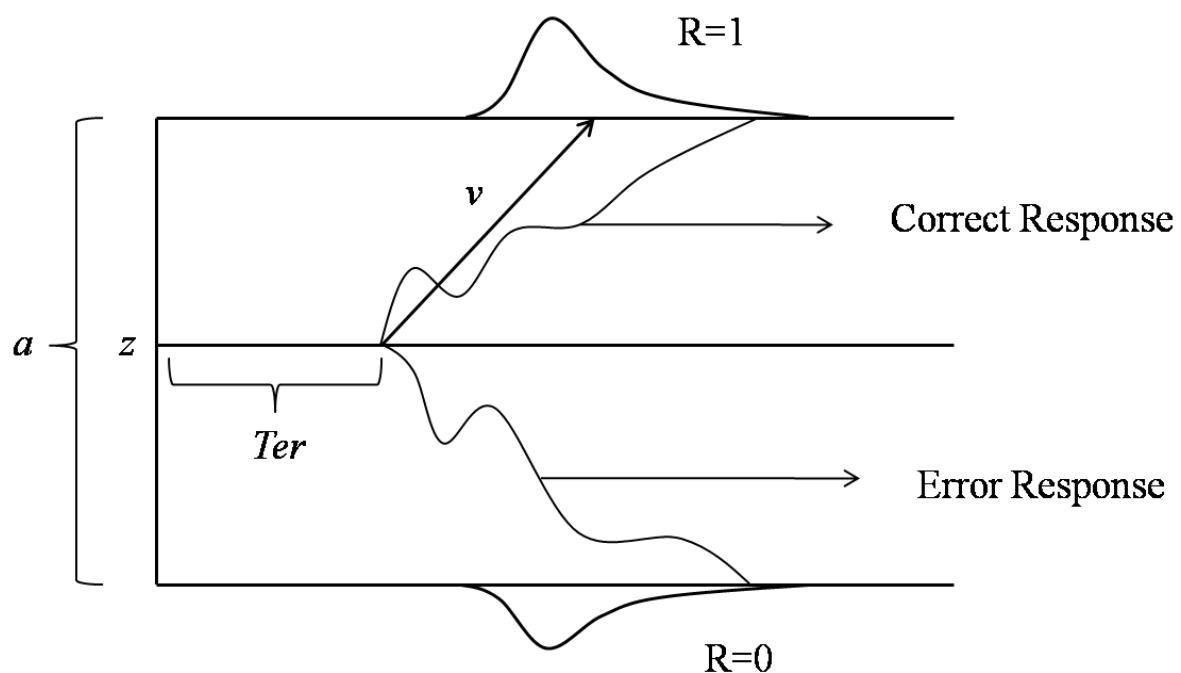they argue contradicts accounts in which ADHD is seen as the result of higher order processing deficits.

Figure 1. Graphical representation of the diffusion model parameters and reaction time distributions for correct (R=1) and error (R=0) responses. *v*=Mean drift rate. *Ter*=Non-decision time. *a*=Boundary between two responses. *z*=starting point of the diffusion process

In the current study, the RDM was employed for a different purpose. In contrast to the design of the Mulder et al. study (2010), the drift rate and the boundary were both allowed to vary between groups so that we could test the relative contribution of deficits in general information processing efficiency (impaired accumulation of information) and impulsive information processing style (indicated by a lower boundary parameter). To examine whether the degree of executive control load affects the differences between groups on these parameters, we used both a simple two choice RT task (2-CRT), which requires minimal executive control, and a conflict control task (CCT), which required considerable levels of inhibitory control. We predicted that ADHD children will differ from controls primarily in terms of information processing efficiency (i.e., a lower drift rate). Furthermore, we predicted that these general information

processing effects would occur irrespective of task specific executive requirements. On the basis of the Mulder et al. study (2010) and the early studies using traditional analytical approaches, we did not predict that the boundary would differ significantly between the groups (i.e., ADHD would not show a more impulsive information processing style).

METHOD

Participants

Seventy children and adolescents with a diagnosis of combined type ADHD and 50 non-clinical controls from the Southampton arm of International Multi-centre ADHD Genetics (IMAGE) study took part in this study. Inclusion criteria were an estimated full IQ of at least 70, age range between 6 and 17 years, and no apparent other major mental health problems, such as autism, epilepsy, brain disorders, or known genetic disorders, such as Down's or Fragile X syndrome. The ADHD group consisted of 60 boys and 10 girls (mean age=12.1 years, SD=2.3), and the control group 33 boys and 17 girls (mean age=12.2 years, SD=2.3). The age difference between groups was not significant (t(118)=.12, p=.9). The ADHD group had a significantly lower IQ than the control group (t(118)=2.97, p=.004). The data analyzed here have already been published in a study exploring the effects of ADHD on inhibitory control (Bitsakou, Psychogiou, Thompson, & Sonuga-Barke, 2008). Results showed that children with ADHD made more errors of commission than controls and these effects were independent of IQ and basic processing speed.

Diagnostic criteria

The full assessment battery for the IMAGE study included a wide range of measures; Conners parent and teacher rating scales (Conners, 1996), Social Communication Questionnaire (SCQ; Berument et al., 1999), parent and teacher versions of the Strengths and Difficulties Questionnaire (SDQ; Goodman, 1997) and Parental Account of Childhood Symptoms (PACS; Taylor, Sandberg, Thorley, & Giles, 1991). PACS is a semi-structured clinical interview developed to provide an objective

measure of behavior. A trained interviewer administered the PACS with parents, who were asked for detailed descriptions of the child's typical behavior in a range of specified situations. Inter-rater reliability was high with product-moment correlations for pairs of interviewers ranging from .79 to .96 (Brookes et al., 2006). The hyperactivity subscale was made up of attention span, restlessness, fidgetiness, and activity level, with other subscales covering defiant, emotional and other comorbid disorders including oppositional defiant disorder (ODD) and autistic spectrum disorder (ASD). A standardized algorithm was applied to the PACS to derive each of the 18 DSM-IV ADHD items. These were combined with items that were scored 2 (pretty much true) or 3 (very much true) in the teacher-rated Conners' ADHD subscales to generate the total number of hyperactive-impulsive and inattentive symptoms of the DSM-IV symptom list. Normal control children were included in the study if they scored below the clinical cut-off of 5 on the hyperactivity-impulsivity subscale of the SDQ, rated both by parents and teachers. Moreover, none of the normal control children had any diagnosed mental disorder according to parental reports.

Tasks

<u>2-Choice Reaction Time Task (2-CRT):</u> This task was selected because it requires only a simple perceptual decision based on the direction indicated by arrows on the computer screen and therefore involves little executive or inhibitory control (Hogan et al., 2005; Bitsakou et al., 2008). Green arrows either pointing to the left or to the right were presented on a computer screen. Participants had to press the mouse buttons indicating the direction of the arrow. 100 stimuli were presented, half requiring left and half requiring a right button press. The inter-stimulus interval was 1500 msec and the stimulus duration was 100 msec. Both speed and accuracy were equally emphasized in the instructions.

<u>Conflict Control Task (CCT):</u> This task is also referred to as a modified Stroop task (Hogan et al., 2005; Bitsakou et al., 2008) because it requires participants to occasionally suppress a dominant tendency to respond in the direction indicated and to respond in the opposite direction, with these conflict trials being indicated by a change in the arrows color. Performance on this task is correlated with standard tasks of inhibitory

control such as the Stop Signal Paradigm (Bitsakou et al., 2008). In the congruent trials the same green arrows as in the 2-CRT were presented and participants had to press the button indicating the direction of the arrow. In the incongruent trials, red arrows were presented and the participants were asked to respond in the opposite direction of these arrows. In total, 100 trials were presented, of which 25% were incongruent. The presentation timings were the same as for the 2-CRT. Both speed and accuracy were equally emphasized in the instructions.

Procedure

Children with ADHD were off-medication for at least 48 hours before testing. The testing also included a Go/No-Go task and a Stop Signal Task, the results of which are reported in the original study (Bitsakou et al., 2008). During the children's neuropsychological testing, the PACS was administered to the parents. No PACS interview was taken from the healthy control children. Full testing took between 120 and 150 minutes and children were allowed to have small breaks during the testing period. The experimenter remained with each child throughout the task. At the end of the session all children received a £5 voucher for their participation. The study had approval from the local NHS ethics committee and written informed consent was obtained from the participants and the parents.

Analysis

Fast-dm software (Voss & Voss, 2007) was used to estimate the parameters of the RDM and evaluate goodness-of-fit. The program uses Partial Differential Equation (PDE) method to estimate model parameters and Kolmogorov-Smirnov (KS) statistics to evaluate model fit. Because there was only one condition in the 2-CRT task this analysis was straightforward. As the CCT consisted of two conditions (congruent and incongruent) we allowed drift rate and non-decision time to vary between conditions because of increased stimulus complexity and motor conflict in the incongruent condition compared to the congruent condition. The other parameters of the RDM, including boundary, were kept constant between conditions. The upper threshold in the model represented the correct responses and the lower threshold, incorrect responses.

When the data is coded this way, the participants can not have a response bias towards one of the boundaries (i.e., upper correct vs. lower incorrect). Therefore, we fixed the bias parameter (i.e., the starting point for the diffusion process) to a value half-way between the upper and lower boundary thresholds (z=0.5) (see also Mulder et al., 2010; supplementary material). Fixing the parameter in this way is also useful for preventing errors in bias estimates which could result from low number of error trials (i.e., <10) in some datasets (A. Voss, personal communication, June 8, 2012). To eliminate the anticipated button presses we excluded responses faster than 100msec. No upper cutoff was applied to exclude slow responses as the inter-stimulus interval was 1500 msec and any response slower than this was not possible. The second reason for not excluding slow responses at a stricter threshold than 1500msec is that this can potentially eliminate slow responses that are commonly observed and of interest in ADHD (Geurts et al., 2008). The participants with >10% outliers were eliminated.

RESULTS

Statistical analysis of the data was completed using SPSS (version 19.0) statistical software. Seven participants were eliminated from the analysis due to a high percentage of outliers.

Accuracy and RT analysis (Table 1)

Table 1 presents the mean RT (MRT) and accuracy data. One-way ANOVA with group (ADHD vs. control) as a between-subject factor was used to explore group differences in RT, accuracy and model parameters on the 2-CRT task. The ADHD group was significantly less accurate than the control group (F(1,111)=19.82, p<.001, d=.85). There was no difference in MRT between groups (F(1,111)=.22, p=.88, d=.09). The CCT data was analyzed using a repeated measures ANOVA with group as a between-subject and executive load (congruent vs. incongruent) as a within-subject factor. In this task, responses were slower in the incongruent condition than the congruent condition (F(1,110)=255.19, p<.001). There was no group difference for MRT (F(1,110)=.53, p=.47, d=.14). The group by congruency interaction was not significant (F(1,110)=1.9, p=.17). More errors were made in the incongruent compared to the congruent condition

(F1,110)=145.03, p<.001) and the ADHD group was less accurate in both the congruent and incongruent conditions (F(1,110)=31.86, p<.001, *d*=1.08). The group by congruency interaction for accuracy was not significant (F(1,110)=2.3, p=.13).

Table 1. Task performance for ADHD and control groups in the 2-CRT task and the CCT.

Measure	ADHD	Control
	Mean (SD)	Mean (SD)
2-CRT	(n=65)	(n=48)
Error percent (%)	26 (13)	15 (12)
MRT (msec)	377 (68)	375 (78)
CCT	(n=64)	(n=48)
Error percent		
Cong. Trial (%)	21 (10)	10 (8)
Incong. Trial (%)	37 (16)	23 (17)
MRT Cong. (msec)	476 (105)	482 (105)
MRT Incong.(msec)	582 (117)	607 (147)

Note. 2-CRT= Two choice reaction time task. CCT= Conflict Control Task. ADHD=Attention-Deficit/Hyperactivity Disorder. MRT=Mean Reaction Time. Cong.=Congruent. Incong.=Incongruent.

Table 2. Estimated model parameters for each group in the 2-CRT task and the CCT.

Measure	ADHD Mean (SD)	Control Mean (SD)
2-CRT	(n=65)	(n=48)
a	0.92 (0.2)	0.89 (0.25)
v	1.96 (1.21)	3.28 (1.56)
Ter	0.2 (0.06)	0.25 (0.07)
CCT	(n=64)	(n=48)
a	1.06 (0.2)	1.05 (0.22)
v		
Congruent	1.74 (0.77)	2.77 (1.1)
Incongruent	1.09 (1.06)	2.28 (1.54)
Ter		
Congruent	0.25 (0.09)	0.31 (0.07)
Incongruent	0.32 (0.13)	0.42 (0.11)

Note. 2-CRT= Two choice reaction time task. CCT= Conflict Control Task. ADHD=Attention-Deficit/Hyperactivity Disorder. *v*= Drift rate. *Ter*=Non-decision time. *a*=Boundary.

Diffusion Model Analysis

Parameter estimates for ADHD and control group derived from RDM analyses are presented in Table 2 for 2-CRT task and CCT. The KS statistic did not indicate misfit for

any participant's data. This confirms that assumptions made for the different conditions within the task described the RT distributions well.

2-CRT

On the 2-CRT, the parameter estimates of drift rate ($F(1,111)=25.79$, p<.001, d=.97) and non-decision time ($F(1,111)=20.53$, p<.001, d=.86) were lower for individuals with ADHD than controls (Table 2). There was no difference between groups for boundary parameter ($F(1,111)=.57$, p=.45, d=.14).

CCT

As with the 2-CRT, children with ADHD had a lower drift rate than controls ($F(1,110)=33.82$, p<.001, d=1.11). There was also a main effect of condition with higher drift rate on congruent trials ($F(1,110)=34.03$, p<.001). The interaction between group and condition was not significant ($F(1,110)=.72$, p=.4). To see the contribution of task type on group differences, the 2-CRT and CCT tasks were also analyzed together with a 2x3 ANOVA with group as a between subject factor and condition (2-CRT, CCT-*congruent* and CCT-*incongruent*) as a within subject factor (Greenhouse-Geisser correction was used for violation of the sphericity assumption). This analysis also produced similar results. The drift rates decreased substantially in the CCT compared to the 2-CRT task ($F(1.86, 204.2)=34.81$, p<.001; 2-CRT> CCT-*congruent* > CCT-*incongruent*). However, the highly significant group difference ($F(1,110)=38.27$, p<.001) was not affected by task or condition, which is indicated by a non-significant interaction between group and condition ($F(1.86, 204.2)=.75$, p=.46). For non-decision time, there was a significant effect of group ($F(1,110)=17.98$, p<.001, d=.81) with children with ADHD having smaller non-decision time than controls. For both groups, non-decision time was greater in the incongruent compared to the congruent condition ($F(1,110)=165.64$, p<.001). A significant interaction effect demonstrated that this shift was less marked in the ADHD than control individuals ($F(1,110)=11.04$, p=.001). The follow-up tests showed that the groups already differed in the congruent condition ($F(1,110)=13.93$, p<.001, d=.71) but this difference became more prominent in the incongruent condition ($F(1,110)=18.58$, p<.001, d=.82). The groups did not differ in boundary parameter ($F(1,110)=.04$, p=.84, d=.04).

We also tested correlations between the RDM parameter estimates across the two tasks in order to examine the extent to which the parameters tapped similar components in the executive and non-executive tasks. There were strong and significant correlations between the RDM parameter estimates for the two tasks. For boundary the correlation between 2-CRT and CCT was .4 (df=110, p<.001). The coefficients were .58 and .60 for correlations between the drift rate in the 2-CRT and the drift rates in the congruent and incongruent conditions of the CCT respectively (df=110, p<.001). For non-decision time they were .57 and .58 (df=110, p<.001). The differences between the correlation coefficients calculated by Fischer's z test were not significant when these were computed separately for the two groups. The correlations for the boundary were 0.34 for the ADHD group and 0.47 for the control group. The drift rate correlations were .52 and .56 for the ADHD group. The same correlations were .44 and .49 for the control group. The non-decision time correlations were .45 and .41 for the ADHD group and .61 and .65 for the control group.

DISCUSSION

The aim of the current study was to explore the basis of performance deficits in ADHD on two tasks: one simple RT task with low levels of executive demands (2-CRT) and one more demanding task with a high executive control load (CCT). There were two questions: First, 'Do the ADHD-related deficits reflect information processing inefficiency or impulsive information processing?' Second, 'Does the relative contribution of these components of information processing to ADHD vary as a function of executive load?'

The Diffusion Model Analysis (DMA) did not provide evidence for an impulsive information processing in the participants with ADHD on both tasks – the groups had similar boundary parameter estimates – suggesting that ADHD participants were no more willing than controls to trade accuracy for speed than controls. This result is consistent with older studies that did not find an ADHD-related SATO difference (Sergeant & Scholten, 1985; van der Meere, Gunning, & Stemerdink, 1996) and also with the previous study using DMA (Mulder et al., 2010). On the other hand, impulsivity is one of the main characteristic of ADHD and there is strong and consistent evidence suggesting that ADHD participants have an impulsive decision making style on tasks

requiring the processing of complex stimuli over longer periods of time such as the Matching Familiar Figures Task where participants have to select a target figure from a set of 5 foils (Sonuga-Barke et al., 1994) or on tasks where choice between small immediate and larger delayed rewards are available (Marco et al., 2009). On these tasks ADHD participants tend to either respond prematurely and make more incorrect decisions or choose the small reward. Reconciling these two set of contrasting results depends on understanding that such tasks engage very different cognitive processes from those employed in reaction time tasks such as the 2-CRT and CCT. These extended tasks, for instance, may provide delay averse responses, whereby ADHD individuals act to avoid extended periods of delay or secure rewards sooner rather than later. Such factors are unlikely to affect performance on RT tasks as the delays are typically already very short. It should also be noted that our findings do not mean that the individuals with ADHD were not more impulsive than the controls. On the contrary, it can only be concluded that increased impulsivity may not be the cause of ADHD-related performance deficits in all types of tasks.

In contrast, we did find strong and consistent evidence for group differences in drift rate showing that ADHD individuals were less efficient in terms of information accumulation. The drift rate-related group differences were remarkably similar for both tasks – that is processing efficiency deficits appeared to play an equally important role in those tasks with little or no executive load and those that required a high degree of inhibitory control. Furthermore, the high correlations between drift rate estimates in the two tasks suggest that variation in performance on two tasks may be determined, in part, by common effects of basic processes determining efficient information uptake and processing.

These findings suggesting information accumulation problems in both tasks are consistent with the idea that the non-executive deficits contribute to task performance in ADHD. Indeed, findings are consistent with previous research reporting an inaccurate response style in ADHD which was independent of the degree of executive load (Rommelse et al., 2007; Van De Voorde et al. , 2010). The implication of these findings for ADHD pathogenesis is that they suggest the contribution of general deficits in information accumulation processes which could disrupt performance both in executive and non-executive tasks.

We also found significant group differences for non-decision time. We made no specific predictions in relation to this parameter as its interpretation is not straightforward because it is thought to equate to a combination of processes including encoding and motor organization. Since this parameter encompasses all extra-decisional processes, it does not relate specifically to performance measured by accuracy. Therefore, even though the ADHD group had overall smaller estimates of non-decision time and less slowing of non-decision time in the incongruent condition, this was not reflected in a performance deficit or an adaptation problem. One possibility, based on previous research, is that this difference may be linked to deficits in motor preparation rather than stimulus encoding in ADHD (Sergeant & van der Meere, 1990a; Sergeant & van der Meere, 1990b). In these studies motor preparation was less efficient in ADHD and this has been shown to be particularly evident during tasks with slow event rates. This finding was supported by electrophysiological studies showing that other indices of response preparation such as lateralized readiness potential and contingent negative variation (Banaschewski et al., 2004; Bourassa et al., 1998; Steger, Imhof, Steinhause, & Brandeis, 2000) and heart rate deceleration were reduced in ADHD (Börger & van der Meere, 2000). However, for now, it is not clear whether the faster non-decision time represents a deficit in motor organization since the performance of the ADHD group is not negatively affected by the difference in this parameter. It should also be kept in mind that faster non-decision times could still be linked to processes other than motor preparation (e.g., encoding time), since non-decisional time is a non-specific component which includes all extra-decisional processes. More research is needed to explore the replicability and the neuropsychological basis of shorter non-decision time in ADHD.

This is the second study using the RDM with individuals with ADHD. Neither study found evidence for an impulsive information processing style in ADHD (i.e., no difference in boundary estimates overall). However the two studies had very different goals. The goal of the Mulder et al. study (2010) was to explore the extent to which individuals with ADHD were able to adjust their SATO style to conform to different types of instructions – they found they were not able to do so. In order to investigate this the drift rate was fixed (by adapting difficulty levels). This meant that the role of general processing efficiency could not be investigated. In contrast, our goal was to compare the separate contribution of drift rate and boundary to ADHD performance. Future research could combine these two approaches to elaborate more clearly the effect of stimulus

complexity and adaptation of information processing style in ADHD by using multiple speed-accuracy instructions and levels of stimulus difficulty to better disentangle the SATO effects from efficiency of information processing.

It is important to acknowledge that the current results do not rule out a role for executive deficits in ADHD – in fact the lower drift rate on the CCT could still, in principle, represent problems with executive functions since the drift rate could be linked to any process involved in producing evidence from the stimulus including higher-order cognitive functions (Rattcliff & van Dongen, 2009). However, by comparing the contribution of drift rate on executive and non-executive tasks and therefore by showing a very similar contribution of these parameters in both tasks, the current results further challenge those accounts of ADHD that see the condition as solely the result of executive dysfunction.

The strengths of the current study include the large and well characterized sample and the use of executive and non-executive tasks. There were however also a number of limitations. First, one might argue that the tasks contained only a moderate number of trials and the CCT particularly contained a small number of incongruent trials relative to congruent trials which could potentially reduce the reliability of the parameter estimation. We tried to overcome this by fixing the bias parameter which ensured that this parameter was not affected by the low number of error trials. Furthermore, it has been shown that the fast-dm program can make fast and accurate parameter estimations with far fewer trials than needed by other programs (Voss & Voss, 2007). In addition, the consistency of the results across two tasks also indicates that the precision of the parameter estimation was high in the analysis of both tasks. Second, there may be some constraints in terms of model selection. Fast-dm does not enable comparison of the fit of different models. Therefore we made empirical assumptions for modeling the CCT. The fit of different models for a task with different complexity levels could be compared with other programs enabling model comparison (Vandekerckhove & Tuerlinckx, 2008). Third, although we had a large sample of ADHD and typically developing children, the lack of a significant difference for the boundary parameter, which represents SATO, could still be due a type II error. For medium (d= .5) to large (d= .8) effect sizes the power of the study was very high (.75 to .99). However for a small sized effect (d=.2) the power was only .18. Therefore the non-significant results for the boundary parameter should be evaluated carefully and more studies are

needed to determine whether or not there is a difference between ADHD and typically developing children in terms of SATO.

In more general terms the DMA has clear advantages over the conventional RT/accuracy analyses. In this study, for instance, the RT analysis revealed no difference between groups because the slower drift rate was offset by faster non-decision time in the ADHD group. The DMA, however, allowed us to disentangle these different components. Furthermore, it was not evident in the conventional analyses whether the lower accuracy was due to lower drift rate or altered boundary conditions but the DMA enabled us to distinguish the relative contributions of SATO and processing efficiency to the general inaccuracy in the ADHD group. The accuracy analysis already demonstrated that stimulus complexity did not affect the control and ADHD group differentially. The DMA confirms this finding by showing that the deficit in information accumulation rate is not affected by stimulus complexity or executive demands.

In summary the current results show highly significant and consistent differences between groups in the efficiency of information processing in both a non-executive and an executive task while providing no evidence for the role of impulsive decision making in ADHD-related task performance deficits. These effects need to be replicated in different populations and to be explored in a broader range of tasks – especially in tasks that examine response to more complex stimuli and long term decision tasks as well as under different instructional conditions and with varying task parameters. Finally, our findings indicate that sophisticated models such as RDM could provide us with a more extensive understanding of the neuropsychological deficits in clinical disorders in terms of individual elements of information processing than would be possible with the classical accuracy and RT analyses.

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CHAPTER 5

EFFECTS OF EVENT RATE ON ADHD INFORMATION PROCESSING: THE ROLE OF MOTOR PREPARATION

ABSTRACT

Background: It has been shown that the individuals with ADHD are differentially sensitive to ER although the neuropsychological basis of these effects is not well understood. A recent Go/No-Go study was consistent with the state regulation deficit model which postulates that ER effects on performance were due to disrupted regulation of activation during motor preparation at ER extremes (very fast and very slow). Here we use a Diffusion Model (DM) analysis to test this motor activation hypothesis more fully. **Methods**: We tested 25 children with ADHD and 29 typically developing children with a simple Go/No-Go task with four different ERs (1, 2, 4, 8 sec). The task performance was analyzed using a DM which estimates separate parameters for information processing efficiency (i.e., drift rate), motor preparation/encoding (i.e., non-decision time) and speed-accuracy trade-off (i.e., boundary). **Results**: The ADHD group had lower processing efficiency (drift rate) and was more cautious (higher boundary) than controls. Slowing of ER, in general reduced processing efficiency. As predicted by the state regulation deficit model, the interaction between ADHD and ER was limited to non-decisional time reflecting over-activation in the fast ER, and under-activation in the slow ER condition. **Conclusions**: This data is consistent with recent DM analyses which suggest that ADHD individuals have deficits in basic information processing reflected in lower efficiency. In contrast, the finding that they were more cautious in their response style seems at odds with the notion of cognitive impulsiveness as a core element of ADHD information processing. There was no evidence that deficits in processing efficiency or increased caution in ADHD were linked to disturbed state regulation processes, however the non-decision time findings are consistent with the idea that children with ADHD have a problem with regulating motor activation at ER extremes.

INTRODUCTION

Attention-Deficit/Hyperactivity Disorder (ADHD) is a prevalent childhood disorder which often persists into adulthood. It is characterized by symptoms of inattention and/or hyperactivity-impulsivity which lead to substantial social and academic impairment (DSM-IV-TR, American Psychiatric Association, 2000). ADHD is associated with deficits in a range of cognitive processes such as response inhibition, planning, vigilance and working memory (see Sonuga-Barke, Sergeant, Nigg, & Willcutt, 2008; Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005 for reviews). There is also accumulating evidence that these deficits are influenced by context - performance of an individual may vary from setting to setting as a function of the motivational and energetic states that they engender (Sonuga-Barke, Wiersema, van der Meere, & Roeyers, 2010). For instance, performance on a wide range of cognitive tasks is affected in non-specific ways by the rate at which stimuli are presented (i.e., event rate (ER; Sergeant, 2005; van der Meere, 2002).

The state regulation deficit (SRD) model proposes that these ER effects occur because children with ADHD have difficulty in properly regulating their energetical state when challenged to do so in sub-optimal settings or states – such as under extremely fast or slow ERs. This is postulated to be linked to activation processes and disrupted effort allocation, especially during the motor preparation states of information processing. It leads to the prediction that, relative to controls, ADHD children's performance would deteriorate at ER extremes (very fast or very slow ERs; van der Meere, Börger, & Wiersema, 2010) because of over-activation at fast ERs and under-activation at slow ERs. To date, several studies have provided robust evidence for the impact of ER on ADHD-related deficits in information processing tasks as predicted by the SRD model (Chee, Logan, Schachar, Lindsay, & Wachsmuth, 1989; Conte, Kinsbourne, Swanson, Zirk, & Samuels, 1986; Metin, Roeyers, Wiersema, van der Meere, & Sonuga-Barke, 2012; Scheres, Oosterlaan, & Sergeant, 2001; van der Meere, Stemerdink, & Gunning, 1995). A meta-analysis of Go/No-Go (GNG) studies comparing the ADHD-related deficits at slow and fast ERs showed that, consistent with the SRD model, ADHD individuals make more impulsive errors on tasks with fast ERs (over-

activation) and have longer RTs (under-activation) on tasks with slow ERs (Metin et al., 2012). Electrophysiological and fMRI studies have also confirmed that children with ADHD have a deficit in adjusting the allocation of effort according to suboptimal ER conditions (Wiersema, van der Meere, Antrop, & Roeyers, 2006; Wiersema, van der Meere, Roeyers, Van Coster, & Baeyens, 2006), problems with motor preparation at slow ERs (Börger and van der Meere, 2000) and show hypo-activation in fronto-striatal networks at slow ERs (Kooistra et al., 2010).

In order to further test the predictions of the SRD model we recently examined reaction time (RT) variability in ADHD and control children across four ER levels on a Go/No-Go (GNG) task. We employed the ex-Gaussian model (Matzke & Wagenmaekers, 2009) which differentiates a number of RT components (*mu*, *sigma*, *tau*). These components better describe the RT distribution and in particular its rightward skewed nature than the classical mean reaction time (RT) and variability measures. The *mu* and *sigma* parameters correspond to the mean and standard deviation (SD) of the normal component of the RT distribution (with *sigma* equating to Gaussian variability). The *tau* parameter represents the exponential component of the variability and is an estimate of the degree of skewness or the positive tail of the RT distribution (which can be equated to occasional long RTs). The key finding in this study was that in keeping with the SRD model children with ADHD had greater sigma at very fast and very slow ER conditions. Despite the consistency of the finding with the predictions of the SRD model it remains to be confirmed that these effects at ER extremes were in fact related to poor regulation of activation during the motor preparation phase of information processing after the decision to respond has been made. It is also possible that they were due to deficits during prior states of information processing (e.g., information extraction).

In this paper we explore this question by using the Diffusion Model (DM) to reanalyze the data from the original ER study. DM is a validated model of decision making (Ratcliff, 1978; Rattcliff & McKoon, 2008; Voss, Rothermund, & Voss, 2004) and offers another alternative to the classical performance measures and ex-Gaussian analysis by providing separate estimates of different components of information processing on the basis of a combined analysis of RTs and errors. It has the potential to allow inferences about the processes implicated in ADHD performance and in particular allows us to disentangle the role of processing inefficiency (drift), impulsive processing style or speed accuracy trade off (boundary) and crucially for the current analysis, non-

decisional processes such as motor response preparation in ADHD deficits. The DM assumes that RT is made up of separate decisional and non-decisional components. The non-decisional component (*T*er) represents encoding and motor execution processes. The decision time is the time interval for the information accumulation process (drift), beginning from the starting point (*z*), to reach the boundary. The steepness of the drift (drift rate-*v*) represents the speed of accumulation of information (i.e., processing efficiency). The boundary (*a*) represents the threshold of accumulated information for a response to be committed reflecting the speed-accuracy trade-off (SATO) or the degree of impulsive information processing style. The higher this boundary is set, the longer it will take for the drift vector to hit the upper boundary but the responses will be more accurate.

The DM has been used to examine ADHD information processing recently. Mulder et al. (2010) compared the ability of individuals with ADHD to adjust SATO (i.e., the boundary parameter) by testing them under two different instructional conditions in which either speed or accuracy was emphasized. They used a perceptual decision making task in which they equated the drift rate across participants by adjusting the stimulus difficulty for each subject in order to isolate case-control differences in the boundary parameter. They did not find a group difference in boundary parameter (or drift rate) per se, but they did find that children with ADHD, compared to controls, were less able to adjust their boundary condition to the instructional demands – they had higher boundaries when speed was emphasized but lower boundaries when accuracy was emphasized. Other studies have given a rather consistent picture. Three of them found that children with ADHD have lower information processing efficiency (lower drift rate) than typically developing children (Karalunas, Huang-Pollock, & Nigg, 2012; Karalunas & Huang-Pollock, 2013; Metin et al, 2013) and two studies reported faster non-decision times (Karalunas & Huang-Pollock, 2013, Metin et al, 2013). The finding relating to non-decisional time might be difficult to interpret because the non-decision time encompasses both stimulus preprocessing (encoding) and post-decisional motor processes. However the previous studies reported that ADHD is associated with deficits at the motor preparatory level rather than at the encoding level (Sergeant, 2005; Sergeant & Scholten, 1985; Sergeant & van der Meere, 1990; van der Meere, van Baal, & Sergeant, 1989). In addition the electrophysiological studies also confirmed these motor preparatory deficits by showing that indices of response preparation such as lateralized

readiness potential and contingent negative variation (Banaschewski et al., 2004; Bourassa et al., 1998; Steger, Imhof, Steinhause, & Brandeis, 2000) and heart rate deceleration were reduced in ADHD (Börger & van der Meere, 2000). Therefore, when evaluated in the light of previous studies, shorter non-decision time is more likely to indicate a difficulty in adjusting motor preparation for the ADHD children. Contrary to what one might expect from the observation of impulsivity in ADHD, no study reported lower boundary for ADHD children.

For this study, we make the following predictions. First, the ADHD children will have lower drift rates than the controls, but there will be no difference in boundary. Previous studies have indicated that the ER has its locus at the motor preparatory level (Sanders, 1983; Sergeant, 2005) and we therefore predicted that the ER manipulation will principally affect the non-decision time. In line with the SRD model we predict that ER will have a differential effect on ADHD outcomes in terms of non-decisional time reflecting problems with activation during the motor preparation stage of processing. More specifically we predict over-activation in the fast ER and under-activation in the slow ER for the ADHD group.

METHODS AND MATERIALS

The study was approved by the Ethics Committee of Ghent University, Faculty of Psychology and Educational Sciences. Written informed consent was taken from all parents and their children participating in the study.

Participants

25 children with ADHD and 29 controls between the ages of 8 to 12 years were tested. The ADHD and the control groups did not differ in age and gender composition. All children were screened for ADHD, oppositional defiant disorder (ODD) and conduct disorder (CD) with the parent version of the Disruptive Behavior Disorder Scale (DBD) (Pelham, Gnagy, Greenslade, & Milch, 1992). The demographic information and the symptom scores on the DBD scale can be found in Table 1. To exclude Autism Spectrum Disorder, the Social Communication Scale (SCQ) (Rutter, Bailey, & Lord, 2003) and the Social Responsiveness Scales (SRS) (Constantino & Gruber, 2005) were administered to both clinical and control

groups. However, none of the children were excluded due to clinical scores on these scales.

Table 1. The characteristics of the ADHD and control group and the scores for comorbid symptoms.

	ADHD (*N* = 25)	Control (*N* = 29)
Age in months[a]	122.4 (19.1)	123.8 (17.7)
Male:Female	16:9	14:15
TIQ[a]	103.6 (13.5)	109.8 (11.2)
HI[ab]	14.78 (1.79)	10.69 (1.05)
IA[abc]	14.76 (1.81)	10.5 (1.18)
ODD[abc]	13.04 (1.95)	10.88 (1.14)
CD[abd]	12.0 (2.02)	10.77 (0.99)

Note: [a] Means and standard deviations (SD), [b] Measured by Disruptive Behavior Disorders Scale, [c] $p < 0.0001$, [d] $p < 0.05$, TIQ = total Intelligence Quotient, HI = Hyperactivity/Impulsivity, IA = Inattention, ODD = Oppositional Defiant Disorder, CD = Conduct Disorder.

The children in the control group were recruited from local schools and scout camps. Children with ADHD were recruited from the community and a formal diagnosis by a clinician was required. The ADHD, ODD and CD diagnoses were ascertained by a DSM-IV oriented parent interview (disruptive behavior module of the Diagnostic Interview Schedule for Children, DISC-IV) (Shaffer, Fisher, Lucas, Dulcan, & Schwab-Stone, 2000) administered by an experienced clinical psychologist. 14 children were classified as ADHD-combined type, 8 children as inattentive type and 3 children as hyperactive-impulsive type. Eight children

received an ODD diagnosis and 3 others had a CD diagnosis. All children had a total IQ (TIQ) score above 75. TIQ was assessed by the short version of the Wechsler Intelligence Scale for Children – 3rd edition (WISC-III) (Grégoire, 2005). The children in the ADHD group had lower TIQ scores than the controls but this difference did not reach statistical significance ($F(1,52) = 3.35$, $p = 0.07$). The summary statistics for TIQ can be found in Table 1.

Experimental Task

All children completed a GNG task programmed using E-prime software (version 2). The stimuli were an upright triangle (Go stimulus) and an inverted triangle (No-Go stimulus). The stimuli were chosen based on a pilot study during which the performance of healthy controls on different tasks was compared across a range of levels of perceptual difficulty. The children were told to respond to every upright triangle and to withhold responding to every inverted triangle. Both speed and accuracy were equally emphasized in the instructions. The order of Go and No-Go stimuli was pseudo-randomized (a No-Go stimulus was always followed by a Go stimulus and maximum four Go stimuli were presented consecutively) with 72% Go and 28% No-Go stimuli. The duration of stimulus presentation was 300 msec. The task was preceded by a 2 minutes practice session. This was followed by 4 blocks of trials presented in a random order; each block had a different inter-stimulus interval (ISIs of 1, 2, 4 and 8 sec). The children were allowed to have small breaks between the sessions.

The duration of each condition was about 10 minutes in total. The 1 sec condition contained 560 stimuli, the 2 sec condition 280, the 4 sec condition 140 and the 8 sec condition 70. All responses up to 1 sec from stimulus onset were recorded for the fastest condition. For the other conditions, the cutoff for recording was 2 sec.

Procedure

All children completed the GNG task before the IQ test. The children completed the computer testing in a quiet room together with an experimenter sitting outside of their sight. The diagnostic interview of the parents of children with ADHD took place in another room with an experienced clinical psychologist. Seventeen children with ADHD were on stimulant medication. They were asked to

discontinue their treatment at least 24 hours before the start of the experiment. All children received 15 euro compensation for their participation in the study.

Analysis

Fast-dm software (Voss & Voss, 2007) was used to estimate the parameters of the DM and evaluate goodness-of-fit. The program uses Partial Differential Equation (PDE) method to estimate model parameters and Kolmogorov-Smirnov (KS) statistics to evaluate model fit. The DM is a model for two choice RT tasks and it assumes two response boundaries. In a GNG task, although the decision process also involves two boundaries (Go and No-Go), the information is only available for the Go boundary. Therefore we adapted the model to fit the single boundary diffusion process: We assumed that for Go stimuli, a response is executed when the drift vector hits the upper Go boundary (see Figure 1). As the responses for the lower boundary are not available, we fixed the starting point to avoid any error due to incorrect bias estimation. Therefore our modified model retained all parameters of the Ratcliff Diffusion Model except for the starting point (z). This adaptation has been successfully used previously (Domenech & Dreher, 2010) to explore the neurobiological basis of decision making in a GNG task with functional neuroimaging. The authors also confirmed that the adapted model estimated the parameters of the original diffusion process reliably. As the task consisted of four conditions with different ERs, the drift rate, non-decision time and the boundary parameters were allowed to vary between conditions. To eliminate the anticipated button presses we excluded responses faster than 100msec. No upper cutoff was applied to exclude slow responses as the responses were recorded maximum up to 2 sec and this produced a natural upper cut-off.

RESULTS

Table 2 reports summary statistics and the results of statistical comparisons for all DM parameters as a function of group and ER. The analyses of conventional performance measures revealed that the ADHD group had slower RTs than controls and the group difference increased as ER slowed. Although the children with ADHD had

higher rates of omission and commission errors than controls, these differences did not reach significance. The ER effect on commission errors was not significant however the fastest and the slowest ERs produced greater percentage of omission errors for both groups.
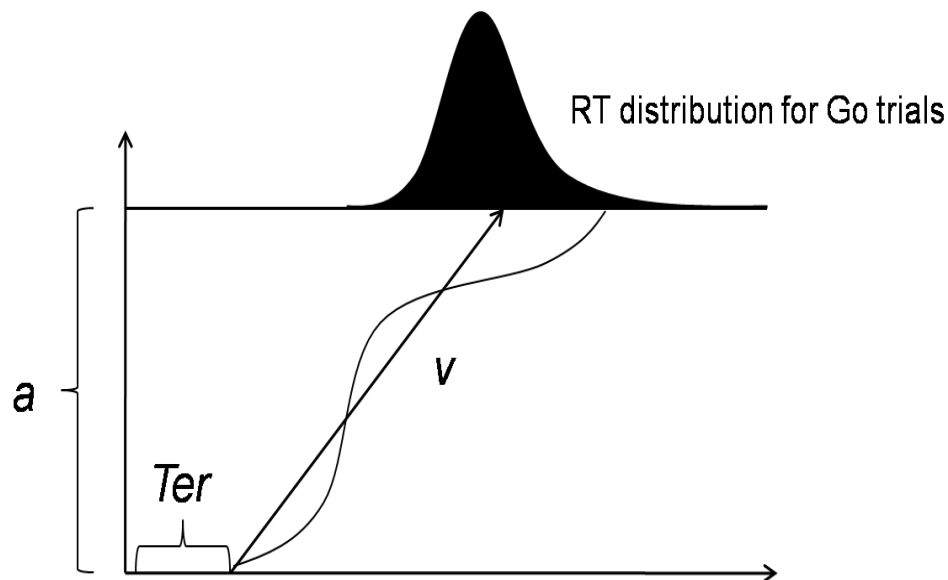

Figure 1. Graphical representation of the single-boundary diffusion model with parameters and reaction time distributions for Go trials. *v*=Mean drift rate. *Ter*=Non-decision time. *a*=Boundary.

Diffusion Model Analysis

Parameter estimates for ADHD and control groups derived from DM analyses are presented in Table 2 as well as the results of statistical comparisons. The KS statistic indicated misfit for only two participants' data confirming that the assumptions made for the different conditions within the task described the RT distributions well. These three participants were excluded from the statistical analysis.

The children with ADHD had significantly lower drift rates than the controls. The drift rate decreased as the ER slowed however the groups were not differentially affected from ER (Figure 2). The boundary parameter was greater in the ADHD group (Figure 3). The fastest and the slowest ER conditions produced lower boundary indicated by a quadratic trend however there was no interaction between group and ER for boundary. For non-decision time, there was no group difference although ER had a very

strong effect - with the non-decision times increasing linearly as the ER slowed. The children with ADHD had shorter non-decision times at fast ERs and slower non-decision times at slow ERs (Figure 4) and the interaction between group and ER was significant with linear contrasts.

Table 2. Means and Standard Deviations (SD) for the variables at each event rate condition.

Variable	Event Rate				ANOVA			ES
	1 sec	2 sec	4 sec	8 sec	Group	ER[b]	Group x ER	
MRT (msec)					$F_{(1,52)}$ 7.35*	$F_{(1,52)}$ 168.9**	$F_{(1,52)}$ 6.06*	0.77
ADHD	438.7 (86.2)	521.0 (111.3)	619.3 (169.6)	715.5 (205.7)				
Control	395.9 (76.5)	456.9 (96.1)	521.0 (125.8)	585.5 (119.9)				
EOC (%)					$F_{(1,52)}$ 2.47	$F_{(1,52)}$ 3.11	$F_{(1,52)}$ 0.03	0.42
ADHD	45.1 (17.0)	43.6 (18.2)	42.5 (25.0)	39.2 (24.6)				
Control	38.2 (14.6)	34.6 (19.3)	33.1 (21.7)	33.4 (23.0)				
EOO (%)					$F_{(1,52)}$ 3.77	$F_{(1,52)}$ 21.62**	$F_{(1,52)}$ 1.15	0.53
ADHD	13.4 (8.5)	6.8 (7.8)	5.6 (7.6)	7.8 (8.3)				
Control	8.0 (9.7)	4.1 (4.1)	3.6 (5.1)	5.2 (7.7)				

					$F(1,52)$	$F(1,52)$	$F(1,52)$	0.92
SDRT					10.47*	34.08**	0.02	
ADHD	167.5	234.4	222.6	234.7				
	(38.4)	(90.9)	(76.0)	(91.5)				
Control	133.2	170.8	170.0	194.0				
	(37.0)	(57.1)	(66.9)	(79.4)				
					$F(1,50)$	$F(1,50)$	$F(1,50)$	0.83
v (drift rate)					8.82*	46.27**	0.007	
ADHD	3.43	3.25	3.1	2.56				
	(0.72)	(0.66)	(0.73)	(0.77)				
Control	4.04	3.7	3.56	3.14				
	(0.96)	(0.75)	(0.83)	(0.85)				
					$F(1,50)$	$F(1,50)$	$F(1,50)$	0.87
a (boundary)					9.86*	11.77*	2.26	
ADHD	1.77	1.84	1.79	1.66				
	(0.24)	(0.31)	(0.31)	(0.31)				
Control	1.59	1.6	1.55	1.48				
	(0.23)	(0.25)	(0.29)	(0.29)				
					$F(1,50)$	$F(1,50)$	$F(1,50)$	0.1
Ter (non-decision time)					0.12	161.0**	5.06*	
ADHD	0.17	0.19	0.30	0.41				
	(0.05)	(0.06)	(0.11)	(0.14)				
Control	0.18	0.22	0.30	0.35				
	(0.06)	(0.06)	(0.08)	(0.11)				

Note: MRT = Mean Reaction Time, EOC = Errors of Commission, EOO = Errors of Omission, SDRT = Standard Deviation of Reaction Time, ER = Event Rate, ES=effect size is Cohen's *d* for the Group effect, [b]ER and interaction analyses have been performed with the use of linear contrasts, *$p < 0.05$, **$p < 0.001$.
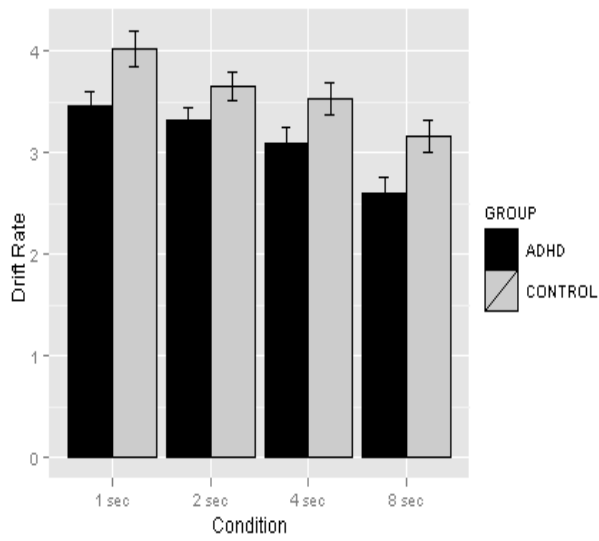
Figure 2. The effect of event rate on drift rate for each group. Error bars=Standard error of the mean.
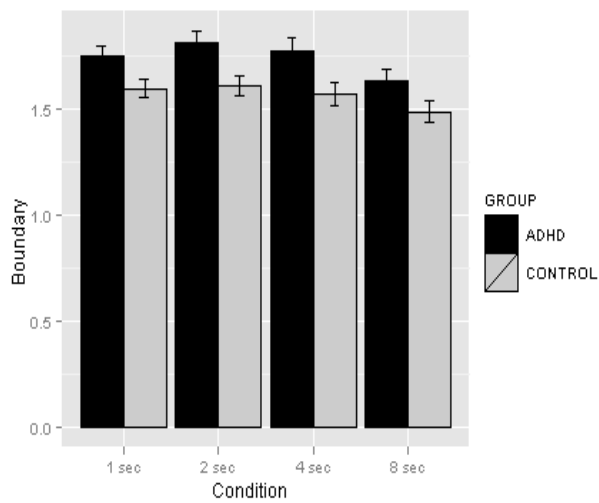

Figure 3. The effect of event rate boundary for each group. Error bars=Standard error of the mean.
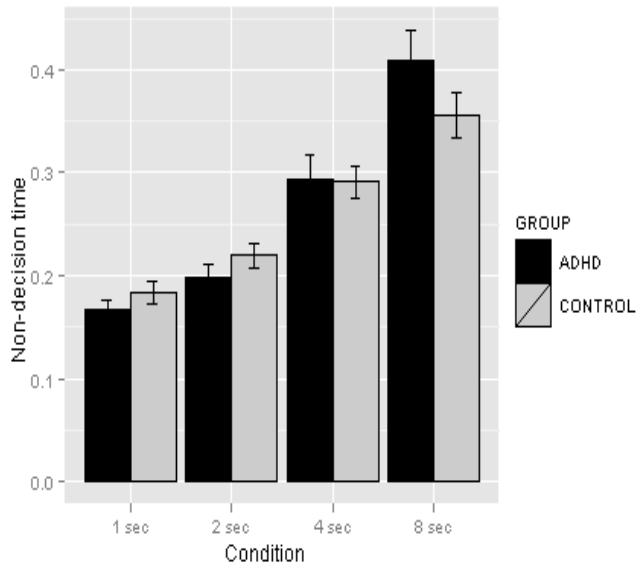
Figure 4. The effect of event rate on non-decision time for each group. Error bars = Standard error of the mean.

DISCUSSION

In this study we explored the neuropsychological basis of ER effects on performance of children with and without ADHD using a DM adapted to the GNG task. Based on previous studies, we predicted that the ADHD group would have slower drift rates and we predicted no difference in boundary parameter. In addition, we predicted that the ER would affect the non-decision time, which includes the motor preparation step, with the ADHD group being more sensitive to this effect. This is because the SRD model postulates that the ER affects the motor preparation level and the ADHD group has a regulatory deficit at this level with fast ER effects producing over-activation and the slow ERs producing under-activation.

As predicted, the ER manipulation exerted its greatest effect on non-decision time with increased non-decision times at slow ERs. In addition, although there was no group difference for non-decision time, there was a significant interaction between group and ER with the ADHD children having shorter non-decision times at fast and longer non-decision times at slow ERs. As mentioned before, the non-decision time comprises both encoding and motor preparation steps. Therefore the ER and the interaction effects may involve both of these steps. However, evidence from previous research suggests that the ER primarily affects the level of motor activation and there is

no evidence that encoding is affected by ER manipulation (Sanders, 1983; Sergeant, 2005). Therefore our findings are more likely to indicate that children with ADHD have over-activation at fast ERs and under-activation at slow ERs.

The speed of information processing was highest at fast ERs and decreased as ER slowed. This finding shows that the under-activation at slower ERs also affects the speed of information uptake. We also found that the children with ADHD had lower drift rates than controls. Together with the current study there have been a number of DM studies which consistently showed that the individuals with ADHD have a slow and sluggish information processing style (Karalunas et al., 2012; Karalunas & Huang-Pollock, 2013; Metin et al, 2013) but the group difference in drift rate was not affected by ER. On the other hand the group difference in drift rate was not affected by ER. This finding suggests that the slower information processing in ADHD may not be sensitive to ER manipulation. However other types of energetic manipulations such as reward or stimulant drugs might increase the speed of information processing and the effects of such factors on drift rate in ADHD are to be explored by future studies.

For boundary, we observed that the fastest and slowest conditions (1 sec and 8 sec ISI) produced the lowest boundary for both ADHD and control children. It is important to note that these conditions also produced the highest rates of omission errors. Therefore the lower boundary at fastest and slowest conditions may be the results of a compensatory strategy by which the participants aimed to alleviate higher rates of omissions. We also observed that the children with ADHD had greater boundary parameters than controls suggesting a problem with regulating the SATO. Increased cautiousness in ADHD appears counterintuitive because impulsivity is one of the main characteristics of ADHD and therefore one might predict that the boundary would be lower for the ADHD group reflecting an impulsive decision making style. However both our study and the previous studies which used DM (Karalunas et al., 2012; Karalunas & Huang-Pollock, 2013; Metin et al, 2013; Mulder et al., 2010) indicate that children with ADHD are in fact not more impulsive in speeded RT tasks but that they have a deficit in regulating the SATO according to the context (Mulder et al.,2010).

While analyzing the same dataset with an ex-Gaussian model (Metin et al., submitted for publication), we found that *mu* increased as a function of ER. In the current study we found the same pattern for the non-decision time parameter of the DM suggesting that the *mu* parameter is related to non-decisional and probably the

motor execution part of the information processing framework. Using the ex-Gaussian model we also found an inverted U pattern for the *sigma* parameter which was accentuated for the ADHD group. This pattern was not observed in the current analysis for any DM parameter. This is probably due to the fact that the Gaussian variability, *sigma*, only weakly affects the DM parameters (Matzke & Wagenmakers, 2009). It is more likely that *sigma* is related to the effort pool (Metin et al., submitted). An increase in *Sigma* at very fast and very slow ERs might indicate that more effort is needed to regulate the level of arousal and activation with the ADHD group being less efficient in effort allocation and thus having greater *sigma* at these conditions. This hypothesis needs to be explored by more objective measures of effort such as event related potentials.

Finally, it is also noteworthy that neither drift rate nor boundary differences were affected from ER. These negative findings indicate that individuals with ADHD show deficits at different information processing stages and not all these deficits are related to state regulation problems. Neuropsychologically, ADHD is a heterogeneous condition (Nigg, Willcutt, Doyle, & Sonuga-Barke, 2005) and a single model may not be sufficient to explain the whole spectrum of neuropsychological dysfunctions. Therefore the future theoretical model of ADHD should take into account the casual heterogeneity and presence of separate etiological pathways (Kuntsi et al., 2010).

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CHAPTER 6

EFFECTS OF ENVIRONMENTAL STIMULATION ON IMPULSIVE CHOICE IN ADHD: A "PINK NOISE" STUDY [1]

ABSTRACT

Background: The preference for sooner smaller over larger later rewards is a prominent manifestation of impulsivity in ADHD. According to the State Regulation Deficit (SRD) model, this impulsive choice is the result of impaired regulation of arousal level and can be alleviated by adding environmental stimulation to increase levels of arousal. **Method**: In order to test this prediction we studied the effects of adding background "pink noise" on impulsive choice using both a classical and new adjusting choice delay task in a sample of 25 children with ADHD and 28 controls. **Results**: Children with ADHD made more impulsive choices than controls. Adding noise did not reduce impulsive choice in ADHD. **Conclusion**: The findings add to the existing evidence on impulsive choice in ADHD but no evidence is found for the SRD model's explanation of this behavioral style. Alternative explanations for impulsive choice in ADHD are discussed.

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[1] Based on Metin, B., Roeyers, H., Wiersema, J. R., Van der Meere, J.J., Gasthuys, R., & Sonuga-Barke, E. (In press). Environmental Stimulation Does Not Reduce Impulsive Choice in ADHD: A "Pink Noise" Study. Journal of Attention Disorders.

INTRODUCTION

Attention-Deficit/Hyperactivity Disorder (ADHD) is a lifespan disorder characterized by symptoms of inattention and/or hyperactivity-impulsivity (DSM-IV-TR, American Psychiatric Association, 2000). These symptoms can lead to substantial deficits in social and academic functioning. The State Regulation Deficit (SRD) model postulates that these symptoms and deficits occur because of problems with regulating energetic factors such as stimulus-related phasic alertness (arousal) and tonic readiness to respond (motor activation) in response to the changing requirements of environmental settings (Sergeant, 2005; van der Meere, 2002). The model is based upon the cognitive energetic framework of Sanders (1983) which incorporates concepts such as effort, arousal and activation into the basic information processing framework so that task performance is predicted to be influenced not only by cognitive capacity but also by environmentally-determined levels of arousal and activation and the extent to which variations in these energetic factors can be managed to ensure optimal performance.

The SRD model has typically been invoked to explain the effect of manipulating contextual factors on information processing performance. For instance, there is a well – established effect of event rate (ER) on performance (Sergeant, 2005; van der Meere, 2002). Several studies have shown that individuals with ADHD are more vulnerable to ER manipulations than their peers across a range of tasks involving different cognitive processes (Chee, Logan, Schachar, Lindsay, & Wachsmuth, 1989; Conte, Kinsbourne, Swanson, Zirk, & Samuels, 1986; Metin, Roeyers, Wiersema, van der Meere, & Sonuga-Barke, 2012; Scheres, Oosterlaan, & Sergeant, 2001; van der Meere, Stemerdink, & Gunning, 1995; see van der Meere, 2002 and van der Meere, Börger, & Wiersema, 2010 for reviews). According to the SRD model a fast ER is predicted to lead to over-activation and fast, impulsive responses; while slow responses and inattentive errors are predicted under slow ER because of under-activation (Metin et al., 2012). In one study non-optimal states were also induced by stimulant medication which normally improves performance under slow ERs but seemed to trigger more errors when combined with a fast ER (van der Meere, Shalev, Börger, & Wiersema, 2009). This finding has been interpreted as the result of the combination of two putative stimulating factors (fast ER and medication).

The effect of external energetic factors on information processing performance in ADHD has been well studied. In contrast, there have been no studies of their effects

on performance on tasks requiring little or no information processing. For instance, children with ADHD prefer smaller sooner (SS) over larger later (LL) rewards more than typically developing children on simple choice tasks (Antrop et al., 2006; Bitsakou, Psychogiou, Thompson, & Sonuga-Barke, 2009; Kuntsi, Oosterlaan, & Stevenson, 2001; Marco et al., 2009; Sonuga-Barke, Taylor, Sembi, & Smith, 1992). Typically this has been explained as either the result of (i) an impulsive drive for immediate reward (IDIR; Marco et al., 2009); (ii) heightened discounting of delayed rewards (Demurie, Roeyers, Baeyens, & Sonuga-Barke, 2012); (iii) an aversion for delay (Sonuga-Barke, Sergeant, Nigg, & Willcutt, 2008) or (iv) a breakdown in inhibitory-based executive processes (Barkley, 1997).

Sonuga-Barke and colleagues recently extended the SRD model to explain impulsive choice in ADHD (Sonuga-Barke, Wiersema, van der Meere, & Roeyers, 2010). According to this extension of the SRD account, impulsive choice in ADHD results from impaired regulation of energetic state created during delay periods. As a consequence, children with ADHD are predicted to avoid low arousing or activating contexts (i.e., long delays) by seeking immediate stimulation or more frequent rewards in the environment (i.e., by choosing SS over LL; Sonuga-Barke et al., 2010). A key prediction of the SRD model is that if arousal or activation is experimentally increased during delay periods to more optimal or acceptable levels, impulsive choices should reduce – children with ADHD will then tend to choose relatively more LL over SS outcomes.

In order to test this prediction we examined if adding extrinsic random environmental noise (in this case "pink noise") during delay affects SS over LL preference in children with ADHD. There is good evidence that adding environmental stimulation in this way modifies arousal level. For instance, a high intensity noise level has been used successfully in several studies to improve attention capacity and selectivity (Baker & Holding, 1993; Davies & Jones, 1975; Hockey, 1970; Söderlund, Sikström, Loftesnes, & Sonuga-Barke, 2010; Söderlund, Sikström, & Smart, 2007; see Davies, 1968 and Sanders, 1983 for reviews) and it has been shown that high intensity noise affects autonomic indices of arousal such as heart rate and skin conductance (Davies, 1968; Hanson, Schellekens, Veldman, & Mulder, 1993). Furthermore, these effects appear to follow an inverted-U shaped curve: Noise increases performance when the subject is in an under-aroused state but addition of noise to an over-aroused state disturbs performance (Davies, 1968; Sanders, 1983). The beneficial effect of noise has also been confirmed in

children with ADHD. Söderlund and colleagues demonstrated that the memory performance of children with attention problems improved under noise conditions while the performance of controls got worse (Söderlund et al., 2007, 2010).

Although no studies have examined the effects of adding random noise on ADHD children's impulsive choice, one study has explored the effects of adding visual stimulation. In this study it was shown that presenting cartoons during delay differentially reduced impulsive choice in ADHD relative to typically developing controls (i.e., decreased preference for SS rewards in children with ADHD; Antrop et al., 2006). These results may be interpreted as a positive effect of environmental stimulation as predicted by the SRD model. They can also be explained by a decrease in the perception of the passage of time brought about by the "non-temporal" stimulation employed (i.e., watching absorbing cartoons will reduce the perception of the length of the delay period). Therefore, "pink noise", which would appear to be neutral with regard to time perception (not absorbing or interesting), provides a specific test of the SRD predictions.

In this study we measured impulsive choice by using two separate paradigms. First, we used a standard choice delay task (CDT) during which the children had to choose between SS and LL rewards (Sonuga-Barke et al., 1992). Second, in or to examine the generalization of the effects of ADHD and noise across tasks we supplemented the original measure with an adjusting choice delay task (A-CDT). In this task the delay for LL was adjusted on each trail, either up or down depending on the choices of the preceding trials, to find the point of delay indifference between SS and LL options. We predicted that children with ADHD would make more impulsive choices on both tasks (i.e., choosing SS more than LL relative to controls and have a lower point of delay indifference). In line with the SRD model, we predicted that adding "pink noise" would reduce impulsive choice in children with ADHD by increasing their preference for LL and increasing the point of delay indifference in the direction of that displayed by typically developing controls.

METHOD

Ethics approval was received from the Ethical Committee of Ghent University, Faculty of Psychology and Educational Sciences. All children and parents gave written informed consent before participating in the study.

Participants

Twenty-five children with ADHD and 28 typically developing controls were recruited for the study. All children were between 8 and 12 years old and had a total IQ (TIQ) above 80. TIQ was assessed by the short form of the Wechsler Intelligence Scale for Children – 3rd edition (WISC-III; Grégoire, 2005). The groups did not differ in mean age ($F(1,51) = .95$, $p = .33$) and TIQ ($F(1,51) = 1.1$, $p = .3$). There were significantly more boys in the ADHD than the control group ($\chi^2(1, N = 53) = 4.77, p = .03$). Detailed information for TIQ, age and gender composition can be found in Table 1. The children did not have a history of hearing loss or a neuropsychiatric condition other than ADHD.

The children in the control group were recruited from local schools and scout camps. All children were screened with the Disruptive Behaviour Scale (DBD; Pelham, Gnagy, Greenslade, & Milch, 1992) for ADHD, Oppositional Defiant Disorder (ODD) and Conduct Disorder (CD). To exclude Autistic Spectrum Disorders the Social Communication Scale (SCQ; Rutter, Bailey, & Lord, 2003) and Social Responsiveness Scale (SRS; Constantino & Gruber, 2005) were administered to both groups. The DBD scores for ODD and CD can be found in Table 1. Children with ADHD were recruited from the community and an official diagnosis by a clinician was required. The ADHD, ODD and CD diagnoses were ascertained by a DSM-IV oriented parent interview (behavior module of the Diagnostic Interview Schedule for Children, DISC-IV; Shaffer, Fischer, Lucas, Dulcan, & Schwab-Stone, 2000) administered by an experienced clinical psychologist. Seventeen children were classified as ADHD-combined type, 6 children as inattentive type and 2 children as hyperactive-impulsive type. In addition, 10 children received ODD diagnosis and one had CD diagnosis. The children using stimulant medications were instructed to discontinue their medication 24 hours before testing.

Table 1. The characteristics of the ADHD and control group and the scores for comorbid symptoms

Measure	Group	
	ADHD (*N* = 25)	Control (*N* = 28)
Age in months[a]	122.1 (14.5)	126.2 (15.9)
Male:Female	22:3	16:12
TIQ[a]	107.4 (10.7)	110.5 (11.3)
ODD[b]		
Mean and SD	12.7 (1.8)	10.7 (.98)
Range[c]	10-16	10-13
CD[b]		
Mean and SD	11.7 (2.3)	11.1 (1.1)
Range[c]	10-19	10-14

Note: [a]Means and standard deviations (SD), [b]Measured by Disruptive Behavior Disorders Scale, [c]Range of standard scores, TIQ = total IQ, ODD = Oppositional Defiant Disorder, CD = Conduct Disorder.

Procedure

The children were tested in a quiet room. During testing an experimenter sat out of sight of the child. The CDT was always completed first and the A-CDT second. The children were told that they would only receive the money that they collected during the tasks and the maximum amount that they could earn in the experiment was 12 euro. However, regardless of the points earned during the tasks, all children received 15 euro. This was accomplished by using a computerized head or tails game after the experimental sessions which always ended with a win. Children were tested for IQ after the choice tasks. Meanwhile the parents of the children with ADHD were interviewed in another room.

Tasks

Two different tasks measuring impulsive choice were programmed using E-prime software (version 2.0). In both tasks the children chose repeatedly between SS and LL rewards. At the start of each trial in both tasks the children saw two coins on the computer screen (5 cent and 10 cent). They were told that if they chose 5 cent, they would receive it immediately; but for the 10 cent reward they would have to wait for a while. The waiting time was displayed under the coins. The coins were displayed on the screen until the children made a response. Immediately after the response the delay period started during which a fixation cross was displayed. The duration of delay was always 2 sec for SS rewarded. The delay to the LL reward varied across task. At the end of each trial participants were shown the amount that they had earned on that trial (i.e., 5 or 10 cent), the total amount of money earned up to that point and the number of remaining trials. This information remained on the screen until the children made a response. There was no post-reward delay period and each new trial followed immediately after the reward was delivered in the previous trial. In both tasks the noise and no-noise trials were blocked and blocks were randomized at the individual level for each participant. The participants were allowed to take a break between the two tasks.

CDT: Children chose between fixed SS (5 cent after 2 sec) and LL (10 cent after 30 sec) options. The task consisted of a total of 40 trials (20 under noise and 20 without noise). The dependent variable was the percentage of LL choices.

A-CDT: In this task the same 5 and 10 cent rewards were used for the SS and the LL option respectively. The delay for SS was always 2 sec (as in the CDT). Initially, the delay for LL was set to 9 sec and adjusted either up or down at the end of each trial as a function of the choice made in that trial. If the child chose SS the delay to LL was reduced, while if the child chose LL the delay to that reward was increased. The increases or decreases in delay were exponential based on the power of 1.3 but were rounded to an integer. The delay for LL decreased until 1.3^3 (2.86) and increased up to 1.3^{13} (39.4) sec. The task consisted of 80 trials. The dependent variable was the adjusted mean delay for a LL reward, reflecting the point of delay indifference between the SS

and LL option. The children completed two sessions of 20 trials under noise and two sessions of 20 trials in the neutral condition.

"Pink Noise"

Standard whole ear headphones were used to deliver 80 dB "pink noise" during the noise sessions. This choice of noise level was made because the same level was previously shown to improve performance of children with ADHD (Söderlund et al., 2007, 2010). "Pink noise" differs from true "white noise" in that the very high frequencies are trimmed to make it less aversive especially at higher intensity levels. The noise level was calibrated regularly throughout the study by using professional sound intensity meters implanted to an artificial head.

Analysis

The statistical analyses was conducted using SPSS statistical software (version 19). The results were analyzed within a single 2 x 2 x 2 ANOVA with noise ("pink noise" versus no noise) and task (CDT vs. A-CDT) as within-subject factors and group (ADHD vs. control) as a between subject factor.

RESULTS

LL preference on the CDT and mean adjusting delay on the A-CDT were strongly correlated ($r = .8$ and $r = .74$ for noise and no-noise conditions respectively). The effect of TIQ and comorbid symptoms (ODD/CD) were explored using correlation analyses, however they were not correlated with performance on either task ($r < .3$ and $p > .05$ for all dependent variables). For the CDT, age correlated with LL preference in the no-noise session ($r = .32$, $p = .02$), however the correlation was not significant for the noise session ($r = .22$, $p = .11$). For the A-CDT, age correlated significantly with the mean adjusting delay in the noise session ($r = .30$, $p = .02$). The correlations for the no-noise session of this task was not significant ($r = .22$, $p = .11$). The inclusion of age as a covariate did not change the results of the analyses presented below.

The summary statistics for task performance can be found in Table 2. The children with ADHD preferred the LL option less than controls ($F(1,51)=8.33$, $p=.006$;

effect size Cohen's $d = .79$). There was no effect of noise on LL preference ($F(1,51)=.09$, $p=.77$) and the interaction between group and noise was not significant ($F(1,51)=.07$, $p=.79$).The interaction between group and task approached significance ($F(1,51)=3.55$, $p=.07$) with greater group difference at A-CDT task (the effects sizes were .72 vs .87 for CDT and A-CDT respectively). There was no interaction between noise and task ($F(1,51)=.05$, $p=.82$) and no three way interaction between noise, task and group ($F(1,51)=.89$, $p=.35$).

Table 2. The performance[a] of the ADHD and control group on both tasks.

Measure	Condition	
	Noise	No-Noise
CDT (% LL preference)		
ADHD	44.2 (28.6)	43.2 (25.9)
Control	61.3 (29.9)	64 (30.8)
A-CDT (Mean Adjusting Delay[b])		
ADHD	12.1 (9.9)	13.2 (9.5)
Control	22 (12.8)	21.4 (12.1)

Note: [a]Means and standard deviations (SD) for each dependent variable, [b]seconds, CDT = Choice Delay Task, A-CDT = Adjusting Choice Delay Task, LL= Large Later reward.

DISCUSSION

In this study, we used two different tasks to test the extension of the SRD model of ADHD performance proposed by Sonuga-Barke and colleagues (2010): the prediction that impulsive choice (preference for SS over LL) in ADHD would be reduced by increasing arousal during delay by adding "pink noise". There were a number of findings of note.

First, as seen in many previous studies children with ADHD chose SS over LL options more often than controls (Antrop et al., 2006; Bitsakou et al., 2009; Kuntsi et al., 2001; Marco et al., 2009; Sonuga-Barke et al., 1992; see also Bidwell, Willcutt, Defries, & Pennington, 2007; Scheres et al., 2006; Sjöwall, Roth, Lindqvist, & Thorell, 2012; for negative results) with case control effect sizes similar to those reported in previous

reviews (Sonuga-Barke et al., 2008). This finding is consistent with a number of theoretical models. For instance, the Delay Aversion (DAv) model, as recently extended (Marco et al., 2009, Sonuga-Barke et al., 2010), postulates that inefficient neural signaling of delayed rewards in dopamine-modulated neural circuits leads to an impulsive drive for immediate rewards (IDIR), which over time creates negative affect in response to delay-rich settings (Sonuga-Barke et al., 2010). In choice settings, such as those presented in the current study, these two components (i.e., IDIR and delay aversion) produce impulsive choice of SS over LL options (Marco et al., 2009). Because a post-reward delay period was not included in our tasks the relative importance of delay aversion and IDIR could not be estimated. Interestingly, performance on the two tasks was correlated but the effect size in the A-CDT was higher than for the classical CDT. This suggests that the A-CDT will be a useful addition to neuropsychological batteries assessing reward related performance in ADHD.

Second, there was no beneficial effect of adding "pink noise" in the ADHD group in terms of reducing impulsive choice or increasing preference for LL options. This suggests that while in principle the SRD model can explain SS over LL preference as an expression of seeking optimally/acceptably arousing settings (Sonuga-Barke et al., 2010), the current results are not consistent with such an account – adding "pink noise" which should increase arousal levels during delay did not reduce SS preferences. However, it should be noted that the cognitive energetic model (Sanders, 1983) and the SRD model (Sergeant, 2005; van der Meere, 2002) postulate that there are two main energetic factors which influence cognitive performance: (i) arousal, which is related to stimulus related alertness and (ii) activation, which is related to tonic motor readiness to respond. Hence, it cannot be excluded that SS preference in ADHD may be related to activation instead of arousal, which would imply that children with ADHD try to increase their motor activation to a desirable state by choosing the more frequent stimulus (i.e., SS reward). Future research should evaluate whether or not this is the case.

Third, there are a number of additional implications of this negative result. Several studies have provided robust evidence for the impact of cognitive energetic factors on ADHD-related deficits in information processing tasks as predicted by the SRD model (Chee et al.,1989; Conte et al., 1986; Epstein et al., 2011; Kuntsi, Wood, van der Meere, & Asherson, 2009; Metin et al., 2012; Scheres et al., 2001; van der Meere, et al., 1995, 2009). Findings from electrophysiological studies have also supported the SRD

model by showing that children with ADHD have a deficit in adjusting the allocated effort in suboptimal settings (Wiersema, van der Meere, Antrop, & Roeyers, 2006; Wiersema, van der Meere, Roeyers, Van Coster, & Baeyens, 2006). Furthermore it has been shown that "pink noise" itself improve information processing performance in ADHD (Söderlund et al., 2010). Given this, it may be the case that cognitive (i.e., tasks with a major information processing demand) and non-cognitive performance in ADHD (i.e., as in simple reward choice tasks used in the current study) are mediated by different neuropsychological systems – a view consistent with recent models highlighting the pathophysiological heterogeneity in ADHD (Kuntsi et al., 2010; Sonuga-Barke et al., 2010). Arousal regulation mainly involves the noradrenergic system (Berridge & Waterhouse, 2003). The noradrenergic neurons originating from the locus coeruleus are distributed to the entire brain and their activation level determines the arousal state of the organism (Aston-Jones, Rajkowski, & Cohen, 1999). On the other hand, delay discounting is mainly associated with dopamine and serotonin systems (Cardinal, 2006; Gregorios-Pippas et al., 2009). The ventral striatum, which receives extensive dopaminergic input from the ventral tegmentum, is involved in coding delayed reward. Our findings suggest that these two systems may be independently involved in ADHD pathogenesis. In terms of its impact on reward related choice performance, extrinsic stimulation may need to be of a particular kind to have an effect. For instance, the DAv model, like the SRD model, predicts that environmental stimulation during delay periods should reduce impulsive choice. However, the DAv model specifies a different mechanism (i.e., environmental stimulation increases the perception of the passage of time and so reduces delay aversion) and makes a different prediction (i.e., only so called non-temporal stimulation that is interesting and engaging will reduce impulsive choice). This effect was seen in the study of Antrop and colleagues (2006) where presenting cartoons during delay normalized impulsive response style.

The current study had many strengths but there were also some limitations. First, there was no direct physiological measure of arousal and so we could not confirm that "pink noise" had the predicted effects on arousal. However, previous studies have confirmed such arousing effect of noise by using both behavioral (Davies, 1968) and electrophysiological measures (Hanson et al., 1993). Second, only one level of "pink noise" was used and if there is an inverted-U shaped relationship between noise level and performance, as predicted by certain accounts (Söderlund, 2007), it is possible that

the noise level was not optimal in this context – either being too low to increase arousal or to high leading to over-arousal. Third, we did not include an alternative noise comparison condition which would allow a direct test of the importance of the non-temporal component of environmental stimuli.

In summary, our results confirm that children with ADHD make more impulsive choices than typically developing children. We did not find any beneficial effect of adding "pink noise" during delay as predicted by models which explain impulsive behavior in ADHD with impaired regulation of arousal. It is possible that impaired arousal regulation and delay aversion make independent contributions to the neuropsychological spectrum of ADHD.

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CHAPTER 7

GENERAL DISCUSSION

ABSTRACT

The aim of this doctoral dissertation was to compare two competing models (State Regulation Deficit and Delay Aversion) of Attention-Deficit/Hyperactivity Disorder (ADHD) based on their predictions for task performance and impulsive choice. In this final chapter we will give an integrated overview of the empirical chapters with recapitulating the goals of the dissertation. Then, we will discuss the implications of the results for the existing neuropsychological theories of ADHD and clinical practice. We will also describe the limitations of the studies and suggest objectives for future research.

OVERVIEW OF THE CHAPTERS

The main goal of this dissertation was to compare State Regulation Deficit (SRD) and Delay Aversion (DAv) models, both of which predict that the performance deficits of individuals with ADHD depend on the environmental and motivational context. The SRD model focuses on arousal, activation, and effort and it postulates that individuals with ADHD have a problem with regulating their arousal and activation levels via allocation of necessary effort required to compensate at sub-optimal settings. The sensitivity of children with ADHD to event rate (ER) manipulation, which affects the level of activation, has been accepted as the hallmark manifestation of the SRD model (for reviews see Sergeant, 2005; van der Meere, 2002). In contrast, the DAv model postulates that the primary deficit arises from the negative affective state induced by delay, which leads to a reduced tolerance for future rewards under some conditions. The increased preference of ADHD children for small sooner (SS) over large later (LL) rewards has been accepted as the hallmark manifestation of the DAv model (Sonuga-Barke, Wiersema, van der Meere, & Roeyers, 2010). In order to compare these two models we used the hallmark manifestations of the two models and explored whether these manifestations are related to one construct but not to the other – whether ER effects can be explained by DAv or whether impulsive choice can be explained by SRD.

In Chapter 2, the SRD and DAv models were compared on their predictions for ER effects on Go/No-Go performance in a meta-analytic study. The SRD model predicted that the ADHD group would have performance deficits both at fast and slow ERs due to over and under-activation, respectively. On the other hand the DAv model predicted deficits only at slow ERs due to longer delay between stimuli. The results showed that the ADHD group made more commission errors at fast ERs and had slower reaction times (RTs) at slow ERs confirming the predictions of the SRD model. The effects at the fast event rate could not be explained by the DAv model. That being said, it is important to note that ER effects cannot explain all deficits in ADHD highlighting the complex pathophysiology of the disorder. For instance, although the magnitude of the case-control effect size (ES) for the standard deviation of reaction time (SDRT) was large, the ESs were not affected by ER suggesting that SDRT was a non-specific marker of SR deficits.

In Chapter 3, we addressed two major limitations of the studies included in the meta-analysis by conducting our own experiment on ER and performance in ADHD. First, most of the studies included only two ERs and when they included three, the range of ERs did not cover very fast and very slow presentation rates. The second issue raised by the meta-analysed studies was related to the measure of reaction time variability. According to the SRD model, variability is a primary manifestation of energetic processes (Sanders, 1983). However we did not find an effect of ER on variability in the meta-analysis. One possible explanation for this negative finding is that most of the previous studies reported a non-specific index of variability (SDRT) which cannot differentiate between the Gaussian variability and the variability caused by occasional slow responses – perhaps linked to attentional lapses. In this study we used a Go/No-Go task with four different ERs covering both very fast and very slow presentation rates. In addition we segregated the non-specific response time variability into Gaussian variability (*sigma*) and variability due to slow responses (*tau*). The SRD model predicted that the *sigma* would be greater for the ADHD group at ER extremes and the *tau* parameter, which represented the attentional lapses, would increase linearly with a greater increase for the ADHD group. The DAv model predicted that that the deficits would manifest only at slow ERs. The results partially confirmed the predictions of the SRD model, with the ADHD group having a greater *sigma* in the 1 sec and 8 sec conditions. However, against the predictions of the SRD model, the ER effect on *tau* was not significant.

Important theories of ADHD postulate that executive dysfunction is the core deficit in ADHD (Barkley, 1997). However, these accounts were challenged by more recent studies that showed that executive dysfunction was neither necessary nor sufficient for ADHD (Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005). According to the SRD model, ADHD children have a problem with regulating the levels of activation and arousal. As these energetic resources affect the basic and executive tasks equally, the performance deficits in ADHD should be the same in tasks with and without executive demands. In Chapter 4, we aimed to explore the relative contribution of basic processing deficits to executive dysfunction. We compared the performance of children with ADHD in two types of tasks: a task that requires executive control and a basic perceptual decision making task. As impulsivity is one of the main characteristics of ADHD, one might expect a fast but inaccurate response style in neuropsychological tasks. However, previous studies showed that children with ADHD have a slow-inaccurate

response style (see van der Meere, 2002 for a review), suggesting problems with information uptake. To explore the contribution of impulsivity and speed of information processing to ADHD-related deficits, we disentangled the basic elements of cognitive processing with a diffusion model (DM) that can estimate separate parameters for different elements, such as speed-accuracy trade-off (boundary), accumulation of information (drift rate), motor preparation, and encoding (non-decision time). We found that regardless of the executive demand, ADHD information processing was characterized by slow processing speed (lower drift rate). We did not find a difference in decision boundary, suggesting that the children with ADHD were no more willing than controls to terminate decision processes prematurely. In addition, the ADHD group had shorter non-decision times in both tasks.

The shorter non-decision time in ADHD suggests deficits at the encoding or motor preparation level. However older studies suggested that the children with ADHD have deficits at motor preparation level and the encoding is intact in ADHD (van der Meere, van Baal, & Sergeant, 1989). According to the SRD model, motor preparation deficit also makes the children with ADHD more sensitive to ER (Sergeant, 2005; van der Meere, 2002). The model predicts that fast and slow ERs produce over and under-activation respectively. In Chapter 5, we re-analyzed the data presented in Chapter 3 with a DM adapted to a Go/No-Go task to test this hypothesis. From the SRD model, we predicted that the ER would affect primarily the non-decision time, which includes the motor preparation process, and that the ADHD group would be more sensitive to ER effects on non-decision time due to deficits at the motor preparation level. The results indicated that the ER affected both the accumulation of information (drift rate), motor preparation (non-decision time) and speed-accuracy trade-off (SATO). Consistent with the predictions of the SRD model the ADHD group had shorter non-decision times at fast ERs and longer non-decision times at slow ERs. In addition, the ADHD children had slower drift rates and greater boundaries, but these group differences were not affected by ER.

In Chapter 6, we tested to what extent poor regulation of arousal state can explain impulsive choice in ADHD. According to the revised SRD model proposed by Sonuga-Barke and colleagues (2010), impulsive choice in ADHD is the results of an attempt to optimize the energetic level. Children with ADHD choose the immediate rewards in an attempt to reach what is for them an optimally stimulating environment –

and they require more stimulation than controls. Therefore the model predicts that the pink noise which increases the level of arousal would alleviate the impulsive choice (Sanders, 1983; Sonuga-Barke et al., 2010). In contrast, the DAv model made no specific predictions for the noise effect as it did not alter the perception of delay. The results were consistent with the DAv model with noise having no effect on impulsive choice in both children with and without ADHD. The results were inconsistent with the SRD model. The pink noise, which increased the arousal state, did not affect impulsive choice.

Is it deficient state regulation or delay aversion?

A summary of the Chapters is presented in Table 1 together with the predictions of the models. The first two studies presented in Chapter 2 and 3 indicated that the ER effects can best be explained by the SRD model, which predicts an inverted U pattern of deficits with fast ERs producing over-activation and slow ERs producing under-activation. In Chapter 2, we observed that the performance corollary of over-activation at fast ERs was a greater percentage of commission errors and the under-activation at slow ERs produced slower RTs. Similarly in Chapter 3, an inverted U pattern of deficits was observed for the *sigma* parameter and this finding can be best explained by the SRD model rather than by the DAv model. In Chapter 4 and 5, we did not aim to compare the SRD and DAv models head to head, but rather tested specific predictions of the SRD model about the effects of executive demands and ER. Consistent with the SRD model, the DM analysis in Chapter 4 showed that ADHD information processing was characterized by slower information uptake, regardless of the executive demands. In addition, in both Chapter 4 and 5 we found deficits related to motor preparation confirming the SRD model predictions. In Chapter 6, we tried to explain a primary manifestation of DAv in ADHD (the increased SS reward preference) with deficits involving the other important energetic pool, namely the arousal. However, the results showed that modification of arousal level with noise did not affect the impulsive choice. These findings together indicate that SR and DAv models cannot explain the manifestations of each other, and therefore they describe independent deficits. The children with ADHD appear to be affected by both types of deficits. The SR deficits make them more sensitive to the environmental factors which affect primarily the behavioural activation while the DAv deficits produce impulsivity.

Table 1. The summary of the Chapters with the models' predictions and findings.

Study	SRD prediction	DAv prediction	Finding
Meta-analysis of ER effects (Chapter 2)	Impulsive errors at fast ERs, slower RTs at slow ERs	Deficits only at slow ERs	In favour of SRD model, but ER cannot explain all deficits
Effects of ER on RT variability (Chapter 3)	Greater *sigma* at fast and slow ERs, greater *tau* at slow ERs	Greater variability only at slow ERs	*Sigma* findings in favour of SRD model, but no effect of ER on *tau*
Contribution of basic processing deficits to executive dysfunction (Chapter 4)	Slow and inefficient processing speed, no effect of executive load	-	Confirming the SRD model (Slower drifts in ADHD group), no effect of executive load to deficits
Effects of ER on ADHD-related deficits (Chapter 5)	ER affects motor preparation. ADHD group more sensitive to ER effects	-	Consistent with SRD predictions for motor preparation. Other type of deficits not affected by ER.
Effects on Pink noise on impulsive choice (Chapter 6)	Pink noise reduces impulsive decision making	No effect of pink noise.	In favour of DAv model

ER=Event Rate, RT=Reaction Time

Implications of the findings for SRD and DAv theories

The SRD model explains the ER effects in terms of deficits at the motor activation stage and effort allocation (Sergeant, 2005; van der Meere, 2002). Our results in Chapter 5 support these predictions by showing that the differential effect of ER mainly relates to the extra-decisional (motor preparation) part of the information processing framework while the deficits involving the decisional components are largely not affected by ER manipulation. According to the model, the suboptimal conditions such as very fast and very slow ERs, cause deficits by producing over and under-activation respectively. Previous studies were not able to disentangle the decisional and extra-decisional stages of the information processing. However newer methods such as DM enabled us to explore the individual contributions of different stages and to better localize the locus of SR deficits. A recently introduced model (Neuroenergetics Mass Action Model, NEMA) proposes that the ADHD-related deficits occur due to inadequate neuronal metabolic supplies (Killeen, Russell, & Sergeant, 2013). The model postulates that attention fluctuates between attentive and inattentive states and individuals with ADHD have insufficient neuronal energy to maintain the attentive state. Therefore, in the slow ERs, which further increase the probability of attentional lapses, the performance deficits become accentuated. From a Cognitive-Energetic perspective (Sanders, 1983), it is plausible that slow ERs produce more attentional lapses. However in Chapter 3, we did not find an effect of ER on *tau*, which was once proposed to be an index of attentional lapses (Leth-Steensen, Elbaz, & Douglas, 2000). We concluded that *tau* may not be a sensitive index of attentional lapses. According to the NEMA, both the probability of a lapse and time required to recover from a lapse are important determinants of performance deficits and the model estimates separate parameters for these constructs. These parameters may provide more sensitive measures for the effect of attention lapses and the cognitive-energetic models could further be developed by integrating the hypotheses related to motor preparation, cognitive effort and attentional lapses.

According to a recent extension of the SRD model the greater SS preference in the ADHD group could be a secondary adaptation to SR deficits: The children with ADHD try to increase their energetic level to a desired stage by choosing the immediately available reward (Sonuga-Barke et al., 2010). Our results in Chapter 6 showed that this

may not be the case. The increased SS reward preference appears to be independent of arousal level. This increased SS preference has been explained by an aversion for delay (Sonuga-Barke et al., 2010), impulsive drive for the immediate reward (IDIR) (Marco et al., 2009), or steeper delay discounting curves (Demurie, Roeyers, Baeyens, & Sonuga-Barke, 2010). According to the IDIR hypothesis, increased SS preference is the result of a primary impulsive drive for immediate reward. On the other hand, according to the DAv model the impulsive choice occurs not only due to IDIR but also due to a general aversion for the delay or a negative affect that develops over-time for delay-rich settings. The DAv model could be improved further by exploring the relative contributions of impulsive drive, delay discounting, and the general aversion for delay to impulsivity in ADHD.

Another important implication of the findings for the DAv model could be about its predictions for the ER effects. Although we did not find evidence supporting these predictions, the experimental setting might also have affected the results. The DAv model makes an important distinction between choice and non-choice settings (Sonuga-Barke et al., 2010). In choice settings, children with ADHD tend to choose the option with shortest delay. In non-choice settings, where delay is externally imposed, they show frustration and increased distractibility. In that sense, the Go/No-Go task that we used to test these predictions is actually a non-choice setting with different ER conditions having equal durations. Therefore the models' prediction for the effect of delay length may hold true, especially for the choice settings where the participants could manipulate the task duration.

Contribution of basic processing deficits to executive dysfunction in ADHD

The study presented in Chapter 4 showed that information processing of children with ADHD is characterized by slow and inefficient information accumulation, and this inefficient processing style did not differ between executive and non-executive tasks. The children with ADHD had lower drift rates in both a simple choice reaction time task and a task that requires conflict control. This finding is consistent with the previous studies that reported that the children with ADHD are impaired even on tasks that require little or no higher-order processing (Rommelse et al., 2007; Van de Voorde, Roeyers, Verté, & Wiersema, 2010). Consequently, while the results do not completely

exclude the role of executive dysfunction in pathophysiology of ADHD, they are compatible with the SRD model which suggests that basic processing deficits involving arousal, activation or effort could explain a big proportion of executive function deficits in ADHD. In addition, we found no group difference for the boundary parameter which reflects the degree of cautiousness. This finding appears counterintuitive because impulsivity is one of the main characteristics of ADHD and one might predict an "acting without thinking" style based on greater impulsivity. The diffusion model (DM) studies conducted so far with children with ADHD also revealed similar results for the boundary parameter (Karalunas, Huang-Pollock, & Nigg, 2012; Karalunas & Huang-Pollock, 2013; Mulder et al., 2010). The DM analysis presented in Chapter 6 showed that individuals with ADHD had even greater boundary estimates, suggesting a more cautious decision making style. Taken together, these studies altogether suggest that impulsivity may not be a key determinant of ADHD performance in speeded reaction time tasks.

The role of neuropsychological heterogeneity

In addition to SR and DAv related deficits we also observed deficits that cannot be explained by both models. For instance, the results presented in Chapter 2 suggest that although both the effect sizes (ES) for commission errors and mean reaction time is affected from the ER, there are still residual deficits that cannot be corrected with energetic manipulation. Furthermore, the magnitude of the group difference for the SDRT was large, but there was no effect of ER on ESs. Similarly in Chapter 3, we observed that the ER affected the *mu* and the *sigma* parameters, but there was no effect of ER on *tau*. In Chapter 6, the results of the DM analysis showed that the children with ADHD were affected at a number of information processing steps and not all of these deficits were related to SR problems. These results altogether suggest that the neuropsychology of ADHD is complex and a single model or construct may not be sufficient to explain the whole spectrum of neuropsychological deficits. Our findings are therefore consistent with the models that suggest the presence of multiple pathways in ADHD (Kuntsi et al., 2010; Sonuga-Barke, 2003).

Besides this complexity in the neuropsychology of ADHD, there is also substantial variation among individuals with ADHD: An individual showing one type of deficit may not be showing another one (Dalen, Sonuga-Barke, Hall, & Remington, 2004; Kuntsi et

al., 2010; Solanto et al., 2001; see Sonuga-Barke, 2003; Sonuga-Barke et al., 2010 for reviews). For instance, it is estimated that only 35% to 50% of individuals with ADHD are impaired in response inhibition, which may also be the case for other types of deficits such as SRDs and DAv (Nigg, Willcutt, Doyle, & Sonuga-Barke, 2005). In this thesis, we also showed that individuals with ADHD are affected from multiple types of deficits and these deficits might vary among individuals. Our results therefore support the role of heterogeneity in ADHD. Future theoretical models of ADHD should acknowledge that individuals with ADHD are not homogeneous in terms of neuropsychological deficits.

LIMITATIONS

There are a number of limitations in this dissertation to note. First, in Chapter 3 we showed that the ADHD group had higher Gaussian variability at very fast and very-slow presentation rates. Although this is a very valuable finding, which confirms the predictions of the SRD model, the cognitive corollary of *sigma* is not certain. We analysed the data further with the DM (Chapter 6) but this inverted U pattern was not observed for any of the model parameters. We concluded that *sigma* might be related to effort allocation. However the DM does not have a separate parameter estimate for the cognitive effort. Therefore, the cognitive basis of *sigma* variability has not been determined.

Second, our ADHD sample contained children from all three DSM-IV subtypes (combined, inattentive and hyperactive/impulsive) and also many participants had comorbid oppositional defiant disorder. It is possible that the subtypes and comorbid disorders affect SR and DAv profiles, creating mixed results for some performance measures. The neurocognitive profiles of different clinical subtypes could not be determined due to moderate sample sizes. In addition to the effect of clinical subtypes the neuropsychological heterogeneity could have affected the results. As stated above, there are multiple types of deficits involved in ADHD and it is possible that only a subgroup of individuals is affected by a certain type of deficit. For instance, the lack of ER effect on all performance measures might indicate a partial response in only a subgroup of individuals. The contribution of neuropsychological heterogeneity could also not be addressed in our studies.

Third, energetic factors encompass arousal, activation, and effort, and we could not evaluate the effect of all factors on ADHD performance in a single study. In Chapter 6, we evaluated the effect of arousal on impulsive choice and we did not find an effect. However, arousal is not the only energetic factor. It is possible that the increased SS reward preference in ADHD might be exclusively due to motor activation, which is not affected by pink noise. Therefore, the findings in Chapter 6 may not be easily compared to those in Chapters 2 and 3 because the ER findings indicate that the regulation of activation stage is impaired in ADHD. Similarly, the deficits in information accumulation and SATO observed in Chapter 5 were not sensitive to ER manipulations. However, these deficits could be affected by other types of manipulations, such as reward which affects the effort pool, and noise, which affects arousal. These issues have not been addressed in our studies due to the single type of manipulation employed.

Fourth, in Chapter 6, the effect of pink noise on impulsive decisions were tested. A methodological limitation of this study was that we could only use one noise level that was commonly used in previous studies (Söderlund, Sikstrom. Loftesnes, & Sonuga-Barke, 2010; Söderlund, Sikstrom, & Smart, 2007). However, according to certain accounts, there might be an inverted U relationship between noise intensity and performance (Söderlund et al., 2007) and this hypothesis could not be tested in our study. It is possible that a different intensity level of noise could have produced different effects on behaviour. For future studies, we recommend using more than one intensity level.

METHODOLOGICAL IMPLICATIONS

Traditionally, the neuropsychological deficits in ADHD have been evaluated with conventional performance measures, such as mean reaction time (MRT), error rate, and SDRT. However, the research presented in this dissertation showed that these measures are not sensitive enough to capture all aspects of neuropsychological deficits. For instance, in Chapter 2 we did not observe an effect of ER on SDRT. As indicated in previous reviews, the SDRT is a non-specific measure of central tendency and greater SDRT is also observed in other neuropsychological disorders (Tamm et al., 2012). Therefore we disentangled the non-specific variability into more specific components

using the ex-Gaussian model. This analysis (Chapter 3) showed that although the ADHD group has both greater Gaussian variability and extreme slow responses that increases the rightward skew of the reaction time distributions, the SR deficits were most obvious when Gaussian variability was analysed. Therefore, it can be concluded that the ex-Gaussian model provides a more sensitive measure for ADHD-related neuropsychological deficits.

The second methodological implication of the experiments is about the use of DM in ADHD research. The DM offers a clear advantage over the conventional performance measures by estimating separate parameters for different steps in information processing. In Chapters 5 and 6, two DM analyses were presented which showed that ADHD information processing is characterized by slower information accumulation (slower drifts) and problems with adjusting motor preparation. In addition, the findings from Chapter 6 showed that children with ADHD might have problems with adjusting the SATO. These findings would not be evident from the conventional MRT, error rate, and SDRT analyses. In summary, it can be concluded that both the ex-Gaussian and diffusion models provide a more sensitive analysis of neuropsychological deficits than the conventional performance measures.

Our results might also have important implications for future ER studies. Previous ER studies used generally two ERs, which did not allow for testing of linear and quadratic types of interactions. In Chapter 3, we used four ERs which made it possible to compare two different hypotheses for the effect of ER on performance. Furthermore, the results showed that the quadratic trend for the *sigma* variability would not be evident without 1 sec and 8 sec conditions. For future studies, it is recommendable to include at least three ERs with 1 sec and 8 sec conditions to detect ADHD versus control differences, especially for the variability measures.

CLINICAL IMPLICATIONS

Our results have clearly indicated that the performance of individuals with ADHD depends on how the information is presented (i.e., event rate) and the changes involving the presentation rate could alleviate some, if not all, aspects of ADHD-related deficits. For instance, in Chapter 2 we showed that a fast presentation rate triggers inhibition

errors in children with ADHD and makes inhibition deficits more prominent. On the other hand a slow presentation rate produces a slow and sluggish response style in children with ADHD. Similarly in Chapter 3, the results indicated that a very fast and a very slow presentation rate triggered variable responses in children with ADHD, suggesting a problem with regulating behaviour at suboptimal conditions. These results might have important implications for the rehabilitation of individuals with ADHD and adjustment of classroom settings for optimal performance. It is apparent that both very fast and very slow presentation rates would cause performance deficits in individuals with ADHD. In addition, it is not known what an optimal presentation rate is and an optimal rate for one task may not be optimal for another. Nevertheless, the pace of teaching can be adjusted on an individual basis, which may require increased use of digital technologies which may optimize the speed of information delivery for each individual. Furthermore, the findings could also be used in the psychoeducational interventions for families. Providing detailed information about the context dependent nature of neuropsychological deficits and using strategies to manipulate these deficits could improve parenting skills.

The findings might also have important implications for the neuropsychological testing of children with ADHD. Currently several neuropsychological tests are being used for evaluation of children with ADHD. However, these tests lack diagnostic sensitivity and specificity (Pineda et al., 2007). One possible explanation for this limitation is that these instruments primarily focus on executive functions and do not evaluate SR and DAv deficits. Integration of measures tapping these deficits to the batteries could increase their clinical utility. Another factor that limits the utility of these instruments could be the current diagnostic nosology that does not take into account the neuropsychological differences between children with ADHD. For instance, a subgroup of individuals with ADHD might have predominantly executive function deficits while another subgroup having predominantly SR deficits and these subgroups might differ in their clinical profiles (Nigg, et al., 2005). The existence of such subtypes has not been confirmed yet. However, further clinical might explore the existence of these neuropsychological subtypes.

FUTURE DIRECTIONS

What brain networks are related to SRDs and DAv in ADHD?

An important goal of future studies could be isolating the neurobiological correlates of SRD and DAv in ADHD. The DAv model suggests that the core deficit in ADHD is the impaired signalling of future rewards in dopaminergic reward pathways, which include ventral tegmental area (VTA), nucleus accumbens (NAcc) and orbitofrontal cortex (OFC). The frustration for the delays may be related to altered function in amygdale, which is involved in coding of the emotional aspects of the delay (Sonuga-Barke et al., 2010). Previous studies showed that the NAcc is hypoactivated for future rewards (Scheres, Milham, Knutson, & Castellanos, 2007) and increasing delays produce amygdala, orbitofrontal cortex, ventral striatum, and insula hyper-activations in ADHD children (Lemiere et al., 2012; Plichta et al., 2009). These studies indicate that two types of deficits involved in delay aversion: impaired reward signalling and altered emotional processing of delays. Future studies could try to identify the relative contribution of these two deficits to the pathophysiology of ADHD.

The neurobiological basis of the SR deficits has been less extensively studied than DAv. Electrophysiological studies showed that children with ADHD have a deficit in allocating necessary effort in suboptimal settings (Wiersema, van der Meere, Antrop, & Roeyers, 2006; Wiersema, van der Meere, Roeyers, Van Coster, & Baeyens, 2006) which is indicated by smaller p3 amplitudes at slow ER settings. The neurobiological basis of p3 and effort needs is not known. However there is evidence for that they may be linked to locus ceruleus (LC) activity (Nieuwenhuis, Aston-Jones, & Cohen, 2005). The LC is the noradrenergic centre located at the rostral brainstem, and animal studies also indicate that it is primarily involved in regulation of arousal state (Aston-Jones, Rajkowski, & Cohen, 1999). Based on this evidence LC appears to be a candidate region for SR deficits. Activity in the LC could be measured directly by functional neuroimaging. Another way to measure LC activity is the measurement of pupil size, which tracks the changes in LC (Gilzenrat, Nieuwenhuis, Jepma, & Cohen, 2010). Future studies could investigate the role of LC in SR deficits by measuring LC activity with functional neuroimaging and pupil size measurement during ER tasks. From the SRD model, one might predict hypo-

activations in LC during a slow ER task, and hyper-activation during a fast ER task reflecting the poor regulation of behaviour state.

The study presented in Chapter 3 showed that the children with ADHD had greater Gaussian variability (*sigma*) at ER extremes. While this finding indicates a problem with regulating performance in sub-optimal conditions and is consistent with deficient state regulation, the neurobiological basis needs to be determined. Similarly, both our two DM studies and the previous studies which used the same method consistently found that ADHD is associated with slower drift rates in both executive and non-executive tasks, indicating slower information processing regardless of the level of processing load. In Chapter 6, we also found that children with ADHD have greater decision boundaries indicating SATO deficits. The neurobiological basis of these deficits is to be explored by studies which could combine diffusion and ex-Gaussian model analyses with functional neuroimaging.

Can neuro-pharmacology elucidate further the SRD effects?

Another important topic for future studies is the neuropsychological mechanism of action of stimulant medications. The stimulants used in the treatment of ADHD increase the dopamine and noradrenaline levels in the central nervous system and they are effective in reducing symptoms and improving cognitive performance (Engert & Pruessner, 2008). However, it is not certain via which neuropsychological mechanisms that these beneficial effects occur. According to the DAv model, the stimulants improve signalling of future rewards by increasing phasic dopamine and reduce perception of time during the task (Sonuga-Barke et al., 2010). On the other hand, the SRD model postulates that the stimulants act by increasing the activation level (van der Meere, Shalev, Börger, & Wiersema, 2009). Therefore, it would predict that at under-activated states (such as slow ERs) the stimulants would improve performance. However at fast-ERs the performance would deteriorate due to a combination of two activating factors (a fast ER and stimulant). This prediction of the SRD model could be explored in randomized controlled trials.

More research on heterogeneity and neuropsychological subtypes

Finally, the results of the research presented in this dissertation consistently showed that the neuropsychological spectrum of ADHD is complex with several types of deficits involved. It is possible that multiple neuropsychological subtypes exist within the ADHD population that differ in their clinical profiles. It is also possible that these different subtypes could benefit from different treatment strategies. Recently, a study attempted to classify a large group of children with and without ADHD according to their executive function profiles (Fair, Bathula, Nikolas, & Nigg, 2012). The results suggest the presence of distinct subtypes within the ADHD and control populations. Future studies could expand this work by exploring subtypes that have predominantly SR or DAv deficits.

<p align="center">**FINAL CONCLUSIONS**</p>

The main goal of this dissertation was to compare two models of ADHD: the SRD and the DAv models. The five studies presented in this dissertation indicated that the SR deficits and DAv are mediated by independent neuropsychological mechanisms, implicating the involvement of separate neural systems: one regulating the level of arousal/activation and the other reward and delay processing. In addition, using the DM we tested the predictions of the SRD model for the role of non-executive processing and motor preparation deficits in ADHD. The results showed that ADHD information processing is characterized by slow and inefficient information processing together with difficulties in adjusting the level of motor preparation and speed-accuracy trade-off. As predicted by the SRD model, the executive deficits made little contributions to these basic deficits. Future studies could aim to identify the neurobiological basis of these basic processing deficits by targeting the neural systems implicated in the regulation of arousal and activation. Lastly, we observed that individuals with ADHD have multiple types of neuropsychological deficits suggesting that the aetiology of ADHD is complex and any single model may not be sufficient to explain the whole spectrum of deficits. Furthermore, individuals with ADHD could be affected by different types of neuropsychological deficits, implicating the role of casual heterogeneity. Large scale

studies are needed to identify the neuropsychological subtypes and clinical differences between these subtypes.

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"Attention Deficit/Hyperactivity Disorder" (ADHD), in het Nederlands "aandachtstekortstoornis met hyperactiviteit", is één van de meest voorkomende psychiatrische stoornissen. ADHD is een ontwikkelingsstoornis die gekenmerkt wordt door ernstige en persisterende symptomen van onoplettendheid, impulsiviteit en/of hyperactiviteit; en leidt tot significante beperkingen in beroepsmatig, schools of sociaal functioneren (Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR), American Psychiatric Association, 2000).

Tot op heden is de etiologie van ADHD nog niet volledig begrepen en bestaan er verschillende neuropsychologische theorieën ter verklaring van de symptomen van ADHD. Lange tijd werd verondersteld dat de symptomen van ADHD het gevolg zijn van een primair tekort in executief functioneren zoals inhibitie, planning, werkgeheugen en "set shifting" (voor een overzicht: zie Barkley, 1997; Castellanos & Tannock, 2002). Recent onderzoek heeft echter aangetoond dat executieve verklaringsmodellen onvoldoende de symptomen van ADHD kunnen verklaren (Willcutt et al., 2005). Bovendien suggereren recentere neuropsychologische theorieën dat tekortkomingen in executief functioneren bij kinderen met ADHD niet statisch zijn; het al dan niet optreden van zwakkere prestaties zou namelijk afhangen van de situationele en motivationele context. Huidig proefschrift focust op twee vooraanstaande neuropsychologische modellen die het dynamische karakter van ADHD benadrukken en in het bijzonder de rol van contextuele factoren: het toestandsregulatiemodel (State Regulation Deficit model (SRD); van der Meere, 2002) en het "Delay Aversion" model (DAv; Sonuga-Barke, Wiersema, van der Meere, & Roeyers, 2010).

Het toestandsregulatiemodel stelt dat prestaties afhankelijk zijn van energetische processen zoals arousal, activatie en effort (Sanders, 1983). Volgens dit model hebben kinderen met ADHD moeilijkheden met het aanpassen van hun energetische interne toestand aan de veranderende eisen uit de omgeving (van der Meere, 2002). Onderzoek heeft aangetoond dat omgevingsfactoren, zoals het manipuleren van de snelheid waarmee informatie wordt aangeboden tijdens een taak, een invloed heeft op de interne toestand. Meer concreet zou een snelle stimulusaanbieding leiden tot een

overactieve toestand en een trage stimulusaanbieding tot een onderactieve toestand. Kinderen met ADHD zouden er niet in slagen om deze sub-optimale toestanden te reguleren, namelijk een onderactieve toestand op te krikken en een overactieve toestand te temperen, waardoor ze zwakke prestaties behalen. Het toestandsregulatiemodel veronderstelt aldus een omgekeerde U relatie tussen de interne toestand en taakprestaties. Aangezien kinderen met ADHD problemen hebben met het reguleren van hun interne toestand, zou deze omgekeerde U functie bij hen uitdrukkelijker tot uiting komen in vergelijking met typisch ontwikkelende kinderen. Onderzoek waarbij de snelheid van stimulusaanbieding werd gemanipuleerd, ondersteunt de voorspellingen van het toestandsregulatiemodel (voor een overzicht zie: Sergant, 2005; van der Meere 2002; Sonuga-Barke et al., 2010).

Het "Delay Aversion model" stelt dat prestaties van kinderen met ADHD hoofdzakelijk worden beïnvloed door intolerantie voor uitstel. Kinderen met ADHD zouden zwakker presteren dan typisch ontwikkelende kinderen in uitgestelde situaties. Volgens dit model is het primair tekort dat aan de grondslag ligt van de symptomen van ADHD een verstoorde codering van toekomstige beloningen. Na verloop van tijd zou dit primaire tekort leiden tot het ontwikkelen van negatief affect ten aanzien van situaties waar men moet wachten (Sonuga-Barke et al., 2010). Onderzoek ondersteunt de voorspellingen van dit model. Meer bepaald stelde men vast dat kinderen met ADHD een sterke voorkeur hebben voor kleine onmiddellijke beloningen boven grotere uitgestelde beloningen. Bovendien lijken kinderen met ADHD gefrustreerd te zijn wanneer een wachttijd extern wordt opgelegd (Marco et al., 2009).

Het Doel van het Proefschrift en een Samenvatting van de Bevindingen

Het hoofddoel van dit proefschrift is het vergelijken van de voorspellingen van het toestandsregulatiemodel en het "Delay Aversion" model. Beide modellen voorspellen dat zwakkere prestaties bij kinderen met ADHD afhankelijk zijn van de situationele en motivationele context. Om beide modellen te vergelijken, baseerden we ons op de kernvoorspellingen van deze twee theorieën: manipulatie van de snelheid van stimulusaanbieding (toestandsregulatiemodel) en de voorkeur voor kleine onmiddellijke beloningen ("Delay Aversion" model). Er werd nagegaan in welke mate deze

manifestaties gerelateerd zijn aan de veronderstelde theorieën. Meer specifiek werd onderzocht of de effecten van manipulatie van de snelheid van stimulusaanbieding ook verklaard kunnen worden door het "Delay Aversion" model en of de impulsieve beloningskeuze verklaard kan worden door het toestandsregulatiemodel. In het eerste inleidende hoofdstuk van dit proefschrift wordt de achterliggende rationale voor deze onderzoeksvragen gedetailleerd weergegeven.

In het tweede hoofdstuk worden aan de hand van een meta-analyse de voorspellingen van beide modellen nagegaan. Ons baserend op de beschikbare literatuur verzamelden we de studies, gepubliceerd tussen 2000 en 2011, waarin gebruik werd gemaakt van een Go/No-Go taak bij kinderen met en zonder ADHD. De taakprestaties van kinderen met ADHD werden vergeleken met die van typisch ontwikkelende kinderen. Daarenboven werd de invloed van snelle en trage stimulusaanbiedingen onderzocht. Het toestandsregulatiemodel voorspelt dat een snelle stimulusaanbieding leidt tot een overactieve toestand en een trage stimulusaanbieding tot een onderactieve toestand; beide situaties zouden leiden tot zwakkere prestaties bij kinderen met ADHD. In tegenstelling tot het toestandsregulatiemodel, voorspelt het "Delay Aversion" model dat zwakkere prestaties bij kinderen met ADHD enkel zouden optreden bij een trage stimulusaanbieding aangezien dergelijke situatie geassocieerd wordt met uitstel. De resultaten van de meta-analyse ondersteunden de voorspellingen van het toestandsregulatiemodel; kinderen met ADHD presteerden zwakker dan typisch ontwikkelende kinderen bij zowel snelle als trage stimulusaanbiedingen. Meer specifiek maakten kinderen met ADHD meer commissiefouten bij een snelle stimulusaanbieding en reageerden ze trager bij een trage stimulusaanbieding. De variabiliteit van de reactietijd werd niet beïnvloed door manipulatie van de snelheid van stimulusaanbieding.

In het derde hoofdstuk onderzoeken we nader het effect van de snelheid van stimulusaanbieding op de variabiliteit van de reactietijd. Kinderen met ADHD en typisch ontwikkelende kinderen maakten een Go/No-Go taak met vier verschillende snelheden van stimulusaanbieding waarbij zowel snelle als trage stimulusaanbiedingen werden opgenomen. Door gebruik te maken van het ex-Gaussian model werd de niet-specifieke variabiliteit van de reactietijd opgesplitst in Gaussian variabiliteit (*sigma*) en variabiliteit te wijten aan trage reacties (*tau*). Het toestandsregulatiemodel voorspelt een grotere *sigma* bij snelle en trage stimulusaanbiedingen bij kinderen met ADHD. Wat betreft *tau,*

wat een dwaling in aandacht weerspiegelt, voorspelt het toestandsregulatiemodel enkel zwakkere prestaties bij trage stimulusaanbiedingen. Het "Delay Aversion" model daarentegen voorspelt dat kinderen met ADHD enkel zwakker zouden presteren bij trage stimulusaanbiedingen en dit voor alle parameters (*sigma* en *tau*). In tegenstelling tot de bevindingen van het tweede hoofdstuk, toonden deze resultaten dat er wel een effect is van de snelheid van stimulusaanbieding op de variabiliteit van de reactietijd bij kinderen met ADHD. Meer concreet vertoonden kinderen met ADHD in vergelijking met typisch ontwikkelende kinderen een grotere *sigma* tijdens heel snelle en heel trage stimulusaanbiedingen, wat de voorspellingen van het toestandsregulatiemodel ondersteunt. Met betrekking tot *tau* werd er echter geen effect van de snelheid van stimulusaanbieding vastgesteld.

In het vierde hoofdstuk worden de voorspellingen van het toestandsregulatiemodel verder onderzocht. Volgens het toestandsregulatiemodel zijn zwakke prestaties bij kinderen met ADHD hoofdzakelijk te wijten aan een gebrekkige regulatie van de interne toestand (arousal/activatie) en niet aan executieve tekorten. Het model veronderstelt bijgevolg dat prestaties van kinderen met ADHD niet beïnvloed worden door executieve taakvereisten. We gingen deze voorspelling na door het analyseren van de prestaties van kinderen met ADHD en typisch ontwikkelende kinderen op twee taken; een eenvoudige twee-keuze perceptuele beslissingstaak en een taak die conflictcontrole vereist. Door gebruik te maken van het "Diffusion Model" werden verscheidene cognitieve basisprocessen nader onderzocht. Meer concreet stellen analyses volgens het "Diffusion Model" ons in staat om afzonderlijke parameters voor de verschillende cognitieve processen in kaart te brengen zoals "speed-accuracy trade-off" (SATO), accumulatie van informatie ("drift rate"), motorische voorbereiding en encodering (niet-beslissingstijd). We stelden vast dat, onafhankelijk van de executieve vereisten, de informatieverwerking van kinderen met ADHD gekarakteriseerd werd door een trage verwerkingssnelheid (lage "drift rate"). Voorts vonden we geen verschillen tussen kinderen met en zonder ADHD met betrekking tot de beslissingsgrens (SATO); dit suggereert dat kinderen met ADHD hun beslissingsproces niet vroegtijdig beëindigen. Daarenboven stelden we vast dat kinderen met ADHD een kortere niet-beslissingstijd vertoonden in beide taken. Overeenkomstig de voorspellingen van het toestandsregulatiemodel, is deze kortere niet-beslissingstijd waarschijnlijk gerelateerd

aan tekortkomingen in motorische voorbereiding en activatie en niet aan moeilijkheden met encoderen.

In het vijfde hoofdstuk wordt dieper ingegaan op de kortere niet-beslissingstijd bij kinderen met ADHD. In principe weerspiegelt een korte niet-beslissingstijd zowel moeilijkheden met motorische voorbereiding als met encoderen. Vroeger onderzoek suggereert echter dat kinderen met ADHD enkel moeilijkheden hebben met motorische voorbereiding en activatie; de encoderingprocessen zouden vlot verlopen (van der Meere, van Baal, & Sergeant, 1989). De vaststelling dat kinderen met ADHD gevoelig zijn voor de snelheid van stimulusaanbieding ondersteunt deze hypothese. Volgens het toestandsregulatiemodel beïnvloedt het manipuleren van de snelheid van stimulusaanbieding immers de motorische voorbereiding en activatie. Snelle en trage stimulusaanbiedingen leiden respectievelijk tot een over- en onderactieve toestand; en kinderen met ADHD hebben moeite om hun interne toestand te reguleren wat onder andere leidt tot problemen met motorische voorbereiding (Sergeant, 2005; van der Meere, 2002). Deze hypothese werd nader onderzocht. Meer concreet werden de taakprestaties uit het derde hoofdstuk opnieuw geanalyseerd door gebruik te maken van het "Diffusion Model", aangepast voor het analyseren van prestaties op een Go/No-Go taak. Op basis van het toestandsregulatiemodel voorspelden we dat het manipuleren van de snelheid van stimulusaanbieding hoofdzakelijk de niet-beslissingstijd, wat onder meer motorische voorbereiding inhoudt, zou beïnvloeden. Daarnaast voorspelden we dat kinderen met ADHD in vergelijking met typisch ontwikkelende kinderen gevoeliger zouden zijn voor de effecten van de snelheid van stimulusaanbieding op de niet-beslissingstijd aangezien kinderen met ADHD moeilijkheden hebben met het reguleren van hun activatieniveau en bijgevolg ook met motorische voorbereiding. De resultaten toonden dat de snelheid van stimulusaanbieding de verschillende parameters van het "Diffusion Model" beïnvloedt: "speed-accuracy trade-off" (SATO), accumulatie van informatie ("drift rate") en motorische voorbereiding en encoderen (niet-beslissingstijd). In lijn met de voorspellingen van het toestandsregulatiemodel hadden kinderen met ADHD een kortere niet-beslissingstijd bij snelle stimulusaanbiedingen en een langere niet-beslissingstijd bij trage stimulusaanbiedingen dan typisch ontwikkelende kinderen. Deze bevindingen ondersteunen de hypothese dat de afwijkende niet-beslissingstijd bij kinderen met ADHD waarschijnlijk gerelateerd is aan tekortkomingen in motorische voorbereiding en activatie en niet aan moeilijkheden met encoderen. Verder stelden we

vast dat kinderen met ADHD een tragere verwerkingssnelheid (lagere "drift rate") en grotere beslissingsgrens (SATO) hadden; deze groepsverschillen werden echter niet beïnvloed door manipulatie van de snelheid van stimulusaanbieding.

In het zesde hoofdstuk wordt nagegaan of de impulsieve beloningskeuze zoals vooropgesteld door het "Delay Aversion" model eveneens kan verklaard worden vanuit het toestandsregulatiemodel. Sonuga-Barke en collega's (2010) stellen in hun herziene uitwerking van het toestandsregulatiemodel dat impulsief keuzegedrag van kinderen met ADHD gezien kan worden als een poging om hun energetische toestand te optimaliseren. Meer bepaald zouden kinderen met ADHD kiezen voor onmiddellijke beloningen zodat een voor hen optimale stimulerende omgeving wordt bekomen. In functie van het bereiken van een optimale interne toestand, zouden kinderen met ADHD meer omgevingsstimulatie nodig hebben dan typisch ontwikkelende kinderen. Op basis van deze veronderstellingen voorspelt het toestandsregulatiemodel dat het luisteren naar roze ruis, hetgeen het arousalniveau verhoogt, leidt tot minder impulsieve keuzes bij kinderen met ADHD. Het "Delay Aversion" model maakt echter geen specifieke voorspellingen omtrent het effect van roze ruis op impulsief keuzegedrag van kinderen met ADHD. Om de voorspelling van het toestandsregulatie te toetsen maakten kinderen met ADHD en typisch ontwikkelende kinderen twee taken waar impulsief keuzegedrag kon worden nagegaan. Roze ruis werd in deze studie gebruikt om de interne toestand (arousalniveau) op te krikken. De resultaten toonden dat roze ruis geen effect had op het impulsief keuzegedrag van kinderen met ADHD. Deze bevindingen kunnen dus het best begrepen worden vanuit het "Delay Aversion" model.

CONCLUSIE

De vijf studies die beschreven worden in dit proefschrift wijzen er op dat toestandsregulatieproblemen en aversie voor uitstel gemedieerd worden door onafhankelijke neuropsychologische mechanismen. Dit impliceert de betrokkenheid van afzonderlijke neurale systemen: één dat instaat voor de regulering van de interne toestand (arousal/activatie) en één dat instaat voor belonings- en uitstelprocessen. Daarnaast onderzochten we aan de hand van "Diffusion Model" analyses de voorspellingen van het toestandsregulatiemodel met betrekking tot de rol van niet-

executieve processen en tekorten in motorische voorbereiding bij prestaties van kinderen met ADHD. De resultaten toonden dat de informatieverwerking van kinderen met ADHD gekarakteriseerd wordt door trage en inefficiënte informatieverwerkingsprocessen die gepaard gaan met moeilijkheden in het reguleren van de interne toestand en het aanpassen van het niveau van motorische voorbereiding en de "speed-accuracy trade-off" (SATO). Overeenkomstig de voorspellingen van het toestandsregulatiemodel worden deze tekortkomingen weinig tot niet beïnvloed door executieve moeilijkheden. Toekomstige studies zou de neurobiologische basis van de vastgestelde moeilijkheden in informatieverwerking bij kinderen met ADHD nader kunnen onderzoeken door de neurale systemen die betrokken zijn bij de regulatie van arousal en activatie in kaart te brengen. Tot slot stelden we vast dat ADHD gekenmerkt wordt door verschillende vormen van neuropsychologische tekorten. Dit suggereert dat de etiologie van ADHD complex is en dat één neuropsychologisch model op zich ontoereikend is om de volledige waaier aan tekortkomingen te verklaren. Verder is het mogelijk dat er bij verschillende kinderen met ADHD verschillende neuropsychologische tekorten aanwezig zijn, wat een causale heterogeniteit impliceert. Grootschalige studies zijn nodig om neuropsychologische subtypes van ADHD en klinische verschillen tussen deze subtypes te identificeren.

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