ADHD: CAN REINFORCEMENT RESOLVE THE PROBLEM?

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CHAPTER 1

General Outline and Statement of The Problem

Introduction

Attention-deficit/hyperactivity disorder (ADHD) is a chronic childhood developmental disorder, with symptoms of inattentiveness, hyperactivity, and impulsivity (American Psychiatric Association APA, 2000). A recent review and meta-regression analysis suggests that the overall pooled worldwide prevalence of ADHD is 5.3%, affecting more boys than girls in a ratio of 4:1 (Polanczyk, de Lima, Horta, Biederman, & Rohde, 2007). The disorder severely disrupts daily life functioning, impairing social, professional as well as family functioning (Barkley et al., 2006; Biederman, Faraone, Spencer, Mick, Monuteaux, & Aleardi, 2006). The prognosis of ADHD is poor: Children with ADHD show increased risk for developing psychiatric or personality disorders as adolescents or adults (Biederman, Monuteaux, et al., 2006; Spencer, 2006). Although the diagnoses continues to be targeted as non-existent or a 'fashion-diagnosis' in the media, a consensus statement signed by more than 70 world-wide experts in the field points to the validity of the diagnosis and its adverse impact on the lives of those diagnosed with ADHD (International consensus statement on ADHD, 2002).

Three subtypes of ADHD have been defined: an inattentive subtype, a hyperactive/impulsive subtype and a combined subtype (APA, 2000). Inattentiveness has been recognized as difficulties with close attention to details, careless mistakes, problems with sustained concentration, daydreaming, frequent shifts in uncompleted activities, difficulties in organizing, chaotic behaviour, being easily distracted by irrelevant stimuli, and forgetfulness. Hyperactivity may manifest itself in restlessness, squirming in one's seat, excessive running, climbing, excessive talking, and being often 'on the go'. Impulsivity is manifested by impatience, difficulty in delaying responses, blurting out answers, difficulty awaiting turns, frequent interruptions on others, and behaviour that may lead to accidents (APA, 2000). Symptoms must be (1) present before the age of 7, (2) pervasive across situations, and (3) impair the child's social and academic functioning.

One of the major issues in identifying the symptoms that are associated with ADHD is the highly variable occurrence of these problems. The fourth revised edition of the Diagnostic and Statistical Manual of Mental Disorders, (DSM-IV-TR) states that the problems with attention and hyperactivity/impulsivity are variable across situations and worsen, when tasks require sustained attention or mental effort, or when tasks lack intrinsic appeal or novelty (APA, 2000). This abnormal response to environmental factors in ADHD has also been observed in an aberrant sensitivity to reinforcement contingencies such as rewards and penalties (see Chapter 2). The increase in behavioural symptoms as a function of task difficulty or task attractiveness suggests that children with ADHD suffer from *motivational problems* that interfere with their behaviour. Motivational processes in humans involve the ability to assign values to objects in the environment, whereas one is tended to work for 'rewards', while avoiding 'punishment'. Motivational problems may, therefore, translate in to an abnormal response to monetary contingencies, such as observed in children with ADHD. Several theoretical frameworks on ADHD have incorporated this aberrant reinforcement sensitivity when explaining the disorder (Casey, Nigg, & Durston, 2007; Castellanos & Tannock, 2002; Douglas, 1989; Doyle et al., 2005; Frank, Scheres, & Sherman, 2007; Haenlein & Caul, 1987; Luman et al., 2005; Nigg, 2005; Quay, 1988a; Sagvolden, Johansen, Aase, & Russell, 2005; Sergeant, Oosterlaan, & Van der Meere, 1999; Sonuga-Barke, 2002; Tripp & Wickens, in press; Wallace & Newman, 1990). The nature of this problem, however, is not well understood.

The aim of the current thesis is to extend the present literature on reinforcement sensitivity in ADHD. By manipulating reward and penalties that are contingent on performance, there is investigated whether neurocognitive deficiencies that are associated with ADHD may be secondary to a motivational deficit such as aberrant reinforcement sensitivity. In addition, autonomic responses to reinforcement are investigated to obtain more insight into the underlying psychophysiological mechanisms.

Aetiology of ADHD

ADHD has been recognized as a disorder that can be explained by both biological as well as psychosocial factors. Recent work has shown that the genetic heritability varies between 60 to 90 percent (Faraone & Doyle, 2001; Faraone & Kahn, 2006; Li, Sham, Owen, & He, 2006; Waldman & Gizer, 2006). Candidate gene studies have identified several genes that are implicated as being (small) contributors to the aetiology of ADHD. Already at an early age, children with ADHD have been found to suffer from brain abnormalities, which emphasize a genetic or early environmental

cause of the disorder (Castellanos et al., 2002; Shaw et al., 2006). Neuroanatomically, there is evidence of smaller total volumes of the cortex of children with ADHD, involving both gray and white matter volume differences (Bush, Valera, & Seidman, 2005; Seidman, Valera, & Makris, 2005). Children with ADHD have been found to show smaller volumes in four specific areas of the brain: (a) the prefrontal cortex (PFC), (b) the corpus callosum, (c) the basal ganglia, and (d) cerebellum (Bush et al., 2005; Seidman et al., 2005). Most of these areas also function abnormally in children with ADHD, specifically the PFC, the anterior cingulate cortex (ACC), the basal ganglia and the cerebellum (see for review Casey et al., 2007). Furthermore, ADHD has been associated with alterations in catecholamine pathways, that may contribute to dysregulation of PFC circuits in this disorder (Arnsten, 2006; Oades et al., 2006). Environmental factors that have been identified as being associated with ADHD are smoking or drinking during pregnancy, maternal infections, or maternal stress (Talge, Neal, & Glover, 2007), complications during birth (premature birth) or low birth weight (Bhutta, Cleves, Casey, Cradock, & Anand, 2002; Linnet et al., 2006), or traumatic brain injury and stroke (Herskovits et al., 1999). Recent studies indicate that prenatal exposure to lead and smoking during pregnancy may activate the genes that have been related with ADHD (Neuman, Lobos, Reich, Henderson, Sun, & Todd, 2007; Swanson et al., 2007). In addition, several psychosocial factors relate with the development of ADHD such as early deprivation (Kreppner, O'Conner, & Rutter, 2001) and the absence of positive parenting (Chronis et al., 2007).

There are several pharmacological and behavioural interventions that have been demonstrated to affect positively the core features of ADHD, and to some extent social and academic functioning (Biederman, Spencer, & Wilens, 2004; Majewicz-Hefley & Carlson, 2007). The most utilized pharmacological intervention for ADHD is treatment with methylphenidate (MPH). MPH is a dopamine transporter antagonist that has been found to improve the behavioural symptoms of ADHD, as well as neurocognitive functioning (Solanto, Anrsten, & Castellanos, 2000) with relatively minor side effects (Rapport & Moffit, 2002). In addition, amphetamines and norepinephrine reuptake inhibitors (atomoxetine) were found to be effective in the treatment of ADHD (Biederman et al., 2004; Prince, 2006). The multi-model treatment (MTA) study on ADHD of the National Institute of Medical Health (NIMH) demonstrated greater effectiveness of pharmacological than behavioural interventions on ADHD symptoms as assessed by parents and teachers (Brown et al., 2005; Jensen, Arnold, Severe, Vitiello, & Hoagwood, 2004). A follow-up of the MTA study, however, demonstrated that the differences in the effectiveness of behavioural and pharmacological interventions diminished over time (Jensen et al., 2007). In addition, despite the benefits of pharmacological interventions, these therapies are unable to completely

ameliorate behaviour problems for all children with ADHD and there is no evidence that MPH improves academic achievement (Hoffman & DuPaul, 2000).

There is strong evidence of considerable comorbidity between ADHD and a number of disorders such as mood and anxiety disorders, anti-social behaviour disorder, learning disorder, motor coordination disorder and pervasive developmental disorder (Kadesjö & Gillberg, 1999; Pliszka, 1998; Spencer, 2006). Children with ADHD with comorbid disorders have been found to show poorer outcomes than children with ADHD-only in terms of social, emotional, and psychological difficulties (Spencer, 2006). For example, ADHD with comorbid conduct disorder (CD) is thought to represent a high risk condition with more severe behavioural problems and poorer prognosis than ADHD or CD alone (Faraone et al., 1998).

An Abnormal Sensitivity to Reinforcement Contingencies?

Several experimental studies have shown that the outcome of the ADHD symptoms may differ, depending on the environment. Research in the 1980's demonstrated that children with ADHD improved in performance when tasks were made more salient, novel, or interesting (Zentall, & Meyer, 1987; Zentall & Shaw, 1980). For example, when hyperactive children performed an attention task, performance was impaired when the child was alone or solely in the presence of the mother, in contrast to when an experimenter was present (Draeger, Prior, & Sanson, 1986; Gomez & Sanson, 1994; Power, 1993). Behavioural activity of children with ADHD diminished more than typically developing children when they saw a (stimulating) cartoon versus a neutral film (Antrop, Buysse, Roeyers, & Van Oost, 2002). Similarly, stimulating children with ADHD with visual cartoons compared to no stimulation normalized their difficulty with waiting (Antrop, Stock, Verte, Wiersema, Baeyens, & Roeyers, 2006). This environment-behaviour interaction has been confirmed in studies that demonstrate an abnormal behavioural sensitivity to contingencies such as reward and punishment (see Chapter 2 of this thesis). These findings point towards motivational problems in ADHD that come to the fore in lower self-rated motivation compared to healthy individuals, preference for easy work, less enjoyment of learning, less persistence, and a greater reliance on external than on internal standards to judge their performance (Carlson, Booth, Chin, & Canu, 2002). An important question is to what extent these problems interfere with the behavioural and intellectual abilities of children with ADHD. One method to study this is to investigate the impact of reinforcement contingencies, such as reward and response cost, on neurocognitive performance of children with ADHD.

The concept of motivation relates to the question of how organisms make choices (see Chapter 4), direct behaviour, and plan actions on the basis of internal evaluation processes regarding their environmental goals, passed experiences, and internal needs (Watts & Swanson, 2002). Humans tend to work for stimuli that are assigned as rewards, while they tend to avoiding aversive stimuli. Since all human behaviour is motivated (except for habits or basic automatic processing such as early visual processing), motivation, reinforcement and behaviour are deeply intermingled (Berridge & Robinson, 2003; Morgane, Galler, & Mokler, 2005). Berridge and Robinson (2003) reviewed the literature on the impact of reinforcement on psychological components and suggested that reward can have an impact on three major psychological components: motivation (wanting), learning, and emotion/affect (liking). The impact of reward on these components is associated with different circuits in the brain. Firstly, reward can increase the desire to want or do something (increasing motivation), which greatly influences behaviour. This is a largely automated process. In terms of task performance, a reward can increase the attention that is allocated to a task, which can increase performance (Sarter, Gehring, & Kozak, 2006). A meta-analysis on the impact of reward on children in classroom situations, demonstrated that by using positive reinforcement (verbal praise, rewards, presents or candy), the intrinsic motivation of children increased, which, in turn, increases performance (Cameron & Pierce, 1994). Secondly, reward can facilitate learning processes, since reward will likely increase the chance of the repetition of behaviour (Schultz, Dayan, & Montague, 1997; Wise, 2004). Otherwise, the omission of reward (or penalty) will decrease the chance of repetition. This process is mediated by dopamine responses to reward, which are suggested to 'stamp in' stimulus-response associations (Wise, 2004). Thirdly, motivation and learning are separated from the more conscious affective component of 'liking': Usually, a reward induces positive emotions such as happiness, while penalty will induce negative emotions such as anxiety.

If children with ADHD suffer from an abnormal sensitivity to reinforcement such as reward or penalty, children with ADHD may show abnormal changes in performance in face of contingencies, show problems with reinforcement learning, show abnormal emotional responses to reinforcement; in this thesis, the first two components are investigated.

Psychophysiological Markers of Abnormal Reinforcement Sensitivity

Children with ADHD have been found to show abnormal psychophysiological responses to reward and penalty, such as abnormal heart rate or skin conductance changes (e.g., Crowell, Beauchaine, Gatzke-Kopp, Sylvers, Mead, & Chipman-Chacon, 2006). While skin conductance responses are mainly controlled by the sympathetic nervous system (SNS), heart rate changes are controlled by both SNS as well as the parasympathetic nervous system (PNS, Brownley, Hurwitz, & Schneiderman, 2000). The SNS and PNS are both part of the autonomic system that plays an important role in regulating physiological arousal and activation, to make the system ready for appropriate behavioural responses (Gray, 1982; 1988; Panksepp, 1982; Porges, 1995). Since reinforcement influences the autonomic system, which activates behavioural changes, studying this system in ADHD may provide more insight into abnormal reinforcement sensitivity.

Sensitivity to Reward and Punishment

According to Gray (1982, 1988) behaviour is modulated by motivational factors through two separate brain systems that are responsible for either behavioural activation (approach behaviour or active avoidance) or behavioural inhibition (extinction behaviour or passive avoidance). Rewards or non-punishment activate the appetitive system (behavioural activation system, BAS), which initiates behaviour and relates to feelings of hope and relief. Aversive stimuli or non-rewards, inhibit (ongoing) behaviour and relate to feelings of anxiety (behavioural inhibition system, BIS). Psychophysiological evidence suggests that both the BIS and the BAS are dominated by the sympathetic nervous system. Gray (1988) suggested that the meso-limbic dopamine pathway, including the ventral tegmental area and ventral striatum, dominates the BAS, which is implicated in mobilizing energy and *increasing heart rate* (Fowles, 1980, 1988). The BIS is controlled by the septo-hippocampal system and is closely related to the Papez loop that depends on noradrenalin and serotonin (Fowles, 1980, 1988). According to Fowles, *increased skin conductance responses* are found to represent activity in the BIS. In addition to the BIS and BAS, Gray (1988) suggested that behaviour is regulated by flight/fight reactions to the perception of immediate danger or rewards, which includes activation of the amygdala (Panksepp, 1982). According to Porges (1995) the activation of the fight/flight system is dependent on (complete withdrawal of) the PNS.

Various psychiatric illnesses have been suggested to be the results of a distortion in the interaction between the BIS, BAS and parasympathetic activity (Beauchaine,

Katkin, Strassberg, & Snarr, 2001). Quay (1988a; 1988b; 1988c; 1997) argued that the behaviour that characterizes children with ADHD (inattentiveness, hyperactivity and impulsivity) is a consequence of an imbalance between BIS and BAS functioning. Children with ADHD would suffer from a weak BIS, resulting in decreased inhibition of initiated responses and an inability to detect and respond to stimuli that signal punishment. Alternatively, Newman (Newman, 1987; Patterson & Newman, 1993; Wallace & Newman, 1990) proposed that ADHD is largely related to the dominance of the BAS over a weak BIS, suggesting that disinhibited behaviour is the result of a lack of attention to signals of penalty in the presence of a reward signal. If Quay (1988a; 1988b; 1988c; 1997) is correct, children with ADHD would display a decreased autonomic sensitivity to penalty, indicating a low BIS, while the suggestions of Newman (Newman, 1987; Patterson & Newman, 1993; Wallace & Newman, 1990) would indicate an additional increased response to instances of reward, indicating a strong BAS over a weak BIS. The studies that investigated BIS and BAS functioning in ADHD yield heterogeneous results. There is some evidence of a weak BIS in ADHD, since ADHD has been associated with reduced noradrenalin precursors (Rogeness et al., 1989) and ADHD groups exhibited reduced urinary noradrenalin metabolites (Sherkim, Dekirmenjian, Chapel, & Davis, 1982; Shekim, Sinclair, Glaser, Horwitz, Javaid, & Bylund, 1987; Yu-cu & Yu-feng, 1984). In addition, ADHD has been associated with low baseline skin conductance activity (Beauchaine et al., 2001) as well as smaller skin conductance reactivity during stress (Boyce, Quas, Alkon, Smider, Essex, & Kupfer, 2001; Van Lang, Tulen, Kallen, Rosbergen, Dieleman, & Ferdinand, 2007; Zahn & Kruesi, 1993). This would confirm low SNS activity in ADHD, although other studies of skin conductance activity in ADHD did not demonstrate these effects (Herpertz et al., 2001; 2003; 2005). No evidence was revealed for increased sympathetic activity to instances of reward that would suggest an overactive BAS (Beauchaine et al., 2001). Chapters 2, 3, 4 and 6 of this thesis investigate heart rate and skin conductance responses of children with ADHD to reinforcement contingencies such as reward and penalty. If children with ADHD suffer from a strong BAS and a weak BIS, larger autonomic responses to reward (or the omission of penalty) and smaller autonomic responses to penalty (or the omission of reward) are expected in children with ADHD compared to typically developing controls.

Heart Rate Variability

In order to maintain an optimal performance or recover from the performance effects of detrimental manipulations, an increase in attentional effort is required (see for review Sarter, Gehring, & Kozak, 2006). For example, when task become more difficult subjects should increase the attention allocation in order to perform well, since difficult tasks require more attention to process information and respond accurately than

easy tasks. This allocation of attention is suggested to be a physiological process and involves changes in electrophysiological brain activity (Barry, Clarke, & Johnstone, 2003) as well as changes in the autonomic system (Brownley et al., 2000; Critchley et al., 2003). The changes in sustained attention are suggested to reflect changes in the variability in heart rate, which are fluctuations in the beat-to-beat interval over a period of time (Hyde & Izard 1997; Mulder & Mulder, 1981). When tasks require active attention, the mid and low frequency (.04 - .15 Hz) fluctuations in heart rate are found to diminish, which is considered as a (primarily) sympathetic measure of task engagement (Brownley et al., 2000; Critchley et al., 2003; Jorna, 1992). A decrease in variability in these frequency bands has been associated with changes in metabolic activity in the brain, for example, when tasks become more difficult (Akselrod, Gordon, Madwed, Snidman, Shannon, & Cohen, 1985; Brownley et al., 2000; Critchley et al., 2000). Children with ADHD compared to typically developing children display an enhanced variability in the mid and low frequency heart rate bands when performing a cognitive task (Börger, Van der Meere, Ronner, Alberts, Geuze, & Bogte, 1999; Börger & Van der Meere, 2000), suggesting difficulties in the intentional control over the allocation of attention. Interestingly, the attention allocation increases not only when tasks become more difficult, but also when tasks are rewarded (Suess et al., 1998). Possibly, children with ADHD suffer from a motivational problem and require external stimulation such as reward and penalty to increase the allocation of attention that is necessary to maintain an optimal performance level (Douglas, 1989; Sergeant et al., 1999). If this is correct, children with ADHD are expected to show abnormal autonomic responses to contingencies such as reward and punishment in terms of low and mid frequency heart rate variability. This is investigated in Chapter 6.

Theoretical Frameworks of ADHD and Abnormal Reinforcement Sensitivity

Several theoretical explanations of ADHD have incorporated motivational problems as the core feature of the disorder (see Chapter 2 for a review), although the theoretical frameworks considerably differ in detail. Some have proposed a *smaller sensitivity to reinforcement* in ADHD: Children with ADHD would suffer from an elevated reward threshold that implies that children with ADHD need more rewards than controls in order to impact their behaviour (Haenlein & Caul, 1987). Similarly, according to a neurobiological model of ADHD (Sagvolden et al., 2005; Johansen, Aase, Meyer, & Sagvolden, 2002) a dysfunction in the dopamine transmission in the fronto-limbic circuitry is responsible for a faster decay of reward and a smaller effects of extinction. Quay (1988a; 1988b; 1988c; 1997) suggested that ADHD is characterized by a

smaller sensitivity to punishment rather than reward, which, according to Newman (Newman, 1987; Patterson & Newman, 1993; Wallace & Newman, 1990) is the result of increased attention that is directed to reward stimuli. Other models, however, have suggested a *greater sensitivity to reinforcement* in ADHD as expressed by increased frustration to the omission of rewards (Douglas, 1989). Sergeant, et al. (1999) and Van der Meere (2002) proposed that a *self-regulation deficit* is responsible for ADHD, which is expressed in a greater behavioural dependence on external reinforcement than on internal goals in ADHD. As a result, when testing the different models regarding an aberrant reinforcement sensitivity in ADHD, one needs to focus on whether children with ADHD are either abnormally sensitive to reinforcement in general (e.g., Sergeant et al., 1999), to the valence of reinforcement (Newman, 1987; Quay, 1988a; Sonuga-Barke, 2002), the magnitude of reinforcement (Haenlein & Caul, 1989) or the frequency of reinforcement (Douglas, 1989; Sagvolden et al., 2005). These four aspects of reinforcement are, therefore, investigated in the current thesis.

Neurocognitive Problems in ADHD: The Search for Endophenotypes

A recent approach in studying the mechanisms that may explain the behavioural and intellectual problems that characterize ADHD has been the search for endophenotypes (Almasy & Blangero, 2001; Castellanos & Tannock, 2002; Doyle et al., 2005; Gottesman & Gould, 2003; Waldman, 2005). Endophenotypes are predisposing (familiar) vulnerability markers that are correlated with the disorder and may explain the relation between the genotype (the genes) and the phenotype (the behavioural symptoms) (Gottesman & Could, 2003; Waldman, 2005). Identifying endophenotypes is useful, since ADHD is a complex disorder in the sense that there is a weak mapping between susceptibility genes and the behavioural symptoms of ADHD (Cornblatt & Malhotra, 2001). Interestingly, neuroanatomical dysfunctions in ADHD show correlations with both the genotype, as well as the fenotype that are larger than the direct correlation between the genotype and the phenotype. This has led researchers to conclude that endophenotypes should be solidly grounded in neuroscience in order to be useful (Castellanos & Tannock, 2002).

Structural and functional imaging studies have shown that three major brain pathways relate to the development of ADHD: the fronto-striatal system, the brain pathway that connects the basal ganglia with the prefrontal cortex, the fronto-cerebellar pathway that connects the cerebellum with the prefrontal cortex, and the fronto-limbic pathway that connects limbic structures such as the amygdala and ventral stria-

tum with frontal cortex (Arnsten, 2006; Castellanos & Tannock, 2002; Nigg & Casey, 2005). The neuroanatomical pathways have led researchers to postulate three neurocognitive endophenotypes that relate to the aetiology of ADHD: *cognitive control, temporal information processing* and an *abnormal sensitivity to reinforcement contingencies* (Bidwell, et al., 2007; Casey et al., 1997; Castellanos, Sonuga-Barke, Milham, & Tannock, 2006, Castellanos & Tannock, 2002; Johansen et al., 2002; Nigg, 2005; Sagvolden et al., 2005).

The fronto-striatal and fronto-cerebellar pathway that connects the (dorsal) striatum and the dorsolateral prefrontal cortex (DLPFC), has been found to be implicated in *cognitive control functions* (or executive control functions) (Casey et al., 1997; Castellanos, Sonuga-Barke, Milham, & Tannock, 2006; Semrud-Clikeman, Steingard, Filipek, Biederman, Bekken, & Renshaw, 2000). Cognitive control is referred to as the ability to adjust flexibly and appropriately to continuous changing environmental demands in relation to internal goals or intentions (Norman & Shallice, 1986; Stuss, Shallice, Alexander, & Pictor, 1995) and is opposed to more automated processes (Posner & Petersen, 1990). Children with ADHD have been found to show cognitive control problems in four areas: working memory (holding information in mind), inhibition (suppressing ongoing motor responses), planning (organizing future action sequences), and interference control (ignore irrelevant information) (Pennington & Ozonoff, 1996; Sergeant, Geurts, & Oosterlaan, 2002; Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005). Furthermore, cognitive control problems in ADHD become evident in the impaired ability to discriminate between good and bad outcomes of responses (Itami & Uno, 2002; Toplak, Jain, & Tannock, 2005). Although there is there is general consensus that children with ADHD suffer from problems with cognitive control (Barkley, 1997; Bidwell, Willcutt, Defries, & Pennington, 2007; Castellanos & Tannock, 2002; Nigg, 2005), the mechanisms of these deficiencies remain unclear. In Chapters 2, 4 and 5 of the current thesis there is investigated whether cognitive control may be secondary to a motivational deficit such as an abnormal sensitivity to reinforcement.

In addition to cognitive control functions, the cerebellum and basal ganglia (both sub-cortical structures) are associated with *temporal information processing:* monitoring the timing of events (Haber, 2003; McClure, Berns, Montague, 2003; Spencer, Zelaznik, Diedrichsen, Ivry, 2003). Temporal information processing is critical for planning, the initiation and suppression of behaviour, but also for the organization of muscle-driven movements of the body (Haber, 2003; Castellanos et al., 2006). This function may therefore play a major role in problems such as motor-restlessness and clumsy behaviour of children with ADHD. Difficulties in temporal information

processing in ADHD are manifested in problems with time discrimination and time (re)production (Toplak, Dockstader, & Tannock, 2006). Children with ADHD seem to have an internal clock that runs too fast (resulting in time underestimations). In addition, problems with temporal organization of motor output are observed such as the well-known pattern of slow and variable responding (Leth-Steensen, Elbaz, & Douglas, 2000; Rubia, Smith, Brammer, & Taylor, 2007; Van Meel, Oosterlaan, Heslenfeld, & Sergeant, 2005a). Subcortical dysfunctions such as those related to temporal information processing are less obviously linked to motivational problems and in Chapter 3 such an attempt has been made by investigating time production performance under various motivational conditions.

Dysfunctions in the fronto-limbic pathway have been associated to problems in motivated behaviour, pleasurable sensations and reward approach (Berridge & Robinson, 2003; Gray, 1988; Schultz, 2000; Wise, 2004). This pathway connects the ventral striatum with the orbital frontal cortex (OFC) and ventral medial prefrontal cortex (VMedPFC; Haber, 2003; Zelazo & Mueller, 2002), which have close connections with the ACC. The input comes mainly from the amygdala and hippocampus. This pathway has been related to an *abnormal sensitivity to reinforcement contingencies* in ADHD (Castellanos & Tannock, 2002; Johansen et al., 2002; Nigg, 2005; Sagvolden et al., 2005). For example, children with ADHD compared to controls prefer immediate small over larger delayed gratification (Sonuga-Barke, Taylor, Sembi, & Smith, 1992; Tripp & Alsop, 1999). Neuroimaging studies have demonstrated that children with ADHD show impaired activity in the ventral striatum during reward anticipation (Scheres, Milham, Knutson, & Castellanos, 2007) that may explain this preference for immediate reward.

The acknowledgement of several endophenotypes in ADHD highlights the importance of studying cognitive control, temporal information processing, and reinforcement deficiencies in concert.

Outline and Aims of the Current Thesis

The studies presented in the current thesis aim to extend the present literature on the role of reinforcement in ADHD. The impact of reward and penalty on neurocognitive performance as well as autonomic responses are studied, under the assumption that people are motivated to work for rewards, while avoiding punishment. Apart from the review of the literature (Chapter 2), around 200 children between 8 and 12 years old participated in the experimental studies (Chapters 3, 4, 5, and 6). In these stud-

ies children with ADHD were compared to typically developing children or a clinical comparison group (Chapter 5). **Chapter 2** reviews the literature on reinforcement sensitivity in ADHD. Five theoretical frameworks are discussed, as well as 22 experimental studies that investigated the impact of reinforcement in children with ADHD on neurocognitive performance, motivation, and autonomic responses. In **Chapter 3**, the impact of reinforcement on motor timing is studied, a basic ability that requires temporal information processing. **Chapter 4** examines decision-making in the face of changing reinforcement contingencies. There is investigated whether children with ADHD are biased by the tendency to search for immediate reward while ignoring the aversive long-term outcomes of their choices. **Chapter 5** reports whether children with ADHD suffer from abnormalities in reinforcement learning. Children with ADHD were compared to typically developing children, as well as a clinical group to investigate the specificity of abnormal reinforcement sensitivity in ADHD. **Chapter 6** reports a study on heart rate responses to reinforcement. Both immediate changes (a measure of feedback monitoring) following reinforcement are reported as well as more slow changes in heart rate variability that are suggested to be indicative of mental effort. **Chapter 7** contains a general discussion of the findings, clinical implication as well as directions for future research. Finally, some concluding remarks are presented.

The current thesis aims to answer three main questions: Firstly, are neurocognitive dysfunctions in ADHD secondary to a motivational deficit such as an abnormal sensitivity to reinforcement contingencies? To answer this question, the impact of reinforcement is investigated on cognitive control (Chapters 2, 4 and 5) and temporal information processing (Chapter 3). Secondly, are children with ADHD sensitive to specific aspects of reinforcement that can explain the underlying mechanisms of a reinforcement deficit in ADHD? Do children with ADHD exhibit an aberrant sensitivity to: instances of reinforcement over feedback-only (e.g., Sergeant et al., 1999: Chapters 2, 3, 4, 5, and 6), the valence of reinforcement (e.g., Newman, 1987; Quay, 1988a; 1988b; 1988c; 1997; Sonuga-Barke, 2002; Wallace & Newman, 1990: Chapters 2, 3, and 6), the magnitude of reinforcement (Haenlein & Caul, 1989: Chapters 3, 4 and 5), or the frequency of reinforcement (Douglas, 1989; Sagvolden et al., 2005: Chapters 4 and 5)? Thirdly, is an abnormal sensitivity to reinforcement accompanied by abnormal autonomic responses to reward and penalty? To answer this question, heart rate and skin conductance responses (Chapters 2, 3, 4, and 6) as well as changes in heart rate variability are measured (Chapter 6).

Chapter 2

The Impact of Reinforcement Contingencies on ADHD: A review and Theoretical Appraisal

Marjolein Luman, Jaap Oosterlaan, and Joseph A. Sergeant, *Clinical Psychology Review*

Abstract

One of the core deficits in attention deficit/hyperactivity disorder (ADHD) is thought to be an aberrant sensitivity to reinforcement, such as reward and response cost. Twenty-two studies (N = 1181 children) employing ADHD and reinforcement contingencies are reviewed from the vantage points: task performance, motivation and psychophysiology. Results indicate that reinforcement contingencies have a positive impact on task performance and levels of motivation for both children with ADHD and normal controls. There is evidence that the effect related to task performance is somewhat more prominent in ADHD. There is some evidence that a high intensity of reinforcement is highly effective in ADHD. Children with ADHD prefer immediate over delayed reward. From a psychophysiological point of view, children with ADHD seem less sensitive to reinforcement compared to controls. While comorbid disorders are suggested to be confounders of the dependent variables, many studies do not examine the effect of ODD and CD. We discuss the implications of the findings for five theoretical frameworks, including the model by Haenlein and Caul (1987), Douglas (1999), the CEM (Sergeant et al., 1999), the dual-pathway model (Sonuga-Barke, 2003) and the BIS/BAS model (Quay, 1988). Results show a discrepancy between the theoretical models and the behavioral findings.

Introduction

Attention deficit/hyperactivity disorder (ADHD) is one of the most prevalent disorders in children and adolescents, characterized by inattentive, hyperactive and impulsive behavior (American Psychiatric Association, 1994). In several theoretical explanations ADHD is thought to be associated with an aberrant sensitivity to reinforcement, including reward, punishment and reinforcement schedules (e.g., manipulation of reinforcement frequency and delays in reinforcement administration) (Douglas, 1989; Haenlein & Caul, 1987; Sagvolden, Johansen, Aase, & Russell, 2004; Sagvolden & Sergeant, 1998; Sergeant, Oosterlaan, & Van der Meere, 1999; Sonuga-Barke, 1995; Wender, 1972; Quay, 1988a, b, c). Since reinforcement is highly associated with motivation, research suggests that an unusually low level of effort or intrinsic motivation accounts for the performance deficits in children with ADHD (August, 1987; Borcherding et al., 1998; Barber, Milich & Welsch, 1996; Sergeant & Van der Meere, 1990; Van der Meere, Hughes, Börger, & Sallee, 1995; Wilkison, Kircher, McMahon, & Sloane, 1995). For example, without supervision or when tasks are extremely boring, the attention span of children with ADHD is very limited (Van der Meere, Shalev, Börger, & Gross-Tsur, 1995).

Haenlein and Caul (1987) suggested that children with ADHD have an elevated reward threshold and, therefore, require higher rates of reinforcement compared to normal children. They hypothesized that children with ADHD, compared to normal children, perform poorer under partial and delayed reinforcement, since the intensity of reward in these conditions is lower compared to conditions of continuous and immediate reinforcement.

Sagvolden and colleagues (Johansen, Aase, Meyer, & Sagvolden, 2002; Sagvolgen, Aase, Zeiner, & Berger, 1998; Sagvolden & Sergeant, 1998; Sagvolden, Johansen, Aase, & Russell, 2004) claimed that the main symptoms of ADHD are caused by a deficit in reinforcement processes, in part, due to a hypo-efficient central nervous dopaminergic system. According to Sagvolden et al. (2004), children with ADHD have a shorter and steeper delay-of-reinforcement gradient. The delay-gradient describes the time interval between the response and reinforcer and its relation to the impact of a reinforcer. The reinforcing effect is largest, when the reinforcer is delivered immediately after the response. In children with ADHD, unlike normally developing peers, only responses in close proximity to a reinforcer will be conditioned. In addition, relatively few correct responses between the delivery of two consecutive reinforcers will be maintained. As a result, the association between response and reinforcer will be less consistent and 'sustained attention' will be impaired. When reinforcers are

powerful and frequent, however, the differences in behavior between children with ADHD and controls is expected to be minimal.

Douglas (Douglas, 1989, 1999; Douglas & Parry, 1994) suggested that children with ADHD are unusually sensitive to reward and suffer from a heightened frustration level in response to the loss of anticipated rewards. Because of the heightened frustration level, performance of children with ADHD is predicted to deteriorate under conditions of partial compared to continuous reward.

Another theoretical position was offered by Quay (1988a, b, c, 1997) who tried to explain ADHD symptoms in terms of Gray's (1982, 1987) psychobiological theory of learning and emotion. Gray developed a theory in which three collaborative brain systems modulate behavior. The two most relevant here are the Behavioral Activation System (BAS), which involves the dopaminergic pathway, nucleus accumbens and ventral striatum, and the Behavioral Inhibition System (BIS), which is located in the septo-hippocampal system. The BAS, according to Gray, is activated by conditions of reward and initiates approach behavior and active avoidance. The BIS is activated by conditions of punishment and non-reward, and interrupts ongoing or anticipated motor behavior. A third system, called the Nonspecific Arousal System (NAS), is activated by both the BIS and the BAS and acts to increase the intensity (speed/force) of behavior. According to Quay (1988a, b, c), in normal children the BIS and the BAS cooperate with one another to meet situational demands. For example, when response inhibition is required, the BIS is activated and temporarily predominates over the BAS. Quay argued that children with ADHD have difficulty in inhibiting ongoing and anticipated motor behavior, because of an underactive BIS. Futhermore, Quay argued that children with ADHD are less responsive to signals of punishment and non-reward.

Fowles (1988) reviewed psychophysiological experiments that provide evidence of two independent psychophysiological measures supporting Gray's psychobiological theory of learning and emotion. Fowles (1980, 1988) noted evidence for increased heart rate in normal adults in face of appetitive stimuli and signals of reward. On basis of these findings, Fowles proposed that heart rate reflects activity in the BAS. In contrast, skin conductance responses increase in the face of aversive stimuli and signals of punishment, and are unaffected by appetitive or rewarding stimuli. The changes in skin conductance were suggested to reflect activity in the BIS.

The role of reinforcement has been examined by Sonuga-Barke (2002), who proposed a dual pathway model of ADHD in which he recognized two distinct subtypes

of the disorder. One subtype is associated with diminished inhibitory control. The other subtype is characterized by a motivational style, in which children with ADHD show aversion to delayed reinforcement, associated with fundamental alternations in reward mechanisms. Children with ADHD were hypothesized to rate immediate rewards as more and future rewards as less valuable compared to control children. Sonuga-Barke acknowledged Sagvolden's (1998) theory concerning a steeper and shorter delay-of-reinforcement gradient in ADHD, as evidence of delay aversion.

In contrast, Sergeant, Oosterlaan, and Van der Meere (1999) hypothesized that children with ADHD suffer from a non-optimal energetic state explained in terms of the Cognitive-Energetic Model (CEM). This model is based on the assumption that information processing is influenced by both computational (process) factors and state factors such as *effort, arousal and activation* (Sanders, 1983; Sergeant, 2000; Sergeant & Van der Meere, 1990; Sergeant & Scholten, 1985; Sergeant et al., 1999). The effort pool controls the state of the lower layers of the model, namely, the arousal and activation pool. Effort (which is related to motivation) is conceived as the energy necessary to meet the demands of the task. Reinforcement contingencies are presumed to have their influence on this pool. The highest level of the CEM is a monitoring system, which is sensitive to 'knowledge of results'. According to the CEM, if children with ADHD suffer from a deficit in the effort pool, performance may be poor due to a non-optimal energetic state. Since reinforcement is expected to activate the effort pool, reinforcement will induce the necessary energy to meet the task demands. As a result, performance on cognitive tasks improves.

In addition, from a clinical perspective, children with ADHD are described as benefiting from reinforcement contingencies. In several behavioral modification programs, reinforcement has proven to be highly effective in the treatment of ADHD (Barkley, 2002). Reinforcement contingencies are found to normalize behavior that characterizes ADHD in school, sports and home settings and to improve academic functioning (Hupp, Reitman, Northup, O'Callaghan, & LeBlanc, 2002; Kelley & McCain, 1995; Pelham et al., 1993; Pelham & Hindshaw, 1992; Rapport, Murphy, & Bailey, 1982). These findings further emphasize the role of reinforcement contingencies in ADHD.

Given, on the one hand, the heterogeneous findings related to ADHD and reinforcement contingencies, on the other hand, the emphasis on reinforcement in several accounts, there is a clear call for a review of the literature related to the impact of reinforcement on ADHD. The aim of this paper is to review the literature regarding sensitivity of children with ADHD to environmental contingencies, such as re-

ward, punishment and reinforcement schedules. First, we will provide an extensive overview of the studies that have focused on task performance, motivation level and psychophysiology of children with ADHD under reinforcement contingencies. Since the publication of the hallmark article by Douglas and Peters (1979), such an attempt has not been made. Secondly, we wish to investigate whether the findings fit into the models encompassing reinforcement contingencies as a central aspect for the theoretical explanations of ADHD, we will focus on possible shortcomings within this field of research.

Organization of This Review

We will compare the performance of children with ADHD and normal controls on different tasks that measure cognitive processing (e.g., inhibition) and response output (e.g., reward choice behavior) under various reinforcement conditions. Next, since motivation and reinforcement are thought to be highly associated (e.g., Sergeant et al, 1999), we will specify the role of motivation. We review psychophysiological measures of heart rate (inter-beat-interval) and skin conductance (skin conductance level and response) under different reinforcement conditions. These measures may provide us with evidence whether children with ADHD suffer from diminished BIS-activity as suggested by Quay (1988a, b, c).

Given the heterogeneous findings in the literature concerning ADHD and reinforcement contingencies, it seems important to acknowledge possible confounding variables that can influence the results. ADHD is highly associated with oppositional defiant disorder (ODD) and conduct disorder (CD) (Angold, Costello, & Erkanli, 1999) and the impact of the possible confounding effects of ODD and CD on the findings are reviewed. ODD and CD were combined because ODD is frequently found to be a developmental antecedent of CD, and because ODD is generally considered a milder form of CD (APA, 1994).

Another important potential confounder may be reinforcement allocation policy. This policy concerns whether reinforcement allocation is based on task performance or whether it is based on task participation (irrespective of response accuracy). The expectancy related to reinforcement occurrence may differ between the two policies, which, according to Schulz (2000), may influence the rate of reinforcement learning and task performance.

Important possible confounders are the specific characteristics of the reinforcer that differ between studies reviewed here. It is acknowledged that neurons in the amyg-

dala seem to be involved in processing the intensity of reinforcement (Schultz, 2001). Neurons in the orbitofrontal cortex, in contrast, can discriminate between different forms of reinforcement, such as liquid or solid reward (Schulz, 2000, 2002). Since ADHD is associated with a deficiency in the orbitofrontal area (Barkley, 1997) and the mesolimbic system (Quay, 1988a, b, c; Sonuga-Barke, 2002, 2003), children with ADHD may be differentially affected by different intensities and forms (e.g., money, tokens, presents) of reinforcement. Finally, the impact of ADHD subtypes, gender, age and IQ are discussed.

Qualitative Overview of Studies Concerning ADHD, Task Performance and Reinforcement Contingencies

This review covers 22 studies published between 1986 and February 2003, which includes 1181 children. The studies were located in PubMed (Medline), PsycINFO and ISI Web of Knowledge databases. We searched for empirical studies that investigated primarily the effect of reinforcement contingencies on task performance of children with ADHD. We searched for studies that investigated the effects of reinforcement contingencies on measures of motivation and psychophysiology. We combined search terms related to ADHD (such as ADHD, hyperactive, attention) with search term related to reinforcement (such as reward, punishment, response cost, reinforcement, feedback, contingencies). The reference lists of published articles were used to locate additional relevant studies.

Dissertations, abstracts as well as clinical studies were not included. In addition, studies that included less than ten subjects in one of the groups of interest were excluded from this review. Furthermore, studies conducted before 1986 were excluded, because of changes in the diagnostic criteria for ADHD, related to the emergence of the third revised edition of Diagnostic and Statistical Manual of Mental Disorders (DSM III-R). Finally, studies that focused on the perception of reward and response cost and imaging studies that did not report performance data were excluded. The main features of the 22 studies is summarized in Table 2.1.

Table 2.1 || Experimental Studies Concerning ADHD, Task Performance and Reinforcement Contingencies

Study by	Subjects	Age	Confounding Variables [a]	Dependent variables	Reinforcement manipulation [b]	Differential Group effects [c]
1. Barber, Milich, & Welsh (1996)	45 ADHD 45 NC	7 - 10	• *Comorbid:* CD, ODD • *Not confounding:* age, gender, IQ as covariate	Related and unrelated paired associate memory task • % Correct	• Tokens cashed for money • Reward delivered on a trial basis • Contingent upon performance • *Conditions:* CR versus PR (50%) versus NR • Between subjects design, subjects randomly assigned to the tasks and conditions • Quantity of reward equal for both groups	• % Correct: -
2. Carlson, Mann, & Alexander (2000)	40 ADHD 40 NC	8 - 12	• *Comorbid:* CD, ODD • *Possible confounding:* age, gender, IQ	Arithmetic task • % Correct • Self rated motivation • Observed motivation	• Tokens cashed for money • Continuous reward on a trial basis • Contingent upon performance • *Conditions:* R versus RC versus NR • Between subjects design, subjects randomly assigned to one of the conditions	• % Correct ADHD: R < RC; NC: - • % Correct R and NR: ADHD < NC; RC: - • Self rated motivation ADHD: R > NR; NC: R, RC > NR • Observed motivation ADHD: RC > R, NR; NC: -
3. Carlson & Tamm (2000)	22 ADHD (combined subtype) 22 NC	8 - 10	• *Comorbid*: CD, ODD • *Not confounding*: age, gender, IQ	Figure Matching task and Jet Pack (game-like task) • % Correct • Self rated motivation • Observed motivation	• Immediate money • Continuous reward on a trial basis • Contingent upon performance • *Conditions:* R versus RC versus NR • Within subjects design, order tasks and conditions balanced	• % Correct ADHD: R, RC > NR; NC: - • % Correct R and NR: ADHD < NC; RC: - • Self rated and observed motivation: -

[a] A variable was considered as not-confounding either when groups were matched or when statistics showed that groups did not differ on this variable.
[b] Total amount of reward may vary between subjects if not mentioned, tokens could be exchanged for reward at the end of the experiment.
[c] For each dependent variable interactions between groups and reinforcement condition are described.

Study by	Subjects	Age	Confounding Variables [a]	Dependent variables	Reinforcement manipulation [b]	Differential Group effects [c]
4. Crone, Jennings, & Van der Molen (2003)	22 ADHD 22 NC	6 - 12	• *Possible confounding:* ODD • *Not confounding:* age, CD, gender, LD IQ as covariate	Go/ No Go Flanker task • % Correct • MRT • Heart rate • Skin Conductance	• Tokens cashed for money • Reward delivered on a trial basis • Contingent upon performance • *Conditions:* CR versus R(66%) & RC(33%) versus R(50%) & RC(50%) • Within subject design, conditions presented in a fixed order	• % Correct ADHD: CR > R(66%)/RC(33%) > R(50%)/RC(50%); NC: - • % Correct R/RC: not reported • MRT: see text • Heart rate: see text • Skin conductance: -
5. Daugherty & Quay (1991)	10 DD+H/ CD 9 ADD 10 CD 9 ID 15 NC	8 - 13	• *Comorbid:* CD • *Possible confounding:* IQ, ODD • *Not confounding:* age, gender, ID	Door opening task (response perseveration task) • Amount of responses • Amount of tokens	• Tokens exchanged for presents • Partially rewarded on a trial basis • Contingent upon quantity of responses • *Condition:* Chance on reward decreases from 90% to 0%, while change on RC increases from 0% to 90%	• Amount of responses: ADD+H/CD, CD > NC, IC • Number of earned tokens: ADD+H/CD, CD < NC
6. Douglas & Parry (1994)	30 ADD+H 30 NC	Range not reported ADD+H M 9.6 SD (2.1) NC: M 9.5 SD (2.0)	• *Possible confounding:* age, CD, gender, IQ, ODD	Penny tossing task • Response Time (RT) *(attention measure)* • Lever pulling force *(frustration measure)*	• Tokens exchanged for presents • Reward delivered on a trial basis • Contingent on the quantity of responses • *Conditions:* CR versus PR(50%) versus PR(30%) NR following each R condition • Between subjects design, subjects randomly assigned to one of the conditions	• RT for NC: CR > PR; ADD+H: - • RT under PR: ADD+H > NC; under CR and NR: - • Lever pulling force ADD+H or NC: - • Lever pulling force CR and PR(50%): - ; PR(30%): ADD+H > NC

[a] A variable was considered as not-confounding either when groups were matched or when statistics showed that groups did not differ on this variable.
[b] Total amount of reward may vary between subjects if not mentioned, tokens could be exchanged for reward at the end of the experiment.
[c] For each dependent variable interactions between groups and reinforcement condition are described.

Study by	Subjects	Age	Confounding Variables [a]	Dependent variables	Reinforcement manipulation [b]	Differential Group effects [c]
7. Iaboni, Douglas, & Baker (1995)	19 ADHD 17 NC	8 - 13	• *Comorbid:* CD, ODD • *Not confounding:* age, IQ, gender (boys only)	Go/no-go discriminative learning task • MRT • Omission errors • Commission errors	• Immediate money • Continuous reward on a trial basis • Contingent upon performance • *Conditions:* For accuracy on Go and No-go trials respectively: R-R versus RC-RC versus R-RC versus RC-R • Within subject design, conditions presented in a random order	• MRT for ADHD: RC < R; NC: - • MRT under R and RC: not reported • Commission and omission errors : -
8. Iaboni, Douglas, & Ditto (1997)	18 ADHD 18 NC	8 - 13	• *Comorbid:* CD, ODD • *Not confounding:* age, IQ gender (boys only)	Repetitive motor task • RT • Heart rate • Skin conductance	• Immediate money • Continuous reward on trial basis • Contingent upon performance • *Conditions:* R versus NR • Within subject design, conditions presented in a fixed order • Quantity reward equal for both groups	• RT: - • Heart rate : See text • Skin conductance level: ADHD: - ; NC: R < NR
9. Konrad, Gauggel, Manz, & Scholl (2000)	31 ADHD 37 TBI 26 NC	8 - 12	• *Possible confounding:* CD, gender, ODD • *Not confounding:* AD/HD subtypes, age, IQ, LD	Stop Task • SSRT • MRT	• Tokens exchanged for presents • Continuous reward on a trial basis • Contingent upon performance • *Conditions :* R versus NR • Between subject design, subjects randomly assigned to one of the conditions after receiving a practice (NR) condition first • Quantity of reward equal for all subjects	• MRT: - • SSRT under R: ADHD, NC < TBI; NR: NC < ADHD, TBI • SSRT in the different groups: -

[a] A variable was considered as not-confounding either when groups were matched or when statistics showed that groups did not differ on this variable.
[b] Total amount of reward may vary between subjects if not mentioned, tokens could be exchanged for reward at the end of the experiment.
[c] For each dependent variable interactions between groups and reinforcement condition are described.

Study by	Subjects	Age	Confounding Variables [a]	Dependent variables	Reinforcement manipulation [b]	Differential Group effects [c]
10. McInerny & Kerns (2003)	30 ADHD 30 NC	6 - 13	• *Possible confounding:* CD, ODD • *Not confounding:* age, gender, IQ	Time reproduction task • Absolute error • Accuracy quotient • Self rated motivation	• Tokens exchanged for presents • Continuous reward on a trial basis • Non informative feedback and reward • *Conditions:* Feedback and R versus feedback and NR • Within subject design, order of the conditions balanced • Quantity of reward and feedback equal for all subjects	• Absolute error for ADHD: NR > R; NC: - • Absolute error NR: ADHD > NC; R: ADHD = NC • Accuracy: not reported • Self rated motivation: -
11. Ooster-laan & Sergeant (1998)	14 ADHD 14 ODD/CD 14 ID 21 NC	7 - 13	• *Comorbid:* CD, ODD • *Possible confounding:* gender • *Not confounding:* age, ID, IQ	Stop task • Chance of inhibition • SSRT • MRT • Accuracy • Self rated motivation	• Tokens exchanged for presents • Continuous reward on a trial basis • Contingent upon performance • *Conditions:* R versus RC • Within subject design, conditions presented in a random order • Quantity of reward equal for all subjects	• Chance of inhibition: - • SSRT: - • MRT: - • Accuracy: - • Self rated motivation: -
12. Pelham, Milich, & Walker (1986)	30 ADD	5 - 11	• *Possible confounding:* CD, ODD • *Not confounding:* age, gender, IQ	Spelling task • Number of errors	• Tokens exchanged for presents • Reward delivered on a trial basis • Contingent upon performance • *Conditions :* CR versus PR(50%) versus NR MPH versus Placebo • Between subject design, subjects randomly assigned to one of the conditions; MPH and placebo balanced within the group	• Number of errors: -

[a] A variable was considered as not-confounding either when groups were matched or when statistics showed that groups did not differ on this variable.
[b] Total amount of reward may vary between subjects if not mentioned, tokens could be exchanged for reward at the end of the experiment.
[c] For each dependent variable interactions between groups and reinforcement condition are described.

Study by	Subjects	Age	Confounding Variables [a]	Dependent variables	Reinforcement manipulation [b]	Differential Group effects [c]
13. Rapport, Tucker, DuPaul, Merlo, & Stoner (1986)	16 ADD+H 16 NC	6 - 8	• *Possible confounding:* CD, ODD • *Not confounding:* ADHD subtypes, age, gender, IQ as covariate	Arithmetic task • Reward choice	• Immediate and delayed presents • Continuous reward after each condition • Contingent upon quantity of responses • *Conditions:* A: Small immediate R or large delayed R versus B: Small immediate R or large immediate R • Within subjects design, conditions presented in a random order	• Reward choice in A: Small immediate reward: ADD+H > NC • Reward choice in B: Small reward < large reward: ADHD = NC
14. Scheres, Oosterlaan, & Sergeant (2001)	24 ADHD 21 ODD/CD 27 ADHD +ODD/CD 41 NC	6 - 12	• *Not confounding:* ADHD subtypes, age, CD, gender, ODD, IQ as covariate	Stop task • % of inhibition • SSRT • Accuracy • MRT • Self rated motivation	• Tokens exchanged for presents • Continuous reward on a trial basis • Contingent upon performance • *Conditions:* R versus NR • Within subject design, conditions presented in a random order • Quantity of reward equal for all subjects	• % of inhibition, SSRT and accuracy: - • Self-rated motivation: - • MRT: Difference between R and NR condition: ADHD+ODD/CD > NC; ADHD > NC (trend)
15. Slusarek, Velling, Bunk, & Eggers (2001)	33 ADHD (combined subtype) 33 Clinical Controls = ID, ODD, CD) 33 NC	6 - 14	• *Possible confounding:* gender, IQ • *Not confounding:* CD, ID, LD, ODD, age as covariate	Stop task • Chance of inhibition: P(i) • SSRT	• Points as reward • Continuous reward on a trial basis • Contingent upon performance • *Conditions:* A: R & RC (amount ratio 1:1) versus B: R & RC (amount ratio 1: 5) • Within subjects design, conditions presented in a random order • Quantity of reward equal for all subjects	• P(i) for ADHD: A < B; CC and NC: - • P(i) in condition A: ADHD < CC, NC; condition B: - • SSRT for ADHD: A > B; CC and NC: - • SSRT in condition A: ADHD > CC, NC; condition B: -

[a] A variable was considered as not-confounding either when groups were matched or when statistics showed that groups did not differ on this variable.
[b] Total amount of reward may vary between subjects if not mentioned, tokens could be exchanged for reward at the end of the experiment.
[c] For each dependent variable interactions between groups and reinforcement condition are described.

Study by	Subjects	Age	Confounding Variables [a]	Dependent variables	Reinforcement manipulation [b]	Differential Group effects [c]
16. Solanto (1990)	20 ADD+H 18 NC	4 - 11	• *Comorbid:* CD, LD, ODD • *Not confounding:* age, gender, IQ, LD	Delayed Responding Task • % Correct	• Immediate money • Continuous reward on a trial basis • Contingent upon performance • *Conditions:* R versus RC • Within subjects design, conditions presented in a random order, both R and RC always alternated by NR condition • Quantity of reward equal for all groups	• % Correct: -
17. Solanto, Wender, & Bartell (1997)	22 ADHD	6 - 10	• *Comorbid:* ID, ODD • *Possible confounding:* age, gender, IQ • *Not confounding:* CD	Continuous Performance Task • d' • Hit rate	• Immediate presents • Continuous reward on a trial basis • Contingent upon performance • *Conditions:* R & RC mixed versus feedback-only MPH versus placebo • Within subject design, conditions presented in a random order, MPH and placebo balanced	• d' and Hit rate: See text
18. Sonuga-Barke, Taylor, Sembi, & Smith (1992)	15 Hyperactives 15 NC	6 - 7	• *Possible confounding:* ODD • *Not confounding:* age, IQ, gender (boys only) • *Confounding:* CD	Reward choice task • Reward choice	• Tokens cashed for money • Continuous reward on a trial basis • Contingent upon performance • *Conditions:* A: small immediate reward or large delayed reward versus B: small immediate reward + post-reward delay or large delayed reward + post reward delay • Within subject design, conditions presented in a random order	• Reward choice in B: small R < large R for both groups • Reward choice in A: See text

[a] A variable was considered as not-confounding either when groups were matched or when statistics showed that groups did not differ on this variable.
[b] Total amount of reward may vary between subjects if not mentioned, tokens could be exchanged for reward at the end of the experiment.
[c] For each dependent variable interactions between groups and reinforcement condition are described.

Study by	Subjects	Age	Confounding Variables [a]	Dependent variables	Reinforcement manipulation [b]	Differential Group effects [c]
19. Tripp & Alsop (1999)	15 ADHD 15 NC	6 - 14	• *Possible confounding:* CD, ODD, gender • *Confounding:* age, IQ	Signal detection task • d' • Response bias • RT	• Tokens exchanged for presents • Partially rewarded on a trial basis • Contingent upon performance • *Conditions:* Discrimination between two alternatives, one alternative is rewarded three times as often ADHD group: MPH versus off medication • Within subjects design, alternatives presented in a random order; MPH and off medication balanced • Quantity of reward equal for both groups	• d' : - • Response bias : - • RT : -
20. Tripp & Alsop (2001)	36 ADHD (combined subtype) 36 NC	5 - 11	• *Comorbid:* CD, ODD • *Possible confounding:* gender • *Not confounding:* age • *Confounding:* IQ	Signal detection task • d' • Response bias • RT	• Tokens exchanged for presents • Partially rewarded on a trial basis • Contingent upon performance • *Condition:* Discrimination between two alternatives, one alternative is coupled to post-reward delay and one to pre-reward delay • Within subject design, alternatives presented in a random order	• d' : - • Response bias : - • RT : -
21. Van der Meere, Hughes, Börger, & Sallee (1995)	13 ADHD 13 ADHD +CD 13 NC	Range not reported For all groups:M: 10.3	• *Possible confounding:* IQ, ODD • *Not confounding:* age, CD, gender (boys only)	Continuous Performance Task • % Correct • RT	• Immediate money • Continuous reward on a trial basis • Reward allocated every 10 seconds • *Conditions:* R versus NR, Amount of reward increases with time • Within subject design, conditions presented in a fixed order: NR – R	• % Correct: - • RT 1st half ADHD and NC: R < NR; ADHD+CD: R > NR • RT 2nd half: ADHD and NC: R > NR; ADHD+CD: R < NR • RT under R and NR: -

[a] A variable was considered as not-confounding either when groups were matched or when statistics showed that groups did not differ on this variable.
[b] Total amount of reward may vary between subjects if not mentioned, tokens could be exchanged for reward at the end of the experiment.
[c] For each dependent variable interactions between groups and reinforcement condition are described.

Study by	Subjects	Age	Confounding Variables [a]	Dependent variables	Reinforcement manipulation [b]	Differential Group effects [c]
22. Wilkison, Kirscher, McMahon, & Sloane (1995)	16 ADHD	8 - 13	• *Possible confounding:* age, CD, IQ, ODD • *Not confounding:* gender (boys only), LD	Reward choice response task • Number of responses • Amount of reward	• Tokens cashed for money • Continuous reward on a trial basis • Contingent upon the quantity of responses • *Conditions:* Reward after an ever increasing number of responses MPH versus off medication • Within subject design, order MPH and off medication condition balanced	• Not reported

[a] A variable was considered as not-confounding either when groups were matched or when statistics showed that groups did not differ on this variable.
[b] Total amount of reward may vary between subjects if not mentioned, tokens could be exchanged for reward at the end of the experiment.
[c] For each dependent variable interactions between groups and reinforcement condition are described.

ADD+H, ADHD = Attention Deficit Hyperactivity Disorder, CD = Conduct Disorder, CR = Continuous Reward, d' = d-prime, measure of sensitivity, ID = Internalizing Disorder (anxiety and mood disorders), LD = Learning Disorder, MPH = Methylphenidate, (M)RT = (Mean) Response Time, NC = Normal Control Group, NR = Non-Reward, ODD = Oppositional Defiant Disorder, PR = Partial Reward, R = Reward, RC = Response Cost, SSRT = Stop Signal Reaction Time, TBI = Traumatic Brain Injury.

Twenty studies in this review compared an ADHD group with a group of normally developing children (control group) without a psychiatric or learning disorder. Two studies did not include a control group, but compared the performance of children with ADHD on and off medication (Pelham, Milich, & Walker, 1986; Wilkison et al., 1995). In three studies included in this review (Daugherty & Quay, 1991; Oosterlaan & Sergeant, 1998; Sonuga-Barke, Taylor, Sembi, & Smith, 1992), the children in the psychiatric groups were not diagnosed according to DSM III, DSM III-R or DSM IV criteria, in contrast with the remaining 19 studies.

Although all the studies discussed in this review investigated the effects of reinforcement contingencies in ADHD, the authors adopted five different approaches to study the effects (see Table 2.1). A first approach was to compare reward with non-reward conditions, to compare reward with response cost conditions, to compare reward, response cost and non-reward conditions, and also to compare mixed reward and response cost with feedback-only conditions. In a second approach, continuous reward schedules were compared to partial reward schedules. In a third approach, reward delay was manipulated. A fourth approach was to study an altered response to reward by manipulating the reward ratio. Changes in the intensity of reward were studied in a fifth approach.

A variety of tasks that study cognitive processing and tasks that study response output were used (e.g., Arithmetric Task, Continuous Performance Task, Choice-Delay Task, Paired Associate Memory Task, Repetitive Motor Task, and a Stop Signal Task). These tasks capture different aspects of cognitive functioning, such as vigilance, working memory, inhibition, perseveration, abstract reasoning, and stimulus detection. Other tasks focus more on aspects of response output such as reward choice behavior. To overcome the problem of heterogeneity in task performance, we focus exclusively on the absolute change in task performance reflected by different dependent measures. This measurement is independent of specific cognitive functions or reward choice studied in this review.

Task Performance

Performance of children with ADHD under several different 'reinforcement conditions' is compared in this section. Reinforcement conditions refer to the different experimental conditions under which task performance is evaluated. Reinforcement may involve (accuracy) feedback only, reward, response cost, as well as a combination of feedback and reward or response cost.

With the exception of six studies, reinforcement was allocated contingent on performance. In six studies, reinforcement was allocated non-contingent on performance, which implies that allocation of reinforcement is not related to response accuracy. In these studies, reinforcement allocation was related to the number of completed trials (Douglas & Parry, 1994; Daugherty & Quay, 1991; Rapport et al., 1986; Wilkison et al., 1995), random reward was provided (McInerny & Kerns, 2003) or reinforcement was allocated at fixed time intervals (Van der Meere, Hughes, Börger, & Sallee, 1995). Response cost conditions are defined as conditions in which incorrect responses result in deduction of reward, with the exception of one study. In this study, in addition to response cost, reward was allocated following correct responses (Crone, Jennings, & Van der Molen, 2003). Under non-reward conditions, children receive neither reward nor response cost. When a non-reward condition immediately follows a reward condition in a within-subject design, this is referred to as an extinction condition. Partial reward conditions are defined as conditions in which a proportion (e.g., 50%) of the correct responses is rewarded in contrast with continuous reward conditions in which all correct responses are rewarded.

Results of children with ADHD and normal controls are reported and ODD/CD groups will be discussed additionally. Main effects of reinforcement condition, main effects of group, and interactions between reinforcement condition and group will be discussed for task performance.

ADHD Versus Normal Controls Under Reward, Non-Reward and Response Cost

Nine studies (see Table 2.2) compared a reward with a non-reward condition. Six of nine studies reported a main effect of reinforcement condition: Across groups, performance improved under reward compared to non-reward. Additionally, across reinforcement conditions, performance of children with ADHD was inferior to controls in five of nine studies. In three studies, a differential effect of reinforcement condition was revealed: Reward compared to non-reward had a positive effect on performance of the ADHD group, whereas performance of controls did not change (Carlson & Tamm, 2000; McInerny & Kerns, 2003), or changed to a lesser extent (Konrad, Gauggel, Manz, & Scholl, 2000). In two studies performance of the ADHD group 'normalized' under reward (Konrad et al., 2000; McInerny & Kerns, 2003). Six of nine studies failed to find a differential effect of reinforcement condition on task performance for the ADHD and control group (Barber et al., 1996; Carlson, Mann, & Alexander, 2000; Iaboni, Douglas, & Ditto, 1997; Scheres, Oosterlaan, & Sergeant, 2001; Solanto, 1990; Van der Meere, Hughes, Börger, & Sallee, 1995). Scheres et al., (2001) revealed a speed-accuracy trade-off for the ADHD group in the reward condi-

tion: while accuracy improved under reward, response times slowed down. Controls did not show this trade-off. The dependent measures used in the studies were accuracy (Barber et al., 1996; Carlson, Mann, & Alexander, 2000; Carlson & Tamm, 2000; McInerny & Kerns, 2003; Van der Meere, Hughes, Börger, & Sallee, 1995; Solanto 1990), (mean) response time (Iaboni et al., 1997; Van der Meere, Hughes, Börger, & Sallee, 1995; Scheres et al., 2001) and Stop Signal Reaction Time (SSRT) (Scheres et al., 2001).

Pelham et al. (1986) compared performance of children with attention deficit disorder (ADD) receiving methylphenidate (MPH) and placebo, under both reward and non-reward conditions. Performance improved under reward compared to non-reward and with MPH compared to placebo. No differential effects of reinforcement condition were revealed for children with ADD on or off medication. The dependent measure was error-rate.

Table 2.2 || Task Performance of Children with ADHD and Normal Controls Under Reward and Non-Reward

Study	Group Effects				
	Reward	Non-Reward	Reward Versus Non-Reward [a]		Dependent Variable
Barber et al. (1996)	ADHD = NC	ADHD = NC			Accuracy
Carlson et al. (2000)	ADHD < NC	ADHD < NC			Accuracy
Carlson & Tamm (2000)	ADHD < NC	ADHD < NC	+	ADHD	Accuracy
Iaboni et al. (1997)	ADHD = NC	ADHD = NC	+	NC, ADHD	RT
Konrad et al. (2000)	ADHD = NC	ADHD < NC	+	NC, ADHD	SSRT
McInerny & Kerns (2003)	ADHD = NC	ADHD < NC	+	ADHD	Absolute error[b]
Van der Meere, Hughes, Börger, & Sallee (1995)	ADHD = NC	ADHD = NC			Accuracy
	ADHD = NC	ADHD = NC			RT
Scheres et al. (2001)	ADHD = NC	ADHD = NC	+	NC, ADHD	SSRT[c]
	ADHD < NC	ADHD < NC	--	ADHD[d]	MRT
Solanto (1990)	ADHD < NC	ADHD < NC	+	NC, ADHD	Accuracy

[a] (+) indicates improvement in performance under reward compared to non-reward, (--) indicates deterioration in performance.
[b] Absolute error indicates a measure of accuracy.
[c] The results for accuracy and % inhibited responses were similar to the results for SSRT.
[d] $p < .10$, marginally significant increase in MRT reflecting a speed-accuracy trade-off.

AD/HD = Attention Deficit/Hyperactivity Disorder, NC = Normal controls, (M)RT = (Mean) Response Time, SSRT = Stop Signal Reaction Time.

Three studies compared the effects of response cost and non-reward conditions (Carlson & Tamm, 2000; Carlson, Mann, & Alexander, 2000; Solanto, 1990). Two studies reported improved performance under response cost compared to non-reward across groups; one study revealed no main effect of reinforcement condition (Carlson, Mann, & Alexander, 2000). All three studies reported a main effect for group: Performance of children with ADHD was worse compared to controls across reinforcement conditions. A differential effect of reinforcement condition has been found in two studies: Performance of children with ADHD improved under response cost compared to non-reward conditions, while performance of controls remained unchanged (Carlson & Tamm, 2000; Carlson, Mann, & Alexander, 2000). In both studies, response cost was found to 'normalize' performance of children with ADHD. Solanto (1990) failed to find a differential effect of reinforcement condition. The dependent measure for all three studies was accuracy.

Reward and response cost conditions were compared in six studies. Table 2.3 shows the results of these studies. A main effect of reinforcement condition was found in three of six studies: Across groups, performance deteriorated under response cost compared to reward (Crone et al., 2003; Iaboni, Douglas, & Baker, 1995; Oosterlaan & Sergeant, 1998). The other studies failed to find any difference in performance between reinforcement conditions (Carlson & Tamm, 2000; Carlson, Mann, & Alexander, 2000; Solanto, 1990). All six studies showed a main effect of group: Performance of children with ADHD was inferior to that of controls across reinforcement conditions. Reinforcement condition differentiated children with ADHD from controls in three of six studies (Carlson & Tamm, 2000; Carlson, Mann, & Alexander, 2000; Crone et al., 2003). In two studies, the performance of the ADHD group improved under response cost compared to reward, while the performance of controls remained unchanged (Carlson & Tamm, 2000; Carlson, Mann, & Alexander, 2000). In both studies, performance of children with ADHD was found to 'normalize' under response cost. Crone and colleagues (2003) found a speed-accuracy trade-off for children with ADHD: While the mean response time improved when the percentage of response cost increased, accuracy deteriorated in these conditions. Controls on the other hand, speeded up when the percentage of response cost increased and remained as accurate compared to the reward-only condition. Three of six studies failed to find a differential effect of reinforcement condition on task performance for the ADHD and control group (Iaboni et al., 1995; Oosterlaan & Sergeant, 1998; Solanto, 1990). The dependent measures were accuracy (Carlson, Mann, & Alexander, 2000; Carlson & Tamm, 2000; Crone et al., 2003; Solanto, 1990), commission errors (Iaboni et al., 1995), (mean) response time (Crone et al., 2003; Iaboni et al., 1995; Oosterlaan & Sergeant, 1998) and SSRT (Oosterlaan & Sergeant, 1998).

Solanto, Wender, and Bartell (1997) compared the performance of children with ADHD between a mixed reward and response cost and a feedback-only condition. Children with ADHD performed the task while receiving medication and placebo. Performance was more optimal under mixed reward and response cost compared to feedback only, although this effect was statistically of marginal significance. Furthermore, within-group differences revealed that children with ADHD on medication performed better than the group receiving placebo (Solanto et al., 1997). There was an interaction between the effect of medication and reinforcement condition: Compared to feedback only, performance of the placebo group improved under mixed reward and response cost. Performance of the medicated group, however, did not improve, when reinforcement was given. When the effects of medication and allocation of reinforcement were compared, medication effects were found to be slightly larger. Dependent measures were hit rate and perceptual sensitivity (d').

Table 2.3 || Task Performance of Children with AD/HD Versus Normal Controls Under Reward and Response Cost

Study	Group Effects				
	Reward	Response Cost	Reward Versus Response Cost [a]		Dependent Variable
Carlson et al. (2000)	ADHD < NC	ADHD = NC	-	ADHD	Accuracy
Carlson & Tamm (2000)	ADHD < NC	ADHD = NC	-	ADHD	Accuracy
Crone et al. (2003)	ADHD < NC	ADHD < NC[b]	-	NC, ADHD	MRT
	ADHD < NC	ADHD < NC	+	ADHD	Accuracy
Iaboni et al. (1995)	ADHD < NC	ADHD < NC	+	ADHD, NC	Commission Errors
	ADHD = NC	ADHD = NC			MRT
Oosterlaan & Sergeant (1998)	ADHD < NC	ADHD < NC			SSRT[c]
	ADHD < NC	ADHD < NC	+	NC, ADHD[d]	MRT
	ADHD = NC	ADHD = NC			Accuracy
Solanto (1990)	ADHD < NC	ADHD < NC			Accuracy

[a] (+) indicates improvement in performance under reward compared to response-cost, (-) indicates deterioration in performance.
[b] This condition involved the allocation of both reward and response cost.
[c] The results for % inhibited responses were similar to the results for SSRT.
[d] $p < .10$, marginally significant effect.

AD/HD = Attention Deficit/Hyperactivity Disorder, NC = Normal controls, (M)RT = (Mean) Response Time, SSRT = Stop Signal Response Time

ADHD Versus Normal Controls Under Partial reward, Non-Reward and Continuous Reward

Three studies compared the impact of partial and non-reward on task performance. In one study, children with ADD were compared receiving both medication and placebo (Pelham et al., 1986). Two studies revealed a reinforcement condition effect: Under partial compared to non-reward, Barber et al. (1996) found that performance deteriorated, while Pelham and colleagues (1986) found that performance improved, although this result was of marginal significance. Douglas and Parry (1994) failed to find a reinforcement condition effect. Children with ADD performed more optimally under medication compared to children receiving placebo (Pelham et al., 1986). No differences in performance were found between children with ADHD and controls. No differential effects of reinforcement condition were revealed (Barber et al., 1996; Douglas & Parry, 1994; Pelham et al., 1986). Dependent measures were response time (Douglas & Parry, 1994), accuracy (Barber et al., 1996) and error-rate (Pelham et al., 1986).

A partial reward condition was compared to continuous reward in three studies. Three studies failed to find main effects of reinforcement condition (Barber et al., 1996; Douglas & Parry, 1994; Pelham et al., 1986). Douglas and Parry (1994) found that reinforcement condition had a differential impact on the performance of children with ADHD and controls: While performance of children with ADHD deteriorated under partial compared to continuous reward, performance of controls was similar in both conditions. In this study, performance of children with ADHD was found to 'normalize' under continuous reward. The remaining two studies revealed no interaction between reinforcement condition and group (Barber et al., 1996; Pelham et al., 1986). The dependent variables in these studies were error-rate (Pelham et al., 1986), (mean) response time (Douglas & Parry, 1994) and percentage correct (Barber et al., 1996).

Douglas and Parry (1994) measured frustration level under both partial and continuous reward, since they predicted frustration level to correlate with task performance. For both the ADHD and control group levels of frustration correlated with performance: Under partial reward, frustration level of children with ADHD increased, while performance deteriorated as noted above. Levels of frustration and performance of normal controls did not differ between the reinforcement conditions.

ADHD Versus Normal Controls Under Immediate and Delayed Reward

Three studies compared task performance under immediate and delayed reward. When children were required to make a choice between an immediate and a delayed reward, children with ADHD chose more often for an immediate reward compared to controls (Rapport, Tucker, DuPaul, Merlo, & Stoner, 1986; Sonuga-Barke et al., 1992; Tripp & Alsop, 2001). They chose more often for the immediate reward, even though the delayed reward was larger (Rapport et al., 1986). In contrast, normal controls chose more often for the larger delayed reward (Rapport et al., 1986) or showed a smaller response bias for the immediate reward (Tripp & Alsop, 2001). In addition, reward choice on earlier trials did not change the preference for an immediate reward for children with ADHD (Rapport et al., 1986; Tripp & Alsop, 2001). Normal controls, however, seemed to incorporate recently gained reward into their reward choice: When previous reward was small (Rapport et al., 1986) or immediate (Tripp & Alsop, 2001), the preference for an immediate (small) reward in the consecutive trial diminished.

When a maximum amount of reward was pre-determined or when the maximum amount of time to complete the task was set, the response pattern of children with ADHD did not differ from normal controls (Sonuga-Barke et al., 1992). Both groups responded in a pattern that maximized the amount of reward. However, when the number of trials was pre-determined, which implied a maximum number of responses, the ADHD group chose more often for the reward that minimized time-on-task. The normal control group maximized their total amount of reward (Sonuga-Barke et al., 1992). Moreover, when overall delay was similar, by adding a post reward delay, Sonuga-Barke et al. (1992) observed that both children with ADHD and normal controls chose for the large delayed reward. The result led Sonuga-Barke to conclude that children with ADHD are extremely sensitive to delay and are delay averse rather than reward maximizers (Sonuga-Barke et al., 1992; Sonuga-Barke, 2000). In contrast to the findings of Sonuga-Barke, however, Tripp and Alsop (2001) found that children with ADHD preferred immediate reward even when overall delay was similar.

ADHD, ODD/CD, and Normal controls Under Different Reward Ratio's

Daugherty and Quay (1991) investigated response perseveration in a two-choice response task, where the chance of receiving reward diminished, while the chance of receiving response cost increased. In this task, reward and response cost were allocated independent of the response choice. Daugherty and Quay (1991) found no differences in the response pattern of children with ADHD and normal controls.

In both groups, the response rate diminished, when the chance of receiving reward declined. In contrast, the response rate of children with CD (and also children with ADHD+CD) remained high. Consequently, children with CD (and children with ADHD+CD) received a smaller total amount of reward compared to the other groups, indicating that their strategy was less profitable.
Wilkison et al. (1995) compared children with ADHD on and off medication in a two-choice response task where the chance of receiving reward diminished. Children with ADHD on medication showed a higher response rate in the face of declining probability of reward compared to children with ADHD off mediation (Wilkison et al., 1995). Consequently, the group receiving medication gained more reward at the end of the experiment. Unfortunately, a normal control group was not included in that study.

Tripp and Alsop (1999) measured performance in a choice task, where one alternative was rewarded three times as often as compared to the other. Children with ADHD on and off medication were compared to controls. Performance of children with ADHD on medication was more optimal compared to both controls and children with ADHD off medication. No interaction between group and reward ratio was revealed. Dependent measures were perceptual sensitivity (d') and response bias.

ODD/CD, ADHD and Normal Controls Under Reward, Non-Reward and Response Cost

Two studies included an ODD/CD group, when task performance was studied in children with ADHD under different reinforcement contingencies (Oosterlaan & Sergeant, 1998; Scheres et al., 2001). Strikingly, in both studies, no differences were revealed between children with ODD/CD and children with ADHD. The same studies compared children with ODD/CD with normal controls. Both studies revealed a main effect of group: Performance of normal controls was more optimal compared to children with ODD/CD. No interaction was found between reinforcement condition and group. Dependent measures were MRT and SSRT.

Summary Task Performance

Firstly, a majority of studies described in this section indicates that reward and response cost have a positive effect on task performance of both children with ADHD and controls. Additionally, in terms of the number of studies showing improvement in performance, the improvement is somewhat more prominent for children with ADHD than in normal controls (Carlson, Mann, & Alexander, 2000; Carlson & Tamm, 2000; Iaboni et al., 1997; Konrad et al., 2000; McInerny & Kerns, 2003; Scheres

et al., 2001; Solanto, 1990). Nine studies that compared reward with response cost conditions found that reinforcement condition did not differentiate performance of children with ADHD from controls.

Secondly, one of three studies showed that performance of children with ADHD deteriorated under partial compared to continuous reward (Douglas & Parry, 1994). When children were required to perform a task under partial and non-reward conditions, no differences were found in four studies that compared children with ADHD (Barber et al., 1996; Crone et al., 2003; Douglas & Parry, 1994) or children with ADD (Pelham et al., 1986) and controls.

Third, compared to controls, children with ADHD seem to choose more often for an immediate than for a delayed reward, irrespective of the previous reward trial and whether the delayed reward was large (Rapport et al., 1986; Sonuga-Barke et al., 1992; Tripp & Alsop, 2001).

Fourth, when reward schedules are manipulated in such a way that the chances of receiving reward diminished over time, no differences in response rate were observed between children with ADHD and controls (Daugherty & Quay, 1991). Children with CD however, showed a high response rate irrespective of diminishing chance on receiving reward, which turned out to be a less profitable response strategy.

Fifth, when reward conditions were compared to a condition of response cost or non-reward authors failed to find any differential effects on task performance in studies where children with ODD/CD were compared to children with ADHD (Oosterlaan & Sergeant, 1998; Scheres et al., 2001).

There are some limitations related to the findings described above that need to be highlighted. The main concern is heterogeneity in the dependent variables employed in the empirical studies. Also, the confounding variables that have been taken into account differ between studies. Furthermore, form, amount and delivery of reinforcement vary, and not all studies make sure that the total amount of reinforcement is similar for all groups. A limitation of a different caliber is that the findings in this review are based on a small number of studies. Finally, a possible ceiling-effect of performance in the control group may confound the findings related to task performance.

Motivation Level

Different methods have been used to assess children's subjective and objective motivation levels. One of the employed methods to obtain subjective motivation is to ask children to rate their motivation to 'perform a specific task' (Scheres et al., 2001), 'to continue with a task' or 'to do a task again' (Carlson, Mann, & Alexander, 2000; Carlson & Tamm, 2000; McInerny & Kerns, 2003; Oosterlaan & Sergeant, 1998). Objective levels of motivation were measured by counting the total number of trials completed, in a task where the number of trials is under the participant's control (Carlson, Mann, & Alexander, 2000; Carlson & Tamm, 2000).

ADHD Versus Normal Controls Under: Reward, Non-Reward and Response Cost

Table 2.4 summarizes the results of four studies that measured levels of motivation of children with ADHD under a reward and non-reward condition. All four studies revealed that across groups, reward had a positive effect on self-rated motivation (Carlson, Mann, & Alexander, 2000; Carlson & Tamm, 2000; McInerny & Kerns, 2003; Scheres et al., 2001). No main effects of group or differential effects of reinforcement condition on self-rated motivation were found.

Two of the four studies included both measures of self-rated and observed motivation. The difference between self-rated and observed motivation is noteworthy. While self-rated motivation increased under reward compared to non-reward, no main effect of reinforcement condition was found for observed motivation (Carlson, Mann, & Alexander, 2000; Carlson & Tamm, 2000). This could indicate that the different mea-

Table 2.4 || Levels of Motivation of Children with AD/HD Versus Normal Controls Under Reward and Non-Reward

Study	Group Effects				
	Reward	Non-Reward	Reward Versus Non-Reward[a]		Motivation Measure
Carlson & Tamm (2000)	ADHD = NC	ADHD = NC	+	NC, ADHD	Self-rated
	ADHD < NC	ADHD < NC[b]			Observed
Carlson, Mann, & Alexander (2000)	ADHD = NC	ADHD = NC	+	NC, ADHD[b]	Self-rated
	ADHD = NC	ADHD = NC			Observed
McInerny & Kerns (2003)	ADHD = NC	ADHD = NC	+	NC, ADHD	Self-rated
Scheres et al. (2001)	ADHD = NC	ADHD = NC	+	NC, ADHD	Self-rated

[a] (+) indicates increased motivation under reward compared to non-reward, (-) indicates decreased motivation.
[b] $p < .10$, statistically of marginal significance.

AD/HD = Attention Deficit/Hyperactivity Disorder, NC = Normal controls.

sures of motivation do not reflect the same concept. Furthermore, Carlson, Mann, and Alexander (2000) found that self-rated motivation was similar across groups, while observed motivation was higher for controls compared to children with ADHD. This difference was of marginal significance. In the Carlson and Tamm study, groups did not differ in terms of self-rated or observed motivation. No differential effects of reinforcement condition were found for observed motivation.

Two studies measured levels of motivation of children with ADHD and controls when comparing a response cost and a non-reward condition (Carlson, Mann, & Alexander, 2000; Carlson & Tamm, 2000). In both studies, self-rated motivation was higher in the response cost condition, although in the Carlson and Tamm study the effect was marginally significant. Carlson, Mann, and Alexander (2000) reported a differential effect of reinforcement condition on self-rated motivation: self-rated motivation of controls was higher under response cost compared to non-reward, while self-rated motivation for children with ADHD remained unchanged. The second study did not find a differential effect (Carlson & Tamm, 2000).

No main effects of reinforcement condition were found for observed motivation. Carlson, Mann, and Alexander (2000) found a differential effect of reinforcement condition: observed motivation of children with ADHD improved under response cost, while observed motivation of controls did not differ between reinforcement conditions (Carlson, Mann, & Alexander, 2000). The other study failed to find an interaction effect between group and reinforcement condition for observed motivation (Carlson & Tamm, 2000).

Three studies included measures of self-rated motivation, when comparing a reward and a response cost condition. Across groups, one study reported higher self-rated motivation under reward compared to response cost (Carlson & Tamm, 2000). Two other studies failed to find any differences in self-rated motivation between reinforcement conditions (Carlson, Mann, & Alexander, 2000; Oosterlaan & Sergeant, 1998). None of the studies reported group differences in self-rated motivation or interaction effects between group and reinforcement condition.

Carlson, Mann, and Alexander (2000) and Carlson and Tamm (2000) measured levels of observed motivation and failed to find a main effect of reinforcement condition. One study reported a differential effect of reinforcement condition: observed motivation of children with ADHD was higher under response cost compared to reward, while controls showed similar levels of motivation in both reinforcement conditions (Carlson, Mann, & Alexander, 2000). The other study failed to find any effects of group and there was no interaction effect between group and reinforcement condition (Carlson & Tamm, 2000).

Summary Motivational Variables

The majority of studies that included measures of motivation found a positive effect of both reward and response cost conditions on self-rated motivation (Carlson, Mann, & Alexander, 2000; Carlson & Tamm, 2000; McInerny & Kerns, 2003; Scheres et al., 2001). Two studies included both measures of observed and self-rated motivation and, while self-rated motivation improved under reinforcement conditions, observed motivation was not affected by either reward or response cost (Carlson, Alexander, & Mann, 2000; Carlson & Tamm, 2000). This result was found for both children with ADHD and controls. No clear differential effects of reinforcement condition on levels of motivation were found for children with ADHD and controls.

Noteworthy in this section is the discrepancy found between observed an self-rated motivation under different reinforcement conditions. This result may indicate that either the measures do not tap into the same concept or that children have difficulties in monitoring their motivation while performing a task. As with the studies investigating task performance, studies into motivation are hampered by the small number of studies that contribute to the findings and differences between variables related to reinforcement (form, amount, and reinforcement allocation policy).

Psychophysiological Variables

Heart rate and skin conductance have been employed in two studies of ADHD and reinforcement contingencies (Crone et al., 2003; Iaboni et al., 1997). Crone et al. (2003) compared psychophysiological responses of children with ADHD and controls under three different reinforcement conditions: One reward-only condition and two mixed reward and response cost conditions (see Table 2.1). In that study, heart rate level and skin conductance level were measured during the different reinforcement conditions and also heart rate responses immediately following reinforcement were obtained (Crone et al., 2003). Heart rate of both children with ADHD and controls increased during the mixed reward and response cost compared to the reward-only condition. Furthermore, heart rate increased following positive reinforcement (reward or escape from punishment) compared to negative reinforcement (punishment or response cost). A main effect for group was found: Heart rate of children with ADHD was higher compared to controls. In addition, reinforcement condition differentiated children with ADHD from controls on heart rate: Compared to controls, heart rate of children with ADHD exhibited smaller differences when responses to positive and negative reinforcement were contrasted (Crone et al., 2003). With respect to skin conductance,

children with ADHD responded like controls and no main effects of reinforcement condition or interactions between group and reinforcement condition were found.

Iaboni et al. (1997) compared the psychophysiological responses of children with ADHD under conditions of reward and non-reward/extinction (see Table 2.1). A main effect of reinforcement condition was found: Hart rate increased during the reward compared to the extinction conditions (Iaboni et al., 1997). In contrast to Crone et al. (2003), Iaboni and colleagues failed to find any main effects of group on heart rate. Heart rate of children with ADHD and controls was differentially affected by the reinforcement conditions: Compared to controls, heart rate of children with ADHD showed smaller differences between the reward and extinction conditions. The heart rate of both groups decreased across the reward trials, however, this habituation commenced earlier for children with ADHD. Over reinforcement conditions, children with ADHD responded like controls with respect to skin conductance level. However, the skin conductance of children with ADHD and controls was differentially affected by reinforcement condition: While skin conductance levels of normal controls increased during the extinction compared to the reward conditions, skin conductance level of children with ADHD remained unchanged (Iaboni et al., 1997).

Thus, both studies found evidence of reduced psychophysiological responding in children with ADHD compared to controls. Compared to controls, children with ADHD exhibited smaller differences in heart rate between the reward and extinction conditions (Iaboni et al., 1997) and in response to positive and negative reinforcement (Crone et al., 2003). Iaboni et al. (1997) found smaller skin conductance levels under extinction compared to reward conditions for children with ADHD compared to controls. This result may indicate that children with ADHD are less sensitive psychophysiologically to reinforcement.

The main limitation here is the small number of studies investigating the effect of external contingencies on heart rate and skin conductance in ADHD. The current studies did not find strong clues for the underlying mechanisms that could account for reinforcement deficits in ADHD.

Confounding variables

Comorbid Disorders

The studies in this review reported on the presence of learning disorders (LD), internalizing disorder (ID) (anxiety and mood disorders), ODD and CD. Nine of 22 studies in this review assessed the possible presence of ODD symptoms in children with ADHD, and all studies reported that a subgroup of children with ADHD classified for a DSM diagnosis of ODD. Twelve studies assessed the possible presence of CD symptoms in children with ADHD, and ten studies reported a comorbid DSM diagnosis of CD. Almost half of the studies (ten studies) included groups of children with an ADHD diagnosis but did not examine possible comorbid ODD in children with ADHD, and one third of the studies (seven studies) did not check for possible comorbid CD. In one of four studies that assessed the possible presence of LD in children with ADHD, a comorbid DSM diagnosis of LD was confirmed. One of six studies that checked for possible ID in children with ADHD reported a comorbid diagnosis of ID for a subgroup of children with ADHD.

When studying ADHD from a psychophysiological perspective, the presence of comorbid anxious and antisocial behavior disorders (ODD and CD) should be taken into account (Quay, 1988a; Gray, 1982). Quay (1988a, b, c) indicated that these psychiatric groups show different psychophysiological responses to reinforcing stimuli. In contrast to children with ADHD, children with oppositional and delinquent behavior disorders were predicted to be oversensitive to signals of reward, because of an overactive BAS. Children with anxious symptoms on the other hand, are predicted to suffer from an overactive BIS and, therefore, are highly sensitive to signals of punishment and non-reward. Interestingly, the comorbid diagnosis of ADHD with an anxiety disorder is suggested to eliminate the dysfunction within the BIS (Quay, 1988a, b, c). In these children, the 'dysfunctional' BIS is hypothesized to normalize due to the combination of an underactive BIS related to ADHD and an overactive BIS related to the anxiety disorder.

Reinforcement Allocation Policy

Reinforcers were administered based on either performance or on task participation. According to Schultz (2000), the rate of reinforcement learning in a task depends on the discrepancy between the occurrence and the predicted occurrence of reward. When reward is based on participation, reward expectancy seems to be highest and reinforcement learning is expected to be lower compared to performance-based re-

inforcement allocation. The two different reinforcement allocation policies were compared in a study by Carlson and Tamm (2000). No differential effects of allocation policy on either performance or motivation level were observed. The majority of studies allocated reinforcement contingent upon the accuracy of the response, which minimized the possible confounding effect of reinforcement allocation policy and maximized stimulus response learning (Schultz, 2000, 2002). More research is needed in order to clarify the role of reinforcement allocation

ADHD subtypes, Gender, Age, and IQ

In this review, three studies explicitly compared the performance of children with ADHD inattentive subtype and ADHD hyperactive/impulsive subtype under different reinforcement contingencies and found no differences (Konrad et al., 2000; Rapport et al., 1986; Scheres et al., 2001). Seven studies included only children with ADHD combined subtype according to the DSM IV or children with ADD+H according to the DSM III. One study included only children with ADD according to DSM III. Since the remaining eleven studies did not provide information on the ADHD-subtypes, no firm conclusions can be drawn on this issue.

Nine studies matched groups on gender. Five studies statistically checked for possible effects of gender and found no differences between boys and girls (Carlson & Tamm, 2000; Daugherty & Quay, 1991; Pelham et al., 1986; Rapport et al., 1986; Solanto, 1990). There seems no reason to suspect any confounding influences of gender on the dependent variables in the remaining eight studies.

Nine studies matched groups on age. Eleven other studies tested for possible group differences in age: Two studies found a difference in age between groups. In one study, age was entered as a covariate in the analyses (Slusarek, Velling, Bunk & Eggers, 2001). These data suggest that age does not have much influence on the dependent variables in this review.

IQ is unlikely to effect the findings noted here. Five studies matched their experimental groups on IQ. All other studies tested for possible group differences in IQ and three studies found a difference in IQ between groups (Rapport et al., 1986; Scheres et al., 2003; Tripp and Alsop, 2001). Two studies entered IQ as a covariate.

Form and Intensity of Reinforcement

In the studies reviewed here, children received either tokens (14 studies), money (five studies), presents (two studies) or diminished inter-trial delays as reinforcement. Children received tokens, which could be exchanged for presents at the end of the experiment (nine studies), or received tokens that could be cashed for money (five studies). The intensity (amount) of reinforcement may differ between studies (p.e., reward allocation of 1, 2, 5 or 10 cents per trial). One study manipulated the intensity of reinforcement (Slusarek et al., 2001). In this study, response cost intensity was found to differentiate children with ADHD from normally developing controls: While in the low intensity condition performance of children with ADHD is less optimal compared to controls, performance of children with ADHD is found to normalize in the high intensity condition.

General Discussion

The goal of this review was twofold. On the one hand, we have charted the behavioral findings regarding the role of reinforcement contingencies in ADHD, an attempt that has not been made for some time (Douglas & Peters, 1979). On the other hand, we wished to study the implications of the behavioral findings for the theoretical frameworks related to this body of research.

We first summarize the results of the studies in this review: We found clear evidence that reward and response cost have a positive effect on performance and on levels of motivation of both children with ADHD and normal controls. Additionally, a performance improvement was reported more often for the ADHD group than for controls (Carlson, Mann, & Alexander, 2000; Carlson & Tamm, 2000; Konrad et al., 2000; McInerny & Kerns, 2003). With respect to the levels of motivation, no significant interactions were found between group and reinforcement condition. Another evident finding is that compared to controls, children with ADHD seem to choose more often for an immediate reward irrespective of the previous reinforcement trial or whether the delayed reward was large (Rapport et al., 1986; Sonuga-Barke et al., 1992; Tripp & Alsop, 2001). Less clear is the role of partial reward. In one of three studies, performance of children with ADHD diminished under partial compared to continuous reward, while performance of controls remained the same (Douglas & Parry, 1994). Furthermore, children with ADHD and normal controls responded in a similar pattern, when response perseveration was measured in a task where the chance on receiving reward diminished (Daugherty & Quay, 1991). When heart rate and skin conductance

measures are investigated, children with ADHD seem to be psychophysiologically less sensitive to reinforcement contingencies (Crone et al., 2003; Iaboni et al., 1997). The decreased sensitivity for reinforcement at a psychophysiological level seems to contrast with the findings related to performance: At a performance level, in some studies, reinforcement contingencies are more beneficial for children with ADHD than for controls (Carlson, Mann, & Alexander, 2000; Carlson & Tamm, 2000; Konrad et al., 2000; McInerny & Kerns, 2003).

We now discuss the implications of the findings in terms of five models described in the introduction. Haenlein and Caul (1987) suggested that children with ADHD require higher amounts of reward in order to perform optimally due to an elevated reward threshold. A more prominent improvement in performance of children with ADHD under reward conditions supports this hypothesis (Carlson & Tamm, 2000; Konrad et al., 2000; McInerny & Kerns, 2003). Partial reward was suggested to result in diminished task performance. The findings, however, only partly support this suggestion, since only one of three studies revealed clear evidence on this issue (Douglas & Parry, 1994). When the chance of receiving reward diminished (Daugherty & Quay, 1991), children with ADHD showed a similar response pattern compared to controls, in contrast to the ideas of Haenlein and Caul. In addition, Haenlein and Caul argued that that medication would lower the reward threshold. When confronted with a diminishing chance of receiving reward, children with ADHD on medication showed a more optimal performance compared to children with ADHD receiving placebo (Wilkison et al., 1995). The psychophysiological findings concerning a diminished sensitivity to reinforcement are in line with the suggestion of an elevated reward threshold. The preference for immediate reward of children with ADHD supports Haenlein and Caul's model, since they suggested that the impact of a reward is larger, when it is administered immediately compared to when it is delayed. A limitation of this model is that Haenlein and Caul did not make any suggestions concerning response cost. Response cost seems to be as effective as reward for children with ADHD, especially when reward intensity is high (Slusarek et al., 2001). As noted above, an elevated reward threshold model of ADHD can account for a considerable number of behavioral findings discussed in this review, questions, however, related the exact elevation of the reward threshold could not be answered.

Douglas (1989, 1999) proposed that children with ADHD are unusually sensitive to reward and suffer from a heightened frustration level in response to the loss of anticipated reward. These suggestions by Douglas are moderately supported: One of three studies found deteriorating performance under partial compared to continuous reward for children with ADHD (Douglas & Parry, 1994). In this study, children

with ADHD exhibited higher levels of frustration compared to normal controls under partial reward. The preference for immediate reward for children with ADHD is in line with the ideas of Douglas. Although the hypothesis of an increased sensitivity to reinforcement is supported by the findings in this review (Carlson, Mann, & Alexander, 2000; Carlson & Tamm, 2000; Konrad et al., 2000; McInerny & Kerns, 2003), no specific predictions were made for the effect of reward or response cost onto performance. The finding that performance of children with ADHD is like controls in a task where the chances on receiving reward diminished contrasts the ideas of Douglas (1989, 1999), since Douglas theorized that children with ADHD are extremely sensitive to the absence of anticipated reward. The diminished psychophysiological responding to reinforcement of children with ADHD may be in contrast with the suggestion of increased reward sensitivity and increased sensitivity to extinction.

According to the CEM, (Sergeant et al., 1999), the contributing role of effort to poor performance in ADHD is caused by a deficit in effort allocation. Since the effort pool is activated by reinforcement contingencies, performance improvement for the ADHD group under both reward and response cost is in line with the CEM. The finding that a higher ratio of reinforcement (continuous versus partial reward, Douglas & Parry, 1994) or a higher intensity of reinforcement (Slusarek et al., 2001) had a differential effect on performance for children with ADHD and controls could also be explained by a lack of effort allocation in ADHD. The preference for immediate reward for children with ADHD, however, is more difficult to explain in terms of the CEM, since the exact specifications of how the effort pool is activated are not provided. According to the CEM, under reward and response cost, improvement in task performance is expected to be associated with an enhanced motivation level. A correlation between improved task performance and motivation level, however, was found in one study only (McInerny & Kerns, 2003). The findings in this review only partly support the CEM on this issue. The psychophysiological findings concerning an underresponsive BIS and BAS could explain the need for external incentives in ADHD for optimal performance. The CEM does not make any specific predictions concerning the preference for immediate reward or concening a diminishing reward ratio. Although findings related to motivation are not in line with the CEM, a sub-optimal energetic state could explain a wide range of behavior related to reinforcement contingencies and ADHD.

Sonuga-Barke (2002, 2003) explained the symptoms of ADHD in terms of two separate dysfunctional brain mechanisms in a dual-pathway model. One pathway is associated with diminished inhibitory responses and the other with increased reward sensitivity. The dual-pathway model predicts delayed and non-continuous reward to

result in diminished task performance for children with ADHD. The preference for immediate reward in children with ADHD is in line with the dual pathway model. Tripp and Alsop (2001), however, found that children with ADHD preferred immediate above delayed reward irrespective whether the overall delay was similar, which contrasts with the findings by Sonuga-Barke et al. (1992). One of three studies revealed evidence for a deteriorating effect of partial reward on performance in ADHD (Douglas & Parry, 1994). The finding that performance of children with ADHD was similar to controls when the chances of receiving reward diminished could not be explained by the dual-pathway model (Daugherty & Quay, 1994). According to Sonuga-Barke, ADHD is in part associated with a dysfunction in the mesolimbic system, which may explain the psychophysiological findings: The regulation of the cardiorespiratory components of the defense and vigilance reactions involves several brain regions, including limbic system structures as the amygdala (Brownley, Hurwitz, & Schneiderman, 2001). If the two pathways of the model are independent, we may expect a double dissociation between the behavioral dysfunctions (inhibition and reward sensitivity) related to the pathways. Future research needs to confirm this prediction. No specific predictions were made concerning the moderating effects of both reward and response cost on performance of children with ADHD.

The fifth model, the BIS/BAS model by Quay (1988a, b, c, 1997), proposed that children with ADHD suffer from a weak BIS, associated with a diminished sensitivity to signals of punishment and non-reward. Psychophysiologically, children with ADHD would show a decreased skin conductance response to conditions of response cost and extinction. The findings related to task performance only partially support Quay's model, since both reward and response cost have a positive effect on performance in ADHD. The psychophysiological findings related to skin conductance, however, are in line with the BIS/BAS model (Iaboni et al., 1997). The findings of Slusarek et al. (2001) concerning a positive effect of response cost in ADHD, when intensity is high may indicate diminished sensitivity to punishment. On the other hand, children with ADHD showed smaller differences in heart rate, when comparing positive with negative feedback, which may indicate an under responsive BAS in addition to an under responsive BIS. When the chance of receiving reward diminished, while response cost levels remain unchanged, response rate of children with ADHD is similar to controls (Daugherty, & Quay, 1991), in contrast to the predictions of the BIS/BAS model. Quay did not make any predictions concerning the timing of reinforcement allocation, motivation or partial versus continuous reward. The behavioral findings in this review provide some support for the BIS/BAS model. However, only a few psychophysiological studies are conducted that may provide evidence for an under responsive BIS (and BAS) in ADHD.

By comparing the behavioral findings and the theoretical models related to reinforcement contingencies in ADHD, some important shortcomings in this field of research are revealed. First, the number of studies contributing to the theoretical models is small: For example, only two studies measured heart rate and skin conductance under different reinforcement contingencies in children with ADHD (Crone et al., 2003; Iaboni et al., 1997). To test the functionality of the models, research in this field should be more theory-driven.

Secondly, all five models showed insufficiencies in explaining the findings in this review (see Figure 2.1). Some important issues, for example, related to response cost, were not taken into account by the models of Haenlein and Caul (1987), Douglas (1989) and Sonuga-Barke (2003). These shortcomings may touch upon the domain specificity of the frameworks that explain the role of reinforcement contingencies in ADHD. The BIS/BAS model, for example, states hypotheses at a psychophysiological and neuro-anatomical level. However, specific suggestions at a performance level are minimal. The CEM, in contrast, explains ADHD at both a performance and a psychophysiological level. The model lacks suggestions at a biochemical or neuro-anatomical level, which are important domains in explaining an aberrant sensitivity to reinforcement in ADHD (Schultz, 2000, 2002; Sonuga-Barke, 2002, 2003). The findings in this review emphasize the complexity of the disorder: different mechanisms (e.g., learning and arousal mechanisms) seem to underlie the behavior related to an aberrant reinforcement sensitivity. In our opinion, a future model of ADHD needs to explain ADHD from a multi-level perspective using a bio-psycho-social approach. The dual-pathway model (Sonuga-Barke, 2003) seems most extensive in describing the impact of reinforcement contingencies in ADHD from diverse domains of functioning, e.g., biochemical and performal. Figure 2.1 shows the five different models described in this review and the extent in which the models are supported by the findings presented here: None of the models seems able to explain all findings in this review.

In the studies reviewed here, different cognitive functions (e.g., inhibition, working memory, time estimation) and reward choice behavior were evaluated. To overcome heterogeneity in the dependent measures in this review, we measured absolute changes in performance, without examining specific cognitive functions or behavior related to reinforcement choice. Research suggested that children with ADHD may suffer from deficits in specific cognitive or executive functions (e.g., Pennington & Ozonoff, 1996). Whether the effect of reinforcement contingencies is function specific remains an issue to be investigated.

Theoretical Models / Review Findings	Elevated reward treshold (Haenlein & Caul, 1987)	Enhanced reward sensitivity (Douglas, 1989)	Cognitive energetic model (Sergeant et al., 1999)	BAS/BIS model (Quay, 1988)	Dual pathway model (Sonuga-Barke, 1995)
Improvement performance under reward and response cost (RC)	+		+ +	+/-	
Preference for immediate reward	+	+ +			+ +
No clear evidence of performance deterioration under partial reinforcement or under diminishing reinforcement ratio	+/-	+/-	+	-	+/-
No correlation between performance and motivation			+/-		
Psychophysiologically less sensitive for reinforcement				+	+

(-), (+/-), (+) and (++) indicate that there is respectively no, weak, some or strong support. An empty box indicates that no predictions are specified by the theoretical model. BAS/BIS = Behavioral Activation System/ Behavioral Inhibition System

Figure 2.1 || The level of support for each of the five theoretical models provided by the findings in this review.

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An important issue is related to the variable 'reinforcement condition'. When comparing the different studies, we found heterogeneity in the reinforcement conditions: Different forms (e.g., money, tokens, presents) or various intensities of reinforcement and reinforcement allocation policies may have a confounding effect on the dependent variables of studies in this review (Fowles, 1988; Schultz, 2000, 2002; Slusarek et al., 2001). Observing differences in reinforcement intensity is important, since several theoretical models consider the degree of reward as being significant in differentiating children with ADHD from controls (e.g., Haenlein and Caul, 1987; Sergeant et al. 1999; Sonuga-Barke et al. 2002, 2003).

Another issue is the possible confounding effects related to the psychiatric groups. For example, a striking finding in this review is that not all studies take comorbid disorders into account. Although several researchers emphasized that ODD/CD groups perform different compared to children with ADHD (Quay, 1988a, b, c), an ADHD group was seldom compared to an ODD/CD group. Two studies that did include a

separate ODD/CD group failed to find any differences in measures of inhibition, between children with ADHD and ODD/CD (Oosterlaan & Sergeant, 1998; Scheres et al., 2001). Future research should seriously take possible diagnoses such as ODD and CD in children with ADHD into account. In particular, when measuring psychophysiological responses, determining the presence of comorbid ODD and CD is important because children with ADHD and children with ODD or CD are hypothesized to show different psychophysiological responses to reinforcement (Quay, 1988a, b, c).

A related question is the possible effect of development factors that may influence the impact of reinforcement in children with ADHD. The prognosis and age of onset of CD, for example, is highly variable (Loeber et al., 2000), longitudinal cross validation studies that systematically investigate the developmental factors in relation to reinforcement contingencies are necessary. Furthermore, the impact of gender on reinforcement sensitivity is never extensively investigated.

In half of the studies, performance of normal controls is superior compared to children with ADHD. Possible performance improvement under conditions of reinforcement, may not have been revealed, due to a ceiling effect in the control group. The use of a paradigm in which task-difficulty is independent on performance would be an elegant solution for this problem. A final issue is the face validity and content validity of the studies in this review. Differences in the intrinsic value of reward or response cost, for example, are difficult to measure and we may question whether 'response cost' or the loss of a reward referrers to a form of punishment; children never actually loose. In addition, the test-retest reliability of most studies is (still) unknown. Finally, the ecological validity of the studies remains an issue to be investigated.

In conclusion: The findings support the suggestion that children with ADHD are aberrantly sensitive to reinforcement and the importance of reinforcement in ADHD is further emphasized by recent imaging research (Castellanos, & Tannock, 2002). The findings are promising: Reward and response cost seem useful methods to improve task performance in children with ADHD. Further research, however, needs to specify to what extent an aberrant sensitivity to reinforcement could account for the problems of inattention, impulsivity and hyperactivity. In addition, the impact of different ADHD subtypes, gender and comorbid ODD and CD should be further investigated. For a more comprehensive investigation of the effect of reinforcement contingencies on task performance, intensity and form of reinforcement could be manipulated. There is a clear call for extension of the current theoretical frameworks, since all five models described above show shortcomings in explaining the findings in this review related to the impact of reinforcement contingencies in ADHD.

Chapter 3

Modulation of Response Timing in ADHD, Effects of Reinforcement Valence and Magnitude

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Abstract

The present study investigated the impact of reinforcement valence and magnitude on response timing in children with ADHD. Children were required to estimate a 1-s interval, and both the median response time (response tendency) and the intra-subject variability (response stability) were investigated. In addition, heart rate and skin conductance were measured to examine the autonomic responses to reinforcement. Feedback-only trials were compared to low response cost trials (response cost for incorrect responses), low reward trials (reward for correct responses), high response cost and high reward trials. In feedback-only trials, children with ADHD underestimated more severely the interval and responded more variably than controls. Children with ADHD, unlike controls, were unaffected by the reinforcement conditions in terms of time underestimations. The variability of responding, on the other hand, decreased under conditions of reinforcement to a larger extent in children with ADHD than controls. There were no indications that children with ADHD were abnormally affected by the valence or magnitude of reinforcement. Furthermore, skin conductance responses increased when feedback was coupled with reinforcement, an effect which was larger in children with ADHD than controls. This could be interpreted as demonstrating that children with ADHD suffer from a diminished awareness of the significance of feedback in the feedback-only condition. The current study suggests that children with ADHD suffer from motivation problems when reinforcement was not available, at least when variability in responding was measured. Underestimations of time may reflect more stable deficits in ADHD.

Introduction

Attention problems, motor restlessness and impulsive responding characterize children with Attention Deficit Hyperactivity Disorder (ADHD) (American Psychiatric Association, APA, 1994). Recently, motivational abnormalities have been identified as crucial in ADHD (Casey, Nigg, & Durston, 2007; Castellanos & Tannock, 2002; Nigg, 2005). Many studies have been designed to investigate whether cognitive performance in ADHD can be modulated by motivation using reinforcement contingencies. Luman, Oosterlaan and Sergeant (2005) reviewed this literature and demonstrated that performance of children with ADHD and controls improved by using appropriate reinforcement. There is some evidence from that review that the improvement is larger for children with ADHD than for controls, which confirms that cognitive problems in ADHD may be partly explained by motivational dysfunctions. In addition to behavioral reports, there is evidence of an abnormal response to reinforcement in ADHD using brain imaging measures (Plessen et al., 2006; Scheres, Milham, Knutson, & Castellanos, 2006; Spencer et al., 2005; Van Meel, Oosterlaan, Heslenfeld, & Sergeant, 2005b).

Although there is general consensus that children with ADHD show an abnormal sensitivity to reinforcement, the nature of this abnormality is unclear. For example, it is not clear whether children with ADHD are abnormally sensitive to either reward, response cost or both. Children with ADHD have been found to show an abnormal sensitivity to reward by preferring an immediate small reward over a larger delayed reward (Rapport, Tucker, DuPaul, Merlo, & Stoner, 1986; Sonuga-Barke, Taylor, Sembi, & Smith, 1992). This has been explained by a shortage in dopamine transmission in the fronto-limbic pathway in ADHD that results in a faster decay of reward (Sagvolden, Johansen, Aase, & Russell, 2005). In contrast, there is evidence that children with ADHD were specifically sensitive to response cost rather than reward, by showing a disproportionally greater improvement in accuracy when faced with response cost than controls in a Figure Matching task and an arithmetic task (Carlson, Mann, & Alexander, 2000; Carlson & Tamm, 2000). Electrophysiological studies confirm the suggestion that individuals with ADHD show abnormalities that are specifically related with processing of response cost (Potts, George, Martin, & Barratt, 2006; Van Meel et al., 2005b). Other performance studies, however, found no differential impact of reward or response cost on performance of children with ADHD compared to normal controls (Iaboni, Douglas, & Baker, 1995; Oosterlaan & Sergeant, 1998).

Using autonomic measures, studies have revealed smaller responses to *both* reward and response cost in ADHD (Crone, Jennings, & Van der Molen, 2003; Firestone & Douglas, 1975; Iaboni, Douglas, & Ditto, 1997). This would converge with the suggestion that children with ADHD suffer from an elevated threshold for experiencing incentives (Haenlein & Caul, 1987), rather than being specifically sensitive to either reward or response cost. Slusarek, Velling, Bunk, and Eggers (2001) studied whether children with ADHD need more reinforcement than controls to improve their performance in a Stop-signal task. Children with ADHD benefited more than controls from large compared to small quantities of response cost (1 versus 5 points loss) by improving the frequency of correct inhibitions, confirming the suggestion that children with ADHD are dependent on intensive external reinforcement to perform well.

The current study was set up to investigate the impact of reward and response cost (investigating the valence of reinforcement) on performance of children with ADHD as well as to test whether children with ADHD suffer from a elevated reinforcement threshold (investigating the magnitude of reinforcement). By investigating these two aspects of reinforcement separately it is possible to disentangle the processes that may underlie reinforcement sensitivity in ADHD in a within subject design (e.g., Haenlein & Caul, 1987; Sagvolden et al., 2005). In addition, knowledge regarding the sensitivity of children with ADHD to specific aspects of reinforcement may inform behavioral interventions for ADHD that make use of reinforcement contingencies (DuPaul, Guevremont & Barkley, 1992; McGoey & DuPaul, 2000; Rapport, Murphy, & Bailey, 1982).

One of the underlying performance deficiencies in ADHD relates to motor timing (Barkley, 1997; Castellanos & Tannock, 2002; Toplak, Dockstader, & Tannock, 2006). Motor timing is hypothesized to consist of two components: an internal clock component, which reflects central time keeping organizations and a motor delay component, which reflects random variability due to organization of motor output (e.g., Harrington, Haaland, & Hermanowicz, 1998). Both components seem to be affected in children with ADHD: Children with ADHD show a time keeping deficiency as observed by problems with time discrimination, time (re)production, and, compared to controls, children with ADHD systematically underestimate time intervals (see for review, Toplak et al., 2006). In addition, motor output problems in ADHD are observed by a well-known pattern of slow and variable responding (Leth-Steensen, Elbaz, & Douglas, 2000; Rubia, Smith, Brammer & Taylor, 2007; Van Meel et al., 2005a). Since reinforcement is found to influence the motor system (Haber, 2003; Schultz, Dayan, & Montague, 1997), it is valuable to investigate whether problems with motor timing in children with ADHD may be secondary to a motivational deficit.

Two studies investigated the impact of reinforcement on motor timing in ADHD. Reward tokens compared to no-reward were found to improve time reproduction performance (3 to 17 s) to a larger extent in ADHD children compared to controls (McInerny & Kerns, 2003). In contrast, using a time production task (1000 ms) no differences in performance improvement were observed between children with ADHD and controls, when either reward or response cost (3 eurocents) were added to performance feedback (Van Meel et al., 2005a). Possibly, the discrepancy in the impact of reinforcement on motor timing in ADHD was related to the differences in time intervals. Larger intervals, such as 3 to 17 seconds, may have invoked delay aversion in children with ADHD, specifically when performance was not reinforced (Sonuga-Barke, 2002; Sonuga-Barke et al., 1992). Otherwise, the magnitude of rewards may have differed between the two studies. Three cents and a promised gift (Van Meel et al., 2005a) may have been perceived as smaller than tokens and a large unwrapped gift that was in sight (McInerny & Kerns, 2003). Furthermore, a counterbalanced blocked design (Van Meel et al., 2005a) may have decreased the motivation for some children to perform well (e.g., when the response cost condition followed the reward condition, children may have been less motivated to perform well than when the response cost condition was presented first).

To accommodate for these issues, the current study investigated the impact of both reinforcement valence and magnitude on motor timing in a task where children were required to produce a 1-s interval. By using a short time interval, the influence of higher cognitive functions, such as sustained attention or working memory, was minimized and the chance of boredom and frustration due to the delay aversion of children with ADHD reduced (Sonuga-Barke, 2002). To study the impact of reinforcement valence and magnitude, five conditions were created: (1) feedback-only, (2) feedback and low response cost, (3) low reward, (4) high response cost, and (5) high reward. Trials from the five conditions were allocated completely randomized. To investigate whether performance differences would be accompanied by psychophysiological abnormalities in response to reinforcement, heart rate (HR) and skin conductance (SC) were measured during the experiment. These measures are valuable when investigating reinforcement sensitivity, since HR and SC responses have been found to differ in response to positive and negative outcomes such as reward and response cost (e.g., Crone et al., 2003; Fowles, 1988). In addition, both measures have been found to differentiate between low and high magnitudes of incentives (Bradley, 2000; Fowles, 1988).

The following hypotheses were tested. First, children with ADHD were expected to perform worse then controls in estimating the 1-s interval (Toplak et al., 2006). Sec-

ond, if children with ADHD suffer from an abnormal sensitivity to either reward (e.g., Sonuga-Barke et al., 1992) or response cost (e.g., Carlson et al., 2000), performance should be differentially affected by reward and response cost compared with their normally developing peers *(the valence hypotheses)*. Otherwise, if children with ADHD suffer from a higher threshold to experience incentives (Slusarek et al., 2001), their performance would be more optimal when the intensity of reinforcement is large compared to small *(the magnitude hypothesis)*, unlike the performance of normal controls. Third, based on earlier findings of attenuated psychophysiological responses to reinforcement in ADHD (e.g., Crone et al., 2003), an abnormal sensitivity to either reward, response cost or both was expected to be associated with smaller HR or SC responses to reinforcement in children with ADHD compared to normal controls.

Methods and Materials

Participants and Selection Procedure

Twenty-five children with ADHD (21 boys) and 30 normal control children (24 boys) aged 7 to 12 participated in this study. Mean age was 121 months (*SD* 17) and 120 months (*SD* 15) for the ADHD and control group, respectively (see Table 3.1).

Children in the ADHD group were recruited through a university affiliated outpatient clinic for ADHD. They were included, when they met the following criteria: (a) a clinical diagnosis of ADHD, (b) IQ score > 80, (c) absence of any psychiatric disorder other than ADHD, oppositional defiant disorder (ODD) or conduct disorder (CD), (d) absence of any neurological disorders as reported by parents, learning disabilities (such as dyslexia or other learning disorder reported by parents as well as severe learning problems noted by the teacher of the child), sensory or motor impairment, (e) no medication other than methylphenidate to control for the impact of psychostimulants on the task results. All children that were on methylphenidate discontinued use at least 24 hours before testing to achieve complete washout (Pelham et al., 1999).

The assessment procedure consisted of three stages. Firstly, to confirm the ADHD diagnosis and assess comorbid ODD and CD, parents were administered the Dutch version of the disruptive behavior disorder section of the Diagnostic Interview Scale for Children (DISC; Shaffer, Fisher, Lucas, Dulcan, & Schwab-Stone, 2000), which is based on the Diagnostic and Statistical Manual of Mental disorders, fourth edition (DSM-IV; APA, 1994). The DISC-IV indicated that ten children met ADHD com-

bined type criteria, 12 children met criteria for ADHD inattentive type, and 3 children met criteria for ADHD hyperactive/impulsive type. Seven children fulfilled additional criteria for comorbid ODD, none were comorbid for CD. Secondly, to ensure symptom pervasiveness, the Dutch version of both the parent and teacher version of the Disruptive Behavior Disorder rating scale (DBD; Pelham, Evans, Gnagny, & Greenslade, 1992) were administered. The DBD consists of 42 items on a 4-point Likert scale (0 = not at all to 3 = very much). The scores on the scales range from 0-27 (9 items) for the Inattention or Hyperactivity/Impulsivity scales, 0-24 for the ODD scale and 0-48 for the CD scale. Children were required to score within the clinical problem range (95th to 100th percentile) on either the Inattention or Hyperactivity/Impulsivity scale of both parent and teacher rating scales. Finally, the Dutch version of the Child Behavioral Checklist (CBCL) and Teacher Rating Form (TRF) were administered (Achenbach & Edelbrock, 1981) as an additional measure of problem behavior, such as attention problems, delinquent and aggressive behavior.

Table 3.1 || Means, Standard Deviations, and Pairwise Group Comparisons for IQ, Age, and Rating Scale Scores.

Measure	Group				
	ADHD (*n* = 25)		Normal Controls (*n* = 30)		Dependent Variable
	M	*SD*	*M*	*SD*	*F*-value (*df* 1,53)
Age in months	120.5	17.4	119.5	15.0	0.1
IQ score	101.3	11.0	105.2	16.8	1.0
DBD parents					
Inattention	16.8[c]	4.9	3.2	3.2	152.8*
Hyperactivity/Impulsivity	15.0[c]	6.3	2.4	2.3	102.9*
ODD	7.3	4.4	2.0	2.0	34.6*
CD	1.6	2.3	0.3	0.6	8.1*
DBD teacher					
Inattention	16.0[c]	5.0	2.7	2.6	161.3*
Hyperactivity/Impulsivity	13.7[c]	6.8	2.6	3.1	65.7*
ODD	5.7	4.5	0.7	1.8	31.2*
CD	1.1	1.6	0.2	0.5	9.1*
CBCL					
Total problem score	67.4[c]	8.4	-	-	-
Attention problem scale	70.9[c]	8.9	-	-	-
TRF					
Total problem score	67.4[c]	9.9	-	-	-
Attention problem scale	66.4[c]	7.8	-	-	-

[c] = scores in the clinical range (> 95th percentile) of that subscale.
* = significant with $p < .01$

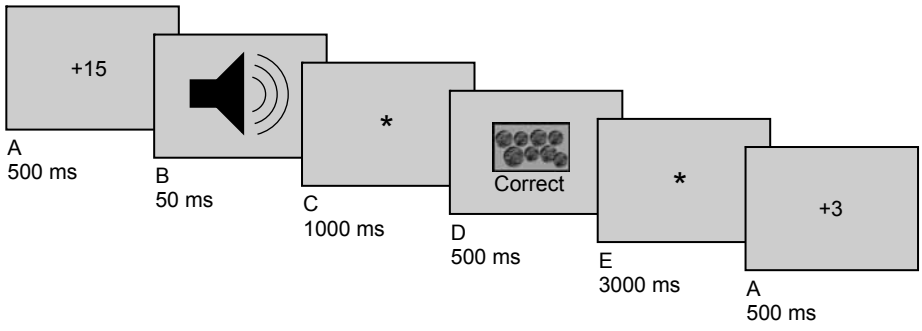
ADHD = Attention Deficit Hyperactivity Disorder; CD = Conduct Disorder; DBD = Disruptive Behavior Disorder rating scale; *M* = Mean; ODD = Oppositional Defiant Disorder; *SD* = Standard Deviation.

Control children were recruited through local elementary schools. They were included, when the following criteria were met: (a) no diagnosis of either ADHD, ODD or CD, (b) scores in the normal range (< 80th percentile) on the ADHD scales of the parent and teacher DBD, (c) IQ score >80, (d) absence of any neurological disorders, learning disabilities, sensory or motor impairment, (e) not taking any medication.

An estimation of the IQ score of each child was obtained by four subtests (Picture Arrangement, Arithmetic, Block Design, and Vocabulary) of the Wechsler Intelligence Scale for Children (WISC-R). These four subtests have been demonstrated to correlate between 0.93 and 0.95 with full scale IQ (Groth-Marnat, 1997).

Reinforced Timing Task

A self-paced time production paradigm adapted from Miltner, Braun and Coles (1997) was employed (see Figure 3.1). In this task, children had to produce a time interval of 1000 ms. The trial started with a colored screen for 500 ms that indicated the start of the reinforcement trial. A green screen signaled that the *reward condition* was applicable; a red screen signaled the *response cost condition*; a blue screen the *feedback-only condition*. Information regarding the *magnitude of reinforcement* was presented in the centre of the colored screen (being either +3, -3, +15, -15). While looking at a fixation cross at the centre of the screen, children heard a brief tone (50 ms, 80 db) through headphones. Following the tone, they pressed a response button, when they thought a 1-s interval had elapsed. Thousand ms after the button press, textual accuracy information appeared on the screen for 500 ms that informed the subject whether the estimation was 'too short', 'too long' (both incorrect) or 'correct'. Accuracy information



A) Background screen turned blue (feedback-only), red (response cost condition) or green (reward condition) for 500 ms. To indicate the magnitude of possible loss/gain, +3, -3, +15 or -15 was presented on the screen. B) Children heard an auditory beep for 50 ms indicating the start of 1-second interval, after which they were required to press the response button. C) A 1000 ms screen with fixation cross separated the button press from feedback presentation. D) Feedback appeared on the screen for 500 ms. E) The screen turned blank for 3000 ms before the next trial started.

Figure 3.1 || The time-course of a time-production trial.

was provided on every trial. A staircase algorithm determined the time window in which a response was considered correct. The boundaries of the initial window were 500 and 1500 ms and narrowed with 100 ms, when a response was correct, while it widened with 100 ms when a response was incorrect (see Miltner et al., 1997). Consequently, this procedure ensured a similar amount of positive and negative feedback (and reward and response cost) for each participant.

Depending on the reinforcement condition, coins indicating gain or loss appeared on the screen. In the reward condition, feedback was accompanied by either a 3 or 15 cents gain when responses were correct, and children received only feedback in case of an incorrect response. In the response cost condition, feedback was accompanied by a 3 or 15 cents loss when responses were incorrect, and children received only feedback following a correct response. In order to clearly distinguish between low and high magnitude of reinforcement, a 1: 5 ratio was used (Slusarek et al., 2001). During the inter-trial interval (3000 ms) the fixation cross re-appeared on the screen. The trials from the five reinforcement conditions were presented in a random order.

Internal clock functioning (e.g., Harrington et al., 1998) was investigated by the response tendency (either over- or underproduction of time, a measure of central time keeping), which was determined by the median time production. The median was used since the data was positively skewed as is common in reaction time distributions (skewness = 3.2, SE = .03) and the median is less sensitive to time production outliers. In addition, the random variability due to organization of motor output (e.g., Harrington et al., 1998) was investigated by the stability of responding, as measured by the intra-subject variability. A measure of the moment-to-moment fluctuations in performance was used that provides an index of local predictability (trial-to-trial variability) and controls for the mean response (Russell et al., 2006). The intra-subject variability = $\sqrt{(\Sigma(RT_i - RT_{i-1})^2/(n - 1)}$, where i = trial number, n = number of trials, and RT = response time. Responses that were more than four standard deviations from a participant's mean were considered as outliers and were excluded to minimize the risk of removing any real data, while still controlling for very extreme observations (Leth-Steensen et al., 2000). In the ADHD group this was 3% of the data points, in the control group 2%.

Procedure

All parents completed a written informed consent prior to the study that was approved by the local ethics committee. Participation was voluntary and travel costs were funded. During the task, children viewed a computer screen, positioned 60 cm

in front of them. The response button was utilized with the right hand and could be moved freely on the table. Standardized task instructions were given. In order to familiarize children with a 1-s interval, children saw a cartoon character that appeared 10 times on the screen for 1 s. Thereafter, a practice session started in which children practiced the feedback-only trials (6 trials), followed by the reward trials (12 trials) and the response cost trials (12 trials). The practice session was repeated until children correctly identified the magnitude and valence of the reinforcer. Finally, children practiced the randomized trials (12 trials). Children received 200 eurocents at the beginning of the task, which was placed in their view. They were instructed to gain as much and lose as little as possible. Participants were informed that their gain or loss would be calculated at the end of the task. At the end of the session, all children were told that their net score was 245 eurocents, which was an (arbitrary) 45 cents gain. Children exchanged their gain for a present worth approximately €5. The task consisted of 300 trials presented in five blocks of 60 trials lasting approximately 6 min per block. Parents received a report on the outcome of the study.

Psychophysiological Recordings

In order to investigate the psychophysiological responses to reinforcement, the electrocardiogram (ECG) and SC level were registered using the Vrije Universiteit Ambulatory Monitoring System-36 (Klaver, De Geus, & De Vries, 1994). The ECG was registered via two active 10 mm Ag/AgCl electrodes attached (a) between the collarbones over the jugular notch of the sternum and (b) under the left breast, 4 cm under the nipple between the ribs. One ground electrode was attached at the right lateral side between the lower two ribs. The continuous signals were sampled at 500 Hz from which R-peak occurrences were detected. Three inter-beat-intervals (IBIs) were extracted following the feedback moment (Crone et al., 2003). IBI0 represented the interval in which the feedback was presented and IBI+1, IBI+2 followed the feedback. The IBIs were corrected by the IBI at time of the button press to control for possible confounding influences of the HR changes related to preparatory response processes (Jennings & Van der Molen, 2002).

SC was measured through two 1 cm^2 AgAg/Cl electrodes, which were attached with Velcro straps to the volar surfaces of the medial phalanges of the index and middle fingers of the left hand. A constant voltage of 0.5 volt was used to register SCL and the signals were amplified and sampled at 10 Hz. Electrolyte gel (0.05 molar NaCL) was applied to the two electrodes. Due to artifacts (possibly due to an increase in random movement), only the first three blocks (180 trials) of SC could be analyzed. The reactive SC was calculated as the difference between the baseline SC (previous to the feed-

back stimulus) and the largest value in the interval 4000 ms following feedback. Psychophysiological data of two children in the control group were missing due to technical problems.

Statistical Analyses

A repeated measures (RM) ANOVA was conducted for the performance measures, with reinforcement condition as within-subject factor and group as between-subject factor. The impact of reinforcement on performance was investigated using three planned contrasts: (a) feedback-only condition versus the (collapsed) reinforcement conditions *(reinforcement contrast)*, (b) reward versus response cost *(valence contrast)*, and (c) high versus low intensity of reinforcement *(magnitude contrast)*. The planned comparisons were orthogonal to (uncorrelated with) every other contrast. To investigate whether performance of children with ADHD and controls changed over the course of the task, the task was divided into 5 blocks (60 trials each).Block was inserted as a within-subject factor in a RM ANOVA with group as between-subject factor.

The impact of the contingencies on HR and SC following feedback were investigated by a RM ANOVA with feedback (positive and negative) and reinforcement condition as within-subject factors and group as between subject factor. Again, the three orthogonal contrasts were employed to test for differences between the reinforcement conditions. For the HR measure, the factor 'sequential IBI' (IBI0, IBI+1, IBI+2) was entered as an additional within-subject factor in the RM analyses.

Greenhousse Geisser adjusted p-values are reported for those analyses in which sphericity assumptions were violated. Effect sizes (partial eta squared, ηp^2) are reported to indicate the proportion of total variance explained by the effect, being either small (.01), medium (.06), or large (.14) (Cohen, 1988).

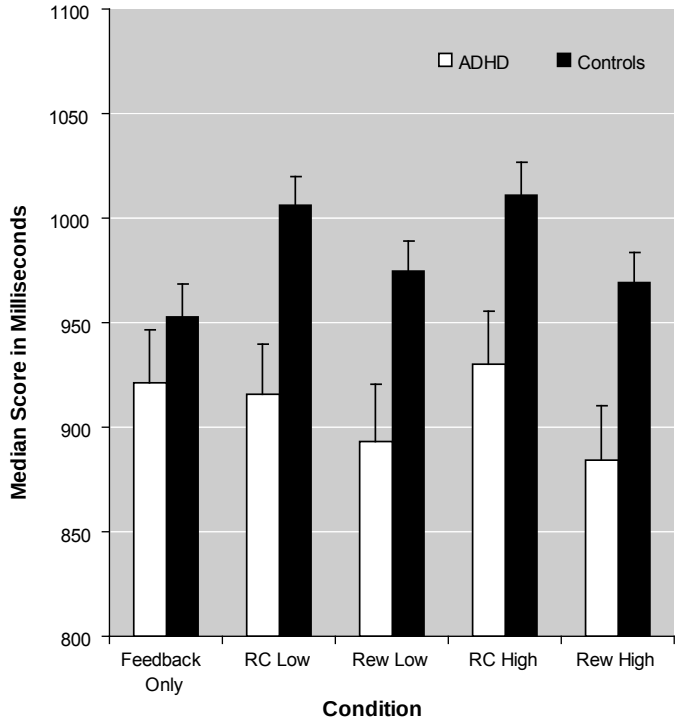
Results

As reported in Table 3.1, children with ADHD did not differ from controls in mean age or estimated full scale IQ. Furthermore, Table 3.1 indicates that groups differed in the expected direction on all scales of both the parent and teacher DBD with higher symptom levels reported for children with ADHD than for controls. Children with ADHD scored within the clinical problem range on the Total Problem scale and the Attention Problem scale of both the TRF and CBCL (see Table 3.1), further demonstrating the validity of our assessment procedure. In addition (not presented in Table

3.1), children with ADHD scored within the clinical problem range on the Externalizing Problem scale of both the CBCL and TRF, as is frequently observed in an ADHD sample (Angold, Costello, & Erkanli, 1999); all other scores (e.g., Internalizing Problem scale) were below the clinical threshold. Results for the ANOVA's testing the impact of the reinforcement conditions to our dependent variables are reported in Table 3.2.

Response Tendency

Figure 3.2 illustrates that children with ADHD underestimated the time interval compared to controls as indicated by a lower median response time. The reinforcement contrast comparing the feedback-only condition to the reinforcement conditions was not significant, but there was an interaction between the reinforcement contrast and group. Follow-up analyses demonstrated that groups did not differ in the feedback-only condition ($p = .28$), in contrast to the reinforcement conditions where children with ADHD more severely underestimated the interval than controls ($p = .003$).



Responses < 1000 ms indicated underestimations and responses > 1000 ms indicated overestimations. RC = Response Cost, Rew = Reward. The figure illustrates the group difference in response tendency and the interaction between group and the reinforcement contrast (feedback-only versus reinforcement conditions).

Figure 3.2 || Response tendency as expressed in terms of median time production (and standard errors) of children with ADHD and normal controls in the reinforced time-production task.

Table 3.2 || Results from the Reinforcement Condition Contrasts Analyses.

Effects / Measure	Group	Reinforcement contrast (Feedback-only – reinforcement)	Valence contrast (reward - response cost)	Magnitude contrast (low - high)
Median response				
Main effect	$F_{5,49}$=7.7, p=.003, η_p^2 =.30	p=.186	$F_{1,53}$=32.9, p<.001, η_p^2=.38	p=.818
Interaction group	-	$F_{1,53}$=10.5, p=.002, η_p^2=.17	p = .837	p=.798
Description of effects	ADHD < NC	FB-only: ADHD = NC RF: ADHD < NC	Reward < Response cost	
ISV				
Main effect	$F_{5,49}$=5.8, p=.019, η_p^2=.09	$F_{1,53}$=10.9, p=.002, η_p^2=.17	p=.106	p=.096
Interaction group	-	$F_{1,53}$= 4.4, p=.040, η_p^2=.08	p=.390	p=.446
Description of effects	ADHD > NC	FB-only: ADHD > NC RF[1]: ADHD > NC		
HR				
Main effect	p=.613	$F_{1,51}$= 5.0, p=.030, η_p^2=.09	$F_{1,51}$=10.5, p=.002, η_p^2=.17	p=.659
Interaction group	-	p = .944	p = .852	p=.324
Description of effects		FB-only < Reinforcement	Reward < Response cost	
SC				
Main effect	p=.300	p=.216	p=.230	p=.156
Interaction group	-	$F_{1,51}$= 4.8, p=.033, η_p^2=.09	p=.526	p=.323
Description of effects		ADHD: FB-only < RF NC: FB-only = RF		

[1] Marginal significant effect.

ADHD = Attention Deficit Hyperactivity Disorder; FB-only = Feedback-only condition; RF = (collapsed) reinforcement conditions; NC = Normal controls

Figure 3.2 shows that while controls reduced their tendency to respond prematurely when reinforcement was added to feedback ($p = .003$), children with ADHD responded similarly in the feedback-only and reinforcement conditions ($p = .25$). The second contrast that tested reinforcement valence was significant: Children responded prematurely in the reward compared to the response cost conditions. Group did not significantly interact with the valence contrast. The magnitude contrast was not significant and no significant interaction between the magnitude contrast and group was observed.

The tendency to respond prematurely diminished over time (912 ms versus 960 ms), as indicated by a main effect of block, $F_{4,50} = 4.1$, $p = .012$, $\eta p^2 = .07$. Groups were not differentiated by the factor block ($p = .87$).

Timing Stability

Figure 3.3 illustrates that the intra-subject variability of time production was larger in children with ADHD than in controls, indicating that time production was less stable in children with ADHD. The reinforcement contrast was significant: Response variability decreased in the reinforcement conditions compared to feedback-only and the reinforcement contrast interacted significantly with group. Figure 3.3 illustrates this interaction: Children with ADHD responded more variably than controls in the feedback-only condition ($p = .008$), while this group difference was smaller and only marginally significant in the collapsed reinforcement trials ($p = .058$). The valence contrast was not significant and this contrast did not interact with group. Variability in time production was larger in the low versus high reinforcement trials as indicated by the magnitude contrast, although this effect was only of marginal significance. No significant interaction between the magnitude contrast and group was found.

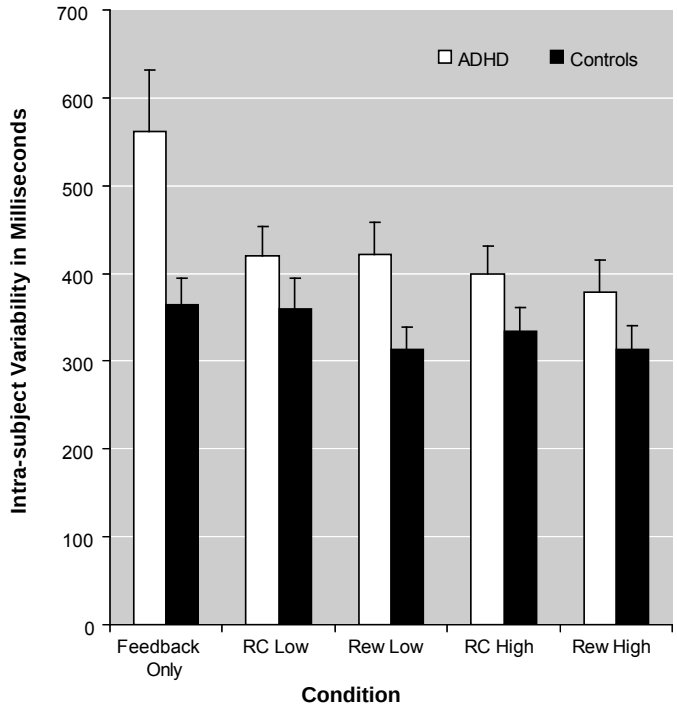
The variability in time production did not change over time; there was no significant effect of block ($p = .64$). Groups were not differentiated by the factor block ($p = .84$).

Psychophysiology

HR Following Feedback

HR was faster following positive than negative feedback, $F_{1,52} = 25.3$, $p < .001$, $\eta p^2 = .33$. The difference between positive and negative feedback did not interact significantly with group ($p = .87$), nor did feedback significantly interact with group and one of the reinforcement condition contrasts (reinforcement, $p = .48$; valence $p = .39$; magnitude $p = .12$). Therefore, the HR responses to positive and negative feedback were collapsed in the analyses described below.

Table 3.2 indicates that the HR response (collapsed over positive and negative feedback) did not differ between children with ADHD and controls. However, there was a interaction between sequential IBI (IBI0, IBI+1 and IBI+2) and group (not presented in Table 3.2), although this just escaped conventional levels of significance, $F_{2,50} = 2.5$, $p = .08$, $\eta p^2 = .05$. This interaction demonstrates that HR of children with ADHD accelerated immediately following feedback (IBI shortening from IBI0 to IBI+1 and IBI+2), in contrast with controls. HR of controls did not differ between IBI0 and IBI+1 and only accelerated (IBI shortened) between IBI+1 and IBI+2. There were no interactions between sequential IBI, group and the reinforcement condition contrasts (reinforcement, $p = .73$, valence $p = .25$, magnitude $p = .93$).



RC = Response Cost, Rew = Reward. The figure illustrates the group difference in timing stability and the interaction between group and the reinforcement contrast (feedback-only versus reinforcement conditions).

Figure 3.3 || Timing stability expressed in terms of the intra-subject variability (and standard errors) of children with ADHD and normal controls in the reinforced time-production task.

Table 3.2 shows that HR accelerated in the (collapsed) reinforcement conditions compared to feedback-only as indicated by a significant effect of the reinforcement contrast. The interaction between group and the reinforcement contrast was not significant. HR in reward trials was faster (lower IBI) than in response cost trials, as indicated by a significant effect of the valence contrast. As shown in Table 3.2, no other significant effects were found.

SC Following Feedback

Children with ADHD exhibited similar SC responses compared to controls. The reinforcement contrast was not significant, however, this contrast interacted significantly with group. Figure 3.4 illustrates that unlike controls ($p = .56$), children with ADHD exhibited a smaller SC response in the feedback-only condition compared to the reinforcement conditions ($p < .01$). As shown in Table 3.2, no other significant effects were found.

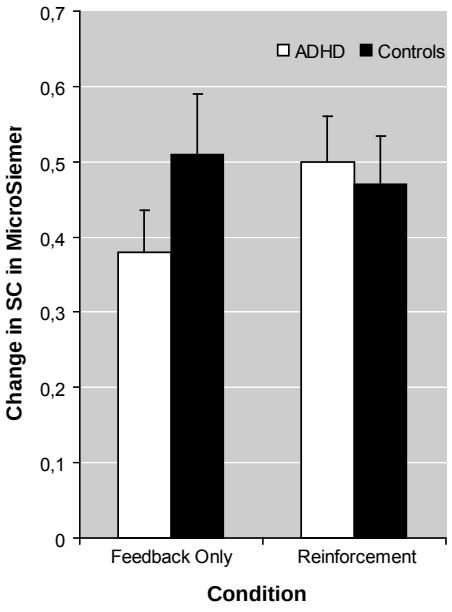


Figure 3.4 || Amplitude of skin conductance responses to feedback (and standard errors) in the reinforced time-production task for children with ADHD and normal controls for a 4000 ms interval following feedback. Data is baseline corrected by the skin conductance at time of the feedback.

Discussion

This is the first study that separated reinforcement valence and magnitude, when investigating motivational modulation of task performance in children with ADHD. We investigated two aspects of motor timing: response tendency (either over- or underproduction of time as indicated by median response time) and response stability (intra-subject variability). In line with previous reports, children with ADHD underestimated the time interval more severely than controls and showed more response variability (Leth-Steensen et al., 2000; Rubia et al., 2007; Toplak et al., 2006; Van Meel et al., 2005a). These findings emphasize that children with ADHD suffer from problems that relate to internal clock functioning as well as the organization of response output (e.g., Harrington et al., 1998). In contrast with our expectations, there were no indications that children with ADHD were abnormally affected by the valence or magnitude of reinforcement. Rather, the impact of reinforcement compared to feedback-only differed between children with ADHD and controls. The intra-subject variability of responding decreased under conditions of reinforcement to a larger extent in children with ADHD than in controls. The tendency to respond prematurely, on the other hand, was unaffected by reinforcement in children with ADHD. In contrast, controls diminished this tendency in the reinforcement conditions compared to the feedback-only condition. Skin conductance responses increased to a larger extent in children with ADHD than in controls when feedback was coupled with reinforcement. No group differences in the HR response to reinforcement were revealed.

The finding that children with ADHD profited from reinforcement to a greater extent than controls when measuring response variability points to an abnormal sensitivity to reinforcement in ADHD. This result corroborates with earlier studies (see for review Luman et al., 2005). The valence hypothesis was not supported: children with ADHD did not show a differential response to reward versus response cost compared to controls. The findings do not converge with the dopamine model of Sagvolden et al. (2005), which suggests that children with ADHD suffer from a faster decay of reward than controls. The preference for a small immediate over a larger delayed reward in children with ADHD (Rapport et al., 1986; Sonuga-Barke et al., 1992) may be more related to delay aversion (APA, 1994; Sonuga-Barke, 2002) than to an abnormal sensitivity to reward. This is confirmed by Antrop et al. (2006), who reported no group differences in reward preference when children were visually stimulated during the waiting period, suggesting that visual stimulation altered their subjective experience of delay. The findings of a greater sensitivity to response cost in children with ADHD compared to controls (e.g., Carlson et al., 2000) were neither supported by our study, nor by others (e.g., Oosterlaan & Sergeant, 1998). Clearly, this issue

needs further investigation. In addition, the magnitude hypothesis was not supported. Our findings could not be explained by an elevated reward threshold in children with ADHD (Haenlein & Caul, 1987). Instead, in the current study, a small amount of reinforcement already motivated children to perform well in terms of the variability of time productions.

Both ADHD and control children exhibited a tendency to press the response button too early in the feedback-only condition (median response < 1000 ms), suggesting that their internal clock ran too fast. A fast internal clock has been reported in an earlier study in ADHD using the same task (Van Meel et al., 2005a) and such a problem may be related to problems with impulsivity or delay aversion in ADHD (Barkley, 1997; Sonuga-Barke, 2002). Controls diminished this tendency when faced with reinforcement and we speculate that control children were motivated by reinforcement to perform adequately. Children with ADHD, in contrast, showed a diminished sensitivity to reinforcement by responding prematurely irrespective of the reinforcement condition. Premature responding in ADHD may reflect a deficiency that is not ameliorable by reinforcement. Similarly, premature responses as measured by the inability to withhold responses in an inhibition task have been found insensitive to manipulations of motivation (Crone et al., 2003; Iaboni et al., 1995; Oosterlaan & Sergeant, 1998).

When looking at the stability of time production in terms of the intra-subject variability, children with ADHD responded less variably when faced with reinforcement compared to feedback-only, almost to a level comparable with controls. Highly variable responses seem characteristic for children with ADHD (Leth-Steensen et al., 2000; Rubia, et al., 2007; Van Meel et al., 2005a), however, this is the first study to show that this response style is sensitive to motivational manipulations. The absence of a group by magnitude interaction, suggest that the prospect of small gains or losses already motivated children with ADHD to respond less variably. Because the variability of time productions in the ADHD group did not change over time, we speculate that there was no decay in the impact of reinforcement on performance. Van Meel et al. (2005a) did not find an interaction between reinforcement condition and group for response variability when studying the individual standard deviation (SD) of responding. In that study children with ADHD more severely underestimated the interval than controls. Possibly, trial-to-trial variability may have been a more accurate measure of intra-subject variability than SD, since it is less sensitive to the mean response (Russell et al., 2006).

The impact of reinforcement on timing variability in the current study converges with evidence of structural and functional brain imaging studies in ADHD. Timing and timing variability problems in ADHD have been associated with the prefrontal cortex, the cerebellum and the basal ganglia (Casey et al., 2007; Rubia et al., 2007; Toplak et al., 2006). A recent paper gathered evidence that reinforcement has a major impact on motor functions, an effect which is mediated by the basal ganglia (e.g., Haber, 2003). Future studies, therefore, may focus on the impact of reinforcement on response variability in children with ADHD using brain imaging techniques.

Psychophysiology

No group differences in the HR response to reinforcement were found, except for a marginal significant group by IBI interaction. In line with previous findings (e.g., Crone et al., 2003), children with ADHD exhibited immediate HR acceleration following feedback, while controls showed a delay in acceleration. HR changes following feedback have been suggested to be related to performance monitoring processes that are responsible for the allocation of attention (Jennings & Van der Molen, 2002). We speculate that an abnormal HR response in children with ADHD points to a dysfunction in the allocation of attention, that may be necessary to decrease their response variability. In contrast with our expectations, the interaction between group and the reinforcement contrast on performance was not accompanied by a group difference in the HR response to reinforcement. This may relate to the age of our participants: Crone, Jennings, & Van der Molen (2004) demonstrated that the monitoring system that is related to HR reactivity (described above) is less active in children as compared to adults.

In terms of SC responses, children with ADHD and controls differed in their reactivity to reinforcement compared to feedback-only. In the ADHD group, SC responses increased in the reinforcement conditions, unlike the SC responses of controls. SC responses have been associated with affective processing of stimuli, such as discriminating between good and bad outcomes (Damasio, 1996). O'Connell, Bellgrove, Dockree, and Robertson (2004) reported smaller SC responses to errors in children with ADHD than in controls. Since children with ADHD demonstrated intact post-error response slowing (an indicator of error detection) in that study, reduced SC responses were interpreted as evidence for a decreased awareness of the significance of errors. In our study, increased SC responses in children with ADHD in the reinforcement conditions may be taken as evidence for an increased awareness of the significance of feedback, which may be associated with the decrease in the variability of responses.

Limitations

An issue in the current study is the presence of comorbid ODD and CD symptoms in the ADHD sample, as specified by scores on the DISC-IV and DBD rating scale. There is substantial overlap between ADHD and anti-social symptoms (Angold et al., 1999), and studies have found an abnormal sensitivity to response cost in ODD/CD measured behaviorally and psychophysiologically (Newman, Wallace, Schmitt, & Arnett, 1997). We examined the contribution of the aggregated parent and teacher reported ODD and CD symptoms as measured by the DBD rating scale to the relationship between reinforcement and all dependent measures. No significant correlations were revealed, except for the SC analyses. The difference in SC between the feedback-only and (collapsed) reinforcement correlated modestly with teacher rated ODD symptoms ($r = .36$). Another limitation is a clear baseline condition in which no feedback was provided. This would have enabled investigation of the impact of feedback (positive, negative) on motivation. Finally, a larger sample size would have increased the power to detect differences between ADHD subtypes, age as well as gender groups.

Conclusions

The current findings indicate that children with ADHD are characterized by a tendency to underestimate time and to show more variability in time production than controls. No evidence was revealed for a differential response to reward and response cost in children with ADHD compared to controls, and no evidence was found for a smaller threshold for experiencing incentives in children with ADHD compared to controls. Rather, the variability in time production decreased to a larger extent in children with ADHD than controls when children were faced with reinforcement compared to feedback-only. This suggests that children with ADHD suffer from motivational problems when performance is not reinforced. The tendency to underestimate time in the ADHD group was less sensitive to our motivational manipulations, which may suggest that these problems cannot be remediated by contingencies. The decreased variability in responding in ADHD in the reinforcement conditions was accompanied by an increase in SC responses to feedback. Possibly, children with ADHD suffered from a diminished awareness of the significance of feedback when reinforcement was not available. There were no group differences in the HR response to reinforcement.

The findings have some important implications. Variability in motor output may translate into diverse domains of motor functioning, such as the planning of simple

and more complex motor behavior (Toplak et al., 2006). Children with ADHD have been found to show problems with motor skills, such as tying shoes, printing letters or playing sports (Karatekin, Markiewicz, & Siegel, 2003) and there is a large overlap between ADHD and motor coordination disorders (Kadesjö, & Gillberg, 1999). Although the present experimental findings suggest that problems related to response variability in ADHD may be modulated by using appropriate reinforcement, clinical studies need to be undertaken to see how these findings are applicable in the clinical setting. The observed normalization of psychophysiological responses to feedback when reinforcement is at stake may suggest that children with ADHD suffer from problems with feedback processing. Such findings call for interventions that focus on the role of reinforcement in enhancing the impact of environmental feedback in children with ADHD. Furthermore, if both reward and response cost are effective in decreasing the variability of motor responses in children with ADHD, reinforcing positive behavior may be as effective as punishing unwanted behavior.

Chapter 4

Decision-making in ADHD: Sensitive to Frequency but Blind to the Magnitude of Penalty?

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submitted for publication

Abstract

Background. Decision-making and reinforcement sensitivity were investigated in 23 children with ADHD and 20 healthy controls using a gambling paradigm. *Methods*. Children were required to choose between three alternatives that carried (A) small rewards and small penalties (advantageous), (B) large rewards and increasing penalties and (C) small rewards and increasing penalties (both disadvantageous). Penalties increased either in frequency or magnitude in two independent conditions. Heart rate (HR) and skin conductance (SC) were measured to examine whether impaired decision-making was accompanied by autonomic abnormalities. *Results*. Children with ADHD showed a maladaptive response style compared to controls by demonstrating a smaller preference for the advantageous alternative, when penalties increased in magnitude. When penalties increased in frequency, children with ADHD performed like controls. Group differences in decision-making attenuated after the task was administered twice. Compared to controls, performance of children with ADHD in the magnitude condition was accompanied by increased HR acceleration following reward and smaller post-selection SC activity. *Conclusions*. The current findings suggest that during decision-making, children with ADHD may be sensitive to the frequency but blind to the magnitude of penalty.

Introduction

Attention-deficit/ hyperactivity disorder (ADHD) is a severe developmental behaviour disorder which is accompanied by attention difficulties, disinhibition and impaired motor-control (American Psychiatric Association, 1994). One of the key issues in ADHD is an abnormal sensitivity to reinforcement (Luman, Oosterlaan, & Sergeant, 2005; Nigg, 2005; Sonuga-Barke, 2002). Children with ADHD have been found to show an increased sensitivity to instances of (immediate) gratification (see Luman et al. 2005 for review). Otherwise, children with ADHD have been found to require more response cost than controls in order to perform accurately (Slusarek, Velling, Bunk, & Eggers, 2001), suggesting that children with ADHD suffer from a diminished sensitivity to negative outcomes. A diminished sensitivity to the negative outcome of behaviour and a craving for immediate reward in children with ADHD becomes apparent in the increased risk for substance abuse (e.g., alcohol, drugs) and pathological gambling (Biederman et al., 2006).

Several theoretical models of ADHD have incorporated an abnormal sensitivity to reinforcement (see Luman et al., 2005), although the models differ greatly in detail. According to the dual-pathway model (Sonuga-Barke, 2002) children with ADHD show both cognitive and motivational problems. According to this model, as a result of a distortions in the cortico-ventral-striatal pathway, children with ADHD are reward-delay averse and are therefore less sensitive to rewards that are not delivered immediately. Several other theoretical models (e.g., Patterson & Newman, 1993; Quay, 1997), suggest that children with ADHD suffer from a smaller sensitivity to punishment (or non-reward) and are therefore focussed on instances of reward. This would be the result of a dysregulation of sympathetic nervous system activity, which has been demonstrated in studies where children with ADHD display smaller galvanic skin conductance responses to penalty than controls (Firestone & Douglas, 1975; Iaboni, Douglas, & Ditto, 1997).

An abnormal sensitivity to reinforcement may influence cognitive processes such as decision-making through unconscious 'somatic marker signals' that arise from bioregulatory processes (Damasio, 1996). Somatic markers develop through the coupling of positive or negative affective experiences with a stimulus, which may gradually result in the acquisition of somatic responses when the stimulus is presented. These responses can automatically be re-activated upon the presentation of a stimulus that is identical or resembles the original stimuli and therefore, the somatic markers differentiate between 'right' and 'wrong' before consciously knowing this. Evidence for this hypothesis comes from the Iowa Gambling Task (IGT) that simulates real-life

decision-making (Bechara et al., 1994). In this task, players are instructed to choose between four decks of cards. Turning a card results in immediate reward, which is either high (deck A or B) or low (deck C or D). In addition to reward, there is an unpredictable penalty, which is larger in decks A and B compared to decks C and D. In the long run, playing from decks A and B is disadvantageous, while playing from decks C and D is advantageous. Healthy subjects were found to develop skin conductance (SC) responses during the course of the task before selecting a card from the disadvantageous decks and choose more cards from the advantageous decks, while not aware (Bechara et al., 1994).

If ADHD is associated with a smaller sensitivity to negative outcomes and larger sensitivity to reward, they may prefer the disadvantageous alternatives (high reward) as compared to healthy controls. Ernst et al. (2003) reported on intact performance on the IGT in adults with ADHD, while Toplak, Jain, and Tannock (2005) demonstrated that adolescents with ADHD showed more disadvantageous choices than controls, especially, when the frequency of penalty was low compared to high. There is some evidence of impaired performance in children with ADHD using the IGT, however, this may be true for a sub-group of children with ADHD without anxiety and depressive symptoms (Garon, Moore, & Waschbusch, 2006; Geurts, Van der Oord, & Crone, 2005).

The current study investigates decision-making in ADHD in face of changing reinforcement contingencies as well as autonomic measures of reinforcement responsiveness. Measures such as heart rate (HR) and SC responses to reinforcement have not been utilized in a gambling paradigm to explain impaired decision-making in ADHD. An adapted version of the IGT was developed that contained an advantageous alternative carrying small rewards and small penalties, and two disadvantageous alternatives that carried either large rewards and large penalties or small rewards and large penalties. This alternative version was developed for three reasons. Firstly, the original four-choice IGT may have been too difficult for children (Geurts et al., 2005), while the two-choice IGT (Kerr & Zelazo, 2004), to our opinion, does not reflect real life decision making since rejecting one alternative automatically led to choosing the other. Secondly, since humans may be more sensitive to detect changes in the frequency than changes in the magnitude of penalty (Lin, Chiu, Lee, & Hsieh, 2007), it is important to separate these two aspects when investigating sensitivity to penalty. In the original IGT, reinforcement magnitude and frequency were manipulated in a single design, which did not allow these two aspects to be assessed in isolation. In our task, penalty increased either in frequency or in magnitude in the disadvantageous alternatives in two separate conditions. Thirdly, in the original task, the amount and

frequency of the contingencies remained stable over the course of the task. In our adapted version, penalty increased over the course of the task to investigate whether (maladaptive) choice behaviour in children with ADHD may 'normalize' when the contingencies are larger or allocated more frequently.

If children with ADHD exhibit a diminished sensitivity to aversive outcomes and an enhanced preference for immediate gratification, they should demonstrate greater preference for the disadvantageous than for the advantageous alternatives, specifically for the disadvantageous alternative carrying large rewards. Group differences should be smallest in the condition where the frequency (compared to the magnitude) of penalty increased, similar to adolescents with ADHD (Toplak et al., 2005). In line with previous findings, abnormal choice behaviour in the ADHD group was expected to be associated with smaller psychophysiological responses to penalty and reward (e.g., Iaboni et al., 1997).

Methods

Participants and Selection Procedure

Twenty-three children with ADHD (M 9.6 years; 5 girls) and 20 normal control children (M 9.1 years; 5 girls), all aged 7 to 12, participated in this study. Background information of the participants is presented in Table 4.1. Children were included, when they met the following criteria: (a) for the control group absence of any psychiatric disorder; for the ADHD group no diagnosis other than ADHD, oppositional defiant disorder (ODD) or conduct disorder (CD), (b) IQ score > 80, (c) absence of any neurological disorders, learning disabilities, sensory or motor impairment, (d) not taking medication except for methylphenidate. All children that were on methylphenidate discontinued use at least 24 hours before testing.

Children in the ADHD group had a clinical ADHD diagnosis and were recruited through the parents association for children with developmental disorders. The assessment procedure consisted of two stages. Firstly, parents were administered the Dutch version of the disruptive behaviour disorder section of the DSM-IV Diagnostic Interview Scale for Children (DISC-IV, Schaffer et al., 2000), to confirm the diagnosis of ADHD. Fifteen children met ADHD combined type criteria, 5 children met criteria for ADHD inattentive type and 3 children met criteria for ADHD hyperactive/impulsive type. Ten children fulfilled criteria for an additional diagnosis of ODD; one other child was comorbid for CD. Secondly, to ensure symptom pervasiveness, the Dis-

ruptive Behavior Disorder rating scale (DBD; Pelham, Evans, Gnagy, & Greenslade, 1992) was administered to both the parent(s) and teacher of the child. Children had to score above the clinical cut-off (> 95th percentile) on either the Inattention or Hyperactivity/Impulsivity scale of both parent and teacher rating scales. Control children were recruited through local elementary schools and were included when they scored in the normal range (< 90th percentile) on all scales of the parent and teacher DBD.

The IQ score of each child was estimated by four subtests (Picture Arrangement, Arithmetic, Block Design, and Vocabulary) of the Wechsler Intelligence Scale for Children (WISC-III). These four subtests have been demonstrated to correlate between .93 and .95 with Full Scale IQ (Groth-Marnat, 1997). IQ scores of children with ADHD that participated in this study were significantly lower than those of controls (see Table 4.1). Correlation analysis revealed no significant relation between IQ and performance on the gambling task (preference for alternative A), neither for period 1 (ϱ = .22, p = .15) nor period 2 (ϱ = .18, p = .25).

Table 4.1 Means, Standard Deviations, and Pairwise Group Comparisons for Age, IQ and Rating Scale Scores.

Measure	Group				
	ADHD (n = 23)		Normal Controls (n = 20)		
	M	*SD*	*M*	*SD*	*F*-value (*df* 1,41)
Age in months	115.9	17.0	113.2	16.5	0.3
IQ score	98.9	11.3	114.7	14.3	15.3**
DBD parents					
Inattention	16.3[a]	4.2	2.6	2.1	175.9**
Hyperactivity/Impulsivity	18.1a	4.2	2.4	2.3	227.1**
ODD	9.3	4.8	0.2	0.4	71.8**
CD	2.7	2.7	1.3	1.5	4.3*
DBD teacher					
Inattention	13.0[a]	5.4	3.6	4.5	37.4**
Hyperactivity/Impulsivity	14.6[a]	6.1	2.1	3.2	68.2**
ODD	6.9	4.7	1.4	2.6	21.5**
CD	2.0	2.2	0.4	1.1	8.1**

a = Clinical score (>95th percentile of this subscale score).
* = p<.05, ** = p<.01.

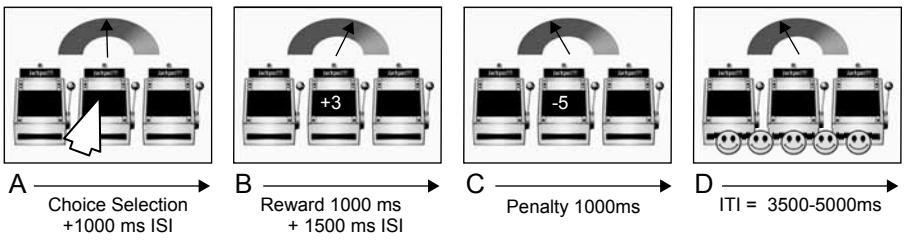
ADHD = Attention Deficit Hyperactivity Disorder; CD = Conduct Disorder; DBD = Disruptive Behavior Disorder rating scale; ODD = Oppositional Defiant Disorder.

Materials

Gambling Task

Children were shown three alternatives presented as Jackpots. The advantageous alternative A carried small rewards (1, 2 or 3 cents) on every trial and small penalties (-2 cents) in one third of the trials (see Appendix 4A). The disadvantageous alternative B carried large rewards (3, 4 or 5 cents) on every trial and large penalties (-8 cents in one third of the trials), the disadvantageous alternative C carried small rewards (1, 2, or 3 cents) on every trial and large penalties (-8 cents in one third of the trials). Children performed the task twice: in a magnitude and a frequency condition, where penalty in the disadvantageous alternatives increased either in magnitude (6 cents every 9 trials) or in frequency (6 cents every 9 trials). Half of the children of each group were presented the magnitude condition first and the other half was presented the frequency condition first.

Children had to choose a Jackpot (10 by 5 cm) by clicking on it (see Figure 4.1). The position of the three alternatives on the screen (left, middle, right) was counterbalanced between subjects. A digital scale (range -100 to +100) monitored the amount of money obtained. After 1000 ms, reward appeared for 1000 ms on the display of the chosen jackpot, printed in green. Fifteen hundred ms after the reward was removed, if applicable, penalty appeared for 1000 ms printed in red (otherwise, the display remained white). The inter-trial interval varied between 3500 and 5000 ms. During this interval, pressing the mouse was ineffective and five 'smileys' disappeared one by one from the screen to indicate when the next choice could be made. Both conditions contained 180 trials.



(a) Children had to press the mouse button on one of the three alternatives. Thousand ms later, (b) reward feedback appeared on the screen for 1000 ms in green ink. Another 1500 ms later, (c) when applicable penalty feedback appeared on the screen for 1000 ms in red ink. (d) During the inter-trial interval of 3500-5000 ms, five 'smileys' disappeared one by one from the screen to indicate when the next trial started.

Figure 4.1 || Time course of a jackpot trial.

Procedure

All parents completed a written informed consent prior to the study that was approved by the local ethical committee. Children were told that they were in a theme park in which they played 'Jackpot'. They had to win as much as possible by choosing between the alternatives. In both conditions, winning over 50 cents was required to receive a gift. After trial 90, the task ended automatically when children choose the same alternative 20 times in a row (so each child played a minimum of 110 trials) to prevent the task from becoming too boring. The remaining trials (to trial 180) were scored as if the child kept choosing this alternative. A break was scheduled between the conditions in which children were administered the WISC-III. At the end of the task, all children received a small present worth €3 irrespective of their performance.

Autonomic Measures

The ECG was registered via two active 10 mm Ag/AgCl electrodes attached (a) between the collarbones over the jugular notch of the sternum and (b) under the left breast, 1.6 inches under the nipple between the ribs. One ground electrode was attached at the right lateral side between the lower two ribs. The continuous signals were sampled at 500 Hz from which R-peak occurrences were detected. On every trial three inter-beat-interval (IBIs) were extracted contingent on the occurrence of reward; when applicable, a second identical window was extracted contingent on the occurrence of penalty. IBI-1 represented the interval preceding the reward and/or penalty; IBI0 represented the interval in which the reward and/or penalty was presented; IBI+1 just followed the reward and/or penalty. Since IBI-1 preceding rewards differed between the conditions ($p < .001$) and interacted significantly between group and condition ($p = .035$), the dependent measure was the difference between IBI+1 and IBI0. For IBI0, no group, condition or group by condition effects were revealed that could invalidate the difference score (p-values > .24). IBIs following reward and penalty were analyzed separately.

SC was measured with two 1 cm^2 AgAg/Cl electrodes that were attached with Velcro straps to the volar surfaces of the medial phalanges of the index and middle fingers of the left hand. A constant voltage of 0.5 volt was used to register SCL and the signals were amplified and sampled at 10 Hz. Electrolyte gel (0.05 molar NaCL) was applied to the two electrodes. Pre-selection SC was calculated as the largest difference between the minimum and maximum in SC level within the interval 2500 ms prior to the (advantageous and disadvantageous) choices, while post-selection SC was calculated as the difference between the minimum and the maximum within

SC level in the interval 2500 ms following the (advantageous and disadvantageous) choices. Only positive reflections of the difference score (the maximum follows the minimum) were incorporated.

Statistical Analyses

To explore choice behaviour over time (nominal data) in a task with three alternatives, an ANOVA such as used in most IGT studies cannot be utilized, since the number of data points in each cell (number of choices for each alternative) greatly differs between the alternatives. Using multilevel nominal logistic regression, time functions of choice behaviour (probabilities of alternatives A, B and C) for ADHD children and controls can be created across the 180 trials of the two conditions (magnitude, frequency). The logistic functions $\log(\pi_{ib}/\pi_{ia})$ of alternative B (high reward and increasing penalty), and $\log(\pi_{ic}/\pi_{ia})$ of alternative C (low reward and increasing penalty) were expressed in a multiple logistic model using alternative A (advantageous alternative) as a baseline category (Agresti, 1996; page 205-211). The probability functions of the three alternatives (π_{ia}, π_{ib} and π_{ic}) summed to 1 for each of the 180 time points. Dummy variables were created for group and condition.

Multilevel models consist of two parts, a fixed part which describes the average time curve, and a random part which describes the between-subject and within-subject variance (Goldstein, 1995). Here, the intercept, group, condition, and time were used to describe the fixed part. The intercept refers to the initial level of the dependent variable. Time was modelled either in a linear or quadratic parameter. The linear parameter describes the slope of the model at each time point. The quadratic factor described the acceleration (or deceleration) of the slope. The model was estimated using MLwiN 2.02 (Rasbash, Browne, Healy, Cameron, & Charlton, 2005).

There were carry-over effects from the first to the second administration (period) of the task as indicated by a significant difference in the intercept (initial choice preference) of $\log(\pi_{ib}/\pi_{ia})$ in period 1 and 2, $X^2_2 = 7.5$, $p < .05$. Initially, children were expected to choose randomly (probability of .33 for each alternative), which was observed in period 1. In period 2, however, the choice probability of the intercept for alternative B was .45, possibly due to a learning history of choice behaviour in period 1. Since group differences were detected in period 1 in the magnitude condition (see Results), the effect of group could not be disentangled from the crossover effect in the analysis of the frequency condition in period 2. Therefore, the frequency condition was excluded from the analyses in period 2. The two periods were analyzed separately with the aim to answer two different questions. In period 1, decision-making problems in chil-

dren with ADHD were investigated and in period 2 the persistency of such problems were studied. In period 1, the parameters of four different groups (ADHD magnitude, ADHD frequency, controls magnitude, control frequency) were inserted in the model; in period 2, the parameters of only two different groups (ADHD magnitude, controls magnitude) were inserted.

HR responses to reward and HR responses to penalty were both submitted to a repeated measures (RM) ANOVA with group as within-subject factor and condition as between-subject factor. The responses were collapsed over the two periods: When period (instead of condition) was inserted as a within-subject factor in the RM ANOVAs no significant group by period interactions on the HR measures were revealed (all $p > .24$). Pre- and post-selection SC were both submitted to a repeated measures ANOVA with condition and choice (advantageous, disadvantageous) as within-subject factors and group as between-subject factor. The responses were collapsed over the two periods: no group by period interactions were revealed for the SC measures (all $p > .38$). Psychophysiological data of two children were missing due to technical problems (one ADHD child and one control child). One other child in the ADHD group completed the frequency condition only and was left out of the psychophysiological analyses.

Results

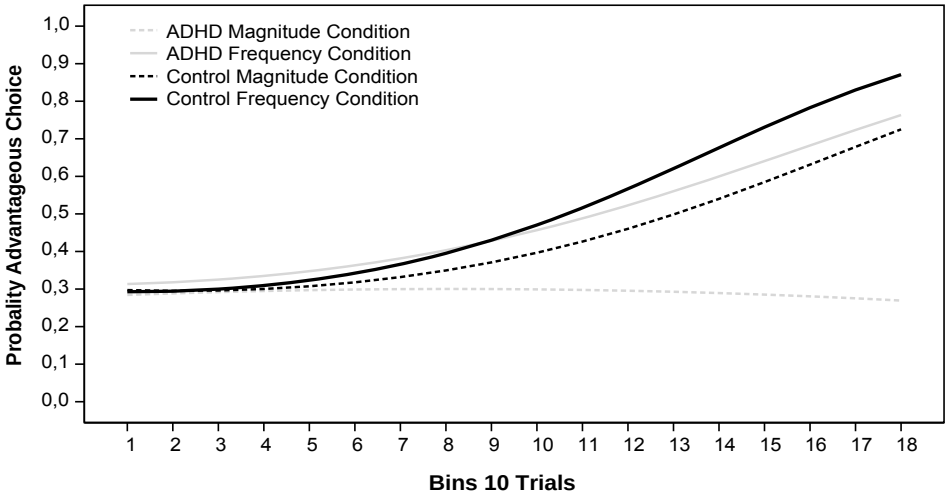
Performance

First, the model is presented for both periods. Three parameters were tested: the intercept (initial choice preference), linear (linear change in choice preference at each time point) and quadratic parameter (acceleration of the change in choice preference), the highest trend being the most informative. Second, the group comparisons of the joint effects of these three parameters (referred to as slope) are presented. To guard against type-1 errors, post-hoc analyses of individual parameters were only performed when significant differences between the slopes were revealed.

Decision-making in Period 1

Choice behaviour was best described by the quadratic trend, joint $X^2_8 = 110.1$, $p < .001$, demonstrating that children increased their preference for the advantageous alternative (A) (see Figure 4.2), while decreasing their preference for the disadvantageous alternatives (B and C). This negative quadratic trend (see Appendix 4B) indicated that the decrease in preference for the disadvantageous alternatives became larger over

time. There was no difference in the decrease in preference for alternative B and C, as indicated by a non-significant difference between $\log(\pi_{ib}/\pi_{ia})$ and $\log(\pi_{ic}/\pi_{ia})$, joint $X^2_{12} < 21.0$, $p > .05$. Figure 4.2 illustrates that children with ADHD and controls differed in their preference for alternative A, when penalty (carried by the disadvantageous alternatives) increased in magnitude, but not when penalty increased in frequency. The slopes of the ADHD group in the magnitude condition differed significantly from the three other groups, joint $X^2_{18} = 75.5$, $p < .001$. Post-hoc tests indicated that the quadratic trend, describing the behaviour of children with ADHD in the magnitude condition, differed from the quadratic trend of the control group in the magnitude condition ($\log(\pi_{ib}/\pi_{ia})$, $X^2_1 = 8.1$, $p < .01$; $\log(\pi_{ic}/\pi_{ia})$, $X^2_1 = 9.7$, $p < .01$), the control group in the frequency condition ($\log(\pi_{ib}/\pi_{ia})$, $X^2_1 = 11.1$, $p < .001$; $\log(\pi_{ic}/\pi_{ia})$, $X^2_1 = 12.5$, $p < .001$), and ADHD group in the frequency condition ($\log(\pi_{ib}/\pi_{ia})$, $X^2_1 = 9.7$, $p < .01$; $\log(\pi ic/\pi ia)$, $X^2_1 = 3.5$, $p < .10$). Figure 4.2 illustrates that children with ADHD in the magnitude condition did not develop any preference for the advantageous alternative (A). In terms of decision-making as measured by the gambling task, children with ADHD seem sensitive to increases in frequency while being blind to increases in magnitude of penalty.



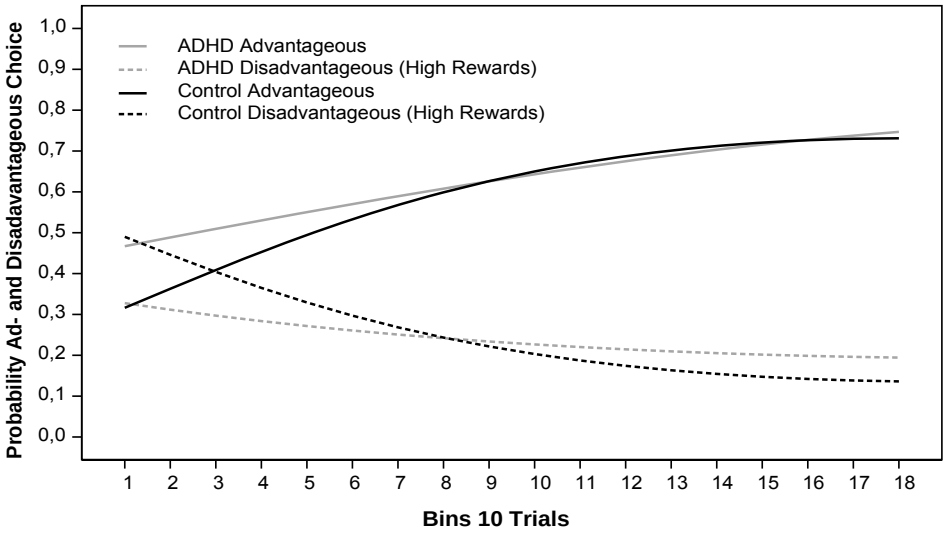
The slopes are described by quadratic trends of a multilevel nominal logistic regression model with random error terms set at 0.

Figure 4.2 || Choice probabilities over time (trial 1-180) for the advantageous alternative A (low reward, low penalty) for children with attention-deficit/ hyperactivity disorder (ADHD) and normal controls (NC) in period 1.

Decision-making in Period 2

Choice behaviour was best described by the quadratic trend, joint $X^2_4 = 15.3$, $p < .01$, which indicated that children increased their preference for the advantageous alternative (A) (see Figure 4.3), and decreased their preference for the disadvantageous alternatives (B and C). The positive quadratic trend (see Appendix 4B) indicated that the decrease in preference for alternatives B and C became smaller over time.

There were significant differences between the slopes of the ADHD and control group, joint $X^2_1 = 19.9$, $p < .01$. Post-hoc analyses showed that this was due to a smaller linear trend for $\log(\pi_{ib}/\pi_{ia})$ in the ADHD compared to the control group, $X^2_1 = 3.8$, $p = .05$ (see Appendix 4B). Figure 4.3 illustrates that over the course of the task, the linear increase in the preference for alternative A was smaller for children with ADHD and controls. This group difference could be explained by the initial preference of controls for the disadvantageous alternative B in contrast to children with ADHD who favoured the advantageous alternative (see Figure 4.3). The findings suggest that when the task was administered twice children with ADHD were able to show adaptive decisions when penalty increased in magnitude.

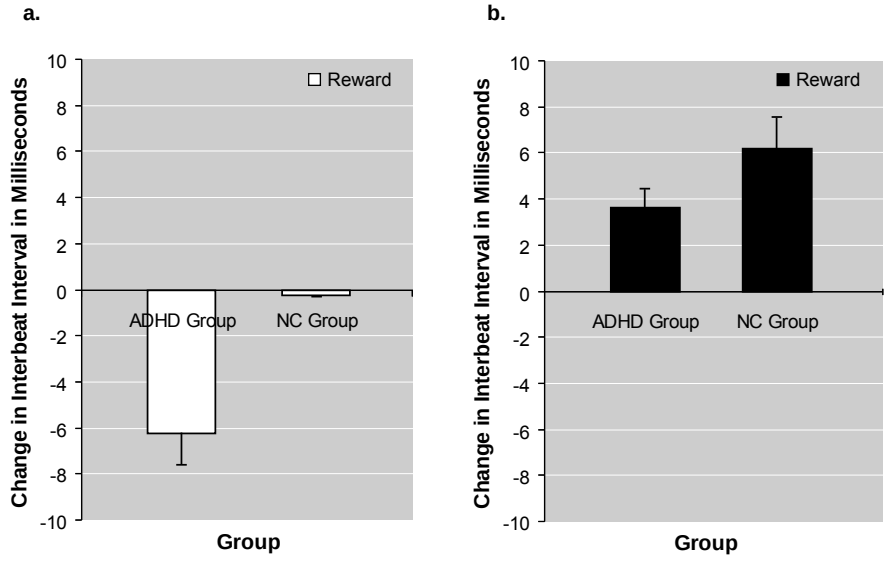


No group differences were revealed for the disadvantageous alternative C (low reward, high penalty). The slopes are described by quadratic trends of a multilevel nominal logistic regression model with random error terms set at 0.

Figure 4.3 || Choice probabilities over time (trial 1-180) for the advantageous alternative A (low reward, low penalty) and the disadvantageous alternative B (high reward, high penalty) for children with attention-deficit/ hyperactivity disorder (ADHD) and normal controls (NC) in the magnitude condition of period 2.

HR Response to Reinforcement

A significant group effect was found for the HR responses to reward, $F_{1,39} = 5.9$, $p = .021$, $\eta p^2 = .15$. Figure 4.4a illustrates that HR in response to reward accelerated in children with ADHD (lower IBI), while controls did not show any evidence for heart rate acceleration. There was an effect of condition, $F_{1,39} = 5.7$, $p = .023$, $\eta p^2 = .14$: The increase in HR following reward was more pronounced in the frequency compared to the magnitude condition. There was no significant interaction between group and condition ($p = .27$). No significant group effect was revealed for HR responses to penalty ($p = .50$). Again, there was an effect of condition: the increase in HR following penalty was more pronounced in the frequency compared to the magnitude condition, $F_{1,39} = 2.2$, $p = .083$, $\eta p^2 = .09$, although the effect was of marginal significance. Group did not interact significantly with condition ($p = .65$).



Responses are averaged over trials, alternatives and conditions. Positive values indicate HR deceleration; negative values indicate HR acceleration.

Figure 4.4 || Heart rate (HR) response (difference between IBI+1 and IBI0) following reward (4a) and penalty (4b) for children with attention-deficit/ hyperactivity disorder (ADHD) and normal controls (NC).

SC Anticipation and SC Responses

Pre-selection SC revealed no significant effects of group, condition, period or choice and no significant interactions were obtained (all $p > .50$).

For post-selection SC, there was no effect of group ($p = .21$), choice ($p = .23$) or condition ($p = .53$). However, group interacted with condition, $F_{1,39} = 17.8$, $p < .001$, $\eta p^2 = .32$. Follow-up analyses showed that in the magnitude condition the SC responses were larger for controls than for children with ADHD, $p = .001$ (see Figure 4.5). In contrast, groups did not differ on SC response in the frequency condition ($p = .49$). The interactions between group and choice as well as choice and condition were not significant (both $p > .49$). There was a 3-way interaction between group, condition and choice, $F_{1,39} = 4.2$, $p = .033$, $\eta p^2 = .11$. Figure 4.5 illustrates this interaction: In the magnitude condition SC responses of controls were larger following disadvantageous compared to advantageous alternatives, while SC responses of children with ADHD showed the opposite pattern (group by choice interaction, $F_{1,19} = 5.5$, $p = .087$, $\eta p^2 = .23$). This group and choice interaction was not observed in the frequency condition ($p = .29$).

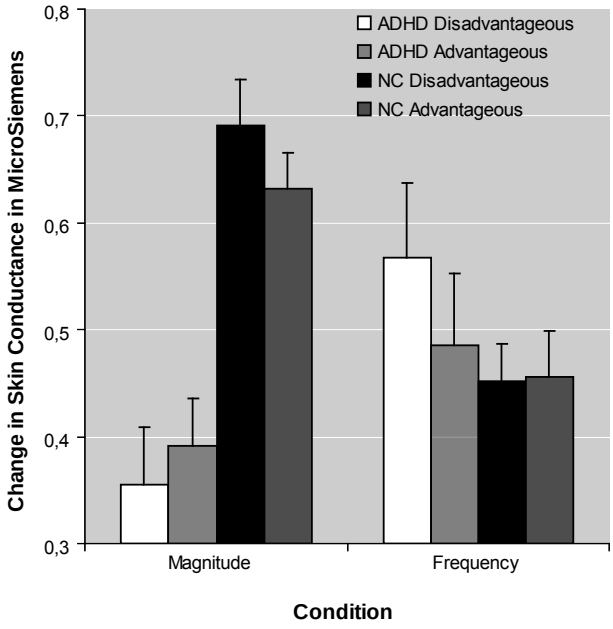


Figure 4.5 || Post-selection skin conductance (SC) to disadvantageous choices (alternative B and C) and advantageous choices (alternative A) for children with attention-deficit/ hyperac tivity disorder (ADHD) and normal controls (NC).

Discussion

Using a 3-choice gambling paradigm it was investigated whether children with ADHD suffered from motivational problems. We tested whether children with ADHD exhibited a diminished sensitivity to aversive outcomes and an enhanced preference for immediate gratification. The task contained an advantageous alternative (small rewards and small penalties), and two disadvantageous alternatives (large rewards and large penalties or small rewards and large penalties). In contrast to the original IGT, penalty carried by the disadvantageous alternatives slowly increased in frequency or magnitude in two separate conditions. This allowed us to track whether (maladaptive) choice behaviour in children with ADHD changed as a result of increased penalty. In addition, psychophysiological responses were measured, which has not been done earlier when studying decision-making in ADHD. All children increased their preference for the advantageous alternative, except for the ADHD group in the magnitude condition, indicating that our task was able to discriminate between groups in terms of decision making.

When penalty increased in magnitude, children with ADHD exhibited a smaller sensitivity to aversive outcomes than controls as indicated by the absence of a preference for the advantageous alternative. Interestingly, when penalty increased in frequency children with ADHD performed like controls. Contrary to prediction, children with ADHD did not display a specific preference for the disadvantageous alternative that carried large rewards (B). Performance in the second period indicated that children with ADHD were able to make advantageous decisions, when penalty increased in magnitude, hence indicating that they learned from past experience. Furthermore, children with ADHD showed abnormalities in their autonomic responses to reinforcement. HR responses following reward accelerated more strongly in children with ADHD than in controls. In addition, in the magnitude condition, SC responses of children with ADHD were smaller than those of controls and were smaller following disadvantageous compared to advantageous choices. This contrasted with the SC responses of controls, which were larger following disadvantageous than advantageous choices.

Although there is evidence of an increased sensitivity to instances of (immediate) gratification in children with ADHD (see Luman et al., 2005) as suggested by Sonuga-Barke (2002), ADHD children did not exhibit any reward driven choice behaviour in the current study. Rather, when making decisions, children with ADHD were blind to increases in penalty, specifically in the condition where the magnitude (and not the

frequency) of penalty increased. A greater sensitivity to frequency than magnitude of penalty concurs with findings in ADHD adolescents using the original IGT (Toplak et al., 2005). Since choice behaviour of ADHD children was only sensitive to penalty when it was administered in a frequent manner, we speculate that the impact of penalty decayed at a faster rate in children with ADHD than controls. These findings are in line with the suggestion that children with ADHD are less sensitive to penalty (e.g., Patterson & Newman, 1993). A faster decay of reinforcement in ADHD has been suggested earlier with respect to reward processing, resulting from a dysfunction in dopamine transmission in the limbic system (Johansen, Aase, Meyer, & Sagvolden, 2002). Tripp and Alsop (1999) showed that children with ADHD compared to controls were extremely sensitive to the last reward received and less sensitive to the overall history of reward. Future studies should verify whether such findings could be replicated, when studying the impact of penalty in ADHD.

In line with previous studies (see Luman et al., 2005), HR findings in the present study suggest abnormal autonomic responses to reward in children with ADHD. Children with ADHD displayed larger HR acceleration following reward than controls, while groups did not differ in HR response to penalty. Reward influences the sympathetic nervous system and increases HR (Fowles, 1988), suggesting that children with ADHD were more aroused than controls when receiving a reward in our study. The HR findings and choice behaviour showed a remarkable contrast: Whereas their HR response to reward was increased in children with ADHD compared to controls, no evidence for an increased preference for alternative B (high reward) was revealed in the ADHD group. In addition, no group differences were revealed in the HR response to penalty, while children with ADHD showed a larger preference for the disadvantageous alternatives than controls (in the magnitude condition). These findings contrast with the somatic marker theory (Damasio, 1996), which suggests that optimal bodily responses are a prerequisite for decision-making.

The findings in the present study indicate that children with ADHD are blind to future consequences of their decisions, despite the increasing penalties. This 'myopia' for future consequences was accompanied by an abnormal SC pattern. In the magnitude condition, children with ADHD displayed smaller SC responses than controls, indicating impaired sympathetic activity following their choices that could have activated an alternative response strategy. In addition, SC responses of children with ADHD were smaller following favourable than unfavourable outcomes, while SC responses of controls showed the opposite pattern, similarly to that of healthy adults (Bechara et al., 1994). The findings in this condition suggest an abnormality in ADHD in discriminating between 'good' and 'bad' (Bechara et al., 1994). In line with

these findings, Van Meel, Oosterlaan, Heslenfeld and Sergeant (2005) demonstrated that compared to controls, children with ADHD demonstrated poor discrimination between positive and negative outcomes on event related potentials that have been associated with affective evaluation. In the frequency condition of the current study, children with ADHD showed intact SC responses that, in line with the somatic marker theory (Bechara et al., 1994), converged with their (intact) performance. Although the group and condition interaction was not significant for the frequency condition, SC responses of controls did not seem to differ between the alternatives, in contrast to the SC responses children with ADHD. Possibly the task in this condition was too easy for control children (see Figure 4.2) and the aversive outcomes did not elicit an arousal response.

This study has some limitations that are worth noting. The study is limited by statistical power, which was exaggerated by the crossover effects of period 1 onto period 2. Another issue is that groups differed in estimated IQ, although it is unlikely that this difference may have affected the present findings, since IQ did not relate to performance on the gambling task (see Method section). Finally, larger inter-stimulus intervals (see Figure 4.1) may have allowed inspection of SC responses in a larger interval than 2500 ms.

Conclusion

The findings point to difficulties for children with ADHD in behaviour regulation in the face of reinforcement. When making decisions, children with ADHD seem sensitive to the frequency of penalty, while being blind to increased magnitude of penalty. This insensitivity to the aversive future outcomes of decisions in ADHD children when the frequency of penalty was small was accompanied by abnormal psychophysiological responses.

If replicated, the findings have important clinical implications, since feedback and reinforcement play a major role in behavioural interventions. If children with ADHD are unable to identify the significance of (large) losses as readily or as reliably as controls, warning children with ADHD regarding the negative consequences of their (undesirable) behaviour should be repeated often, since raising the intensity of the negative consequences may be ineffective.

Appendix 4A || Gain and Penalty Carried by the Alternatives in the Frequency and Magnitude Condition

	Gain			Penalty		
Alternative	**A**	**B**	**C**	**A**	**B and C**	**B and C**
Trial					**Magnitude Condition**	**Frequency Condition**
1	1	3	1			
2	3	5	3	-2		-8
3	2	4	2		-8	
4	1	3	1			-8
5	2	4	2	-2	-8	
6	3	5	3			
7	2	4	2	-2		-8
8	3	3	3		-8	
9	1	5	1			
10	2	4	2			
11	1	5	1	-2	-14	-8
12	3	3	3			
13	3	5	3			-6
14	2	3	2			
15	1	4	1	-2	-8	-8
16	3	5	3			
17	1	4	1			-8
18	2	3	2	-2	-8	-8
19	1	3	1	-2		
20	3	5	3			
21	2	4	2	-2	-14	-6
22	1	3	1			
23	2	4	2			-8
24	3	5	3		-8	-8
25	2	4	2			
26	3	3	3			-6
27	1	5	1	-2	-14	-6
28	2	4	2	-2		
29	1	5	1			-6
30	3	3	3	-2	-14	-8
31	3	5	3			
32	2	3	2			-8
33	1	4	1	-2	-14	-6
34	3	5	3			-8
35	1	4	1		-14	
36	2	3	2			

Gains of all three alternatives, as well as penalty of alternative A are similar in the magnitude and frequency condition. Only 36 trials are presented.

Appendix 4B || Parameters of the Multilevel Nominal Regression Model for Period 1 and Period 2

Period 1					
Group		**Log**	**Intercept (*SE*)**	**Linear effect (*SE*)**	**Quadratic effect (*SE*)**
ADHD Magnitude	(*n* = 11)	(π_{ib}/ π_{ia})	0.37 (0.18)	-0.57 (0.88)	0.73 (0.63)
		(π_{ic}/ π_{ia})	0.09 (0.20)	-0.23 (0.91)	0.17 (0.66)
ADHD Frequency	(*n* = 12)	(π_{ib}/ π_{ia})	0.13 (0.18)	0.13 (0.88)	-2.13 (0.67) **
		(π_{ic}/ π_{ia})	0.06 (0.19)	-0.48 (0.91)	-1.65 (0.72) *
NC Magnitude	(*n* = 11)	(π_{ib}/ π_{ia})	0.32 (0.18)	0.10 (0.91)	-1.90 (0.70) **
		(π_{ic}/ π_{ia})	-0.04 (0.20)	0.94 (0.96)	-2.97 (0.76) **
NC Frequency	(*n* = 9)	(π_{ib}/ π_{ia})	0.37 (0.20)	-0.23 (1.03)	-2.83 (0.82) **
		(π_{ic}/ π_{ia})	-0.04 (0.22)	0.90 (1.07)	-3.69 (0.87) **
Period 2					
Group		**Log**	**Intercept (*SE*)**	**Linear effect (*SE*)**	**Quadratic effect (*SE*)**
ADHD	(*n* = 11)[1]	(π_{ib}/ π_{ia})	-0.30 (0.27)	-1.79 (0.90)*	0.74 (0.70)
		(π_{ic}/ π_{ia})	-0.78 (0.28)	-1.21 (1.06)	-0.61 (0.93)
NC	(*n* = 9)	(π_{ib}/ π_{ia})	0.57 (0.30)	-4.42 (1.00)	2.16 (0.80)*
		(π_{ic}/ π_{ia})	-0.40 (0.31)	-2.89 (1.11)	1.59 (0.91)[2]

* $p < .05$, ** $p < .01$ for a two-sided test.
[1] One child in the ADHD group did not complete the magnitude condition in period 2.
[2] $p < .10$

ADHD = Attention-deficit/ Hyperactivity Disorder; NC = Normal Controls; Log (π_{ib}/ π_{ia}) = β_{0b} (intercept) + β_{1b} time (linear trend) + β_{2b} time^2 (quadratic trend); Log (π_{ic}/ π_{ia}) = β_{0c} + β_{1c} time + β_{2c} time^2. Time = trial 1 to trial 180.

Chapter 5

Is it Reward Frequency or Magnitude that Drives Reinforcement-Learning in ADHD?

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Abstract

Background. Children with attention-deficit/hyperactivity disorder (ADHD) show an impaired ability to use feedback in the context of learning. Using a stimulus-response learning task it was investigated whether (1) children with ADHD displayed flatter learning curves, (2) reinforcement-learning in ADHD was sensitive to either reward frequency, magnitude, or both, and (3) altered sensitivity to reward was specific to ADHD. *Method*. Performance of 23 boys with ADHD aged 8-12 was compared to that of 30 age-matched normal controls (NC). To examine the specificity of reinforcement-learning problems, the ADHD group was compared to a group of clinical controls (CC); 21 boys with a clinical diagnosis of autism spectrum disorder. Rewards were delivered contingent on performance and varied both in frequency (low, high) and magnitude (low, high). *Results*. The findings showed that, although learning rates were comparable across groups, both clinical groups committed more errors than normal controls. In contrast to the NC group, children with ADHD were unaffected by frequency and magnitude of reward, while the NC group and, to some extent, the CC group showed improved performance, when rewards were delivered infrequently versus frequently. *Conclusions*. Children with ADHD show difficulties in stimulus-learning, which was insensitive to motivational modulation. We speculate that children with ADHD were less sensitive to the over-arousing impact of frequent rewards, due to a low level of psychophysiological arousal.

Introduction

In children with attention-deficit /hyperactivity disorder (ADHD) there is evidence of impaired ability to use feedback in the context of learning. This is observed both in an impaired ability in ADHD to detect errors as indicated by decreased electrophysiological brain potentials associated with error processing in response inhibition tasks (Liotti, et al., 2005; Van Meel, et al., 2007) or an inability to adjust behaviour following errors as indicated by reduced post-error response time slowing (Sergeant & Van der Meere, 1988; Wiersema, et al., 2005). Further, children with ADHD show an impaired feedback monitoring as indicated by decreased heart rate responses following performance feedback (Luman et al., 2007). All these reports, however, measured behaviour in tasks where the appropriate response was well-established. Studies on the acquisition of new behaviour in children with ADHD remain scarce.

In the process of learning, reinforcement plays a significant role, since contingencies such as reward and punishment that follow behavioural responses increase or decrease the chance of repetition of that behaviour (Schultz, 2000; Wise, 2004). Physiologically, this reinforcement-learning is mediated by dopamine which facilitates learning by 'stamping in' stimulus-response associations (Wise, 2004). Children with ADHD compared to normal controls (NC) show an abnormal sensitivity to reinforcement, as demonstrated by an intensified response to recently received rewards, while being less responsive to more distant rewards (Sonuga-Barke et al., 1992; Tripp & Alsop, 1999). A review of the impact of reinforcement on cognitive task performance in ADHD revealed some evidence that appropriate motivational stimulation (such as reward or response cost) may improve cognitive functioning to a larger extent in children with ADHD than in controls (Luman, et al., 2005). The studies in that review, however, all assessed the impact of reinforcement on over-learned responses. Learning of new behaviour using reinforcement contingencies is likely to be impeded in ADHD due to their abnormal response to reinforcement.

According to Sagvolden and colleagues (2005) the behaviour that characterizes ADHD can be explained by hypo-dopaminergic functioning in the fronto-striatal pathway. As a consequence, children with ADHD compared to healthy controls should show a faster decay of reward that influences reinforcement-learning through an inefficient stimulus-response coupling, specifically when reinforcement is delivered infrequently (Johansen et al., 2002; Sagvolden et al., 2005). Indeed, in ADHD children frequent compared to infrequent rewards decreased the variability of responding (Aase & Sagvolden, 2006), increased response speed in a Figure Matching task (Douglas & Parry, 1994), and improved decision making abilities in the face of reinforcement (To-

plak et al., 2005). Other studies, however, have failed to replicate a detrimental effect of infrequent reinforcement in ADHD (Pelham et al., 1986; Barber et al., 1996; Tripp & Alsop, 1999). An issue in the studies on reinforcement frequency and ADHD is that most studies did not distinguish whether reward frequency or reward magnitude modulated the behaviour of children with ADHD, since frequent rewards are necessarily associated with a larger amount of reward. It has been shown that increasing the magnitude of reinforcement (penalty) significantly ameliorated inhibitory deficits in ADHD in a Stop Task paradigm (Slusarek et al., 2001). Together, these studies show some support for the view that performance in ADHD is affected by the intensity of reinforcement rather than the time interval between stimulus and reward, as suggested by Sagvolden et al. (2005). The need for intense reinforcement concurs with the suggestion of Haenlein and Caul (1987) that children with ADHD suffer from a decreased sensitivity to reinforcement as a result of an elevated reward threshold. This elevated reward threshold would explain why children with ADHD need either immediate or larger, or more frequent rewards in order to profit from reinforcement in a similar way to controls.

Consequently, the goal of the current study was three-fold. Firstly, the present study investigated whether children with ADHD demonstrate reinforcement-learning problems as reflected by slower acquisition rates during a stimulus-response learning task. Secondly, this study independently assessed the impact of frequency and magnitude of reinforcement on stimulus-response learning, testing the model of Sagvolden et al. (2005) and of Hainlein and Caul (1987). Third, the specificity of reinforcement-learning problems in children with ADHD was examined by comparing the performance of the ADHD group to the performance of a clinical control (CC) group: A group of children with a primary clinical diagnosis of autism spectrum disorder (ASD). Unlike children with ADHD, children with ASD are characterized by problems in communication as well as stereotypical patterns of behaviours and interests (American Psychiatric Association; APA, 2000). An ASD group is included since the occurrence of ADHD and ASD overlap (APA, 2000) and both groups show problems with cognitive control that are as severe or even more severe in ASD than ADHD (Geurts et al., 2004; Happé et al., 2006). In addition, children with ASD may suffer from motivational abnormalities, since they showed less efficient learning of contingencies compared to healthy controls in a decision making paradigm (Johnson et al., 2006) and performed more similar to healthy controls when performance in a sustained attention task was coupled to tangible reinforcers (Garretson et al., 1990).

Reinforcement-learning was investigated by examining the accuracy and speed of response acquisition. Children with ADHD were expected to show impaired response

acquisition reflected by flatter learning curves. If children with ADHD are dependent on frequent reinforcement to perform accurately, one would expect an effect of frequency. Conversely, if children with ADHD require more intense reinforcement than controls, they are expected to perform optimally under intense reinforcement, showing an effect of reinforcement magnitude. To check whether children were aware of the reinforcement manipulations, children completed a visual analogue scale following each condition, registering children's subjective experience of their gain. If children in the CC group show motivational problems like children with ADHD, no group differences in the impact of reward on reinforcement-learning is expected.

Method

Participants and Selection Procedure

Seventy four boys between the ages of 8 to 12 participated in this study: 23 boys with ADHD, 21 with ASD and 30 normal controls (NC) (see Table 5.1 for background information). Children in the ADHD and ASD groups were recruited from special-educational services, through a university affiliated clinic and through the university webpage on which parents of children were asked for voluntary participation in a scientific study. Children in the NC group were recruited through local elementary schools.

Children were included when the following criteria were met: (a) no psychiatric diagnosis (NC group), or a clinical diagnosis of either ADHD (without ASD) or ASD (with possible comorbid ADHD) by a health care professional (clinical groups), (b) IQ score > 70, (c) absence of any psychiatric disorder, other than ASD, ADHD, oppositional defiant disorder (ODD) or conduct disorder (CD) (clinical groups), (d) absence of any neurological disorder, learning disability, sensory or motor impairment, (e) not taking any medication other than methylphenidate.

The assessment procedure of the ADHD group consisted of two stages. Firstly, to confirm the ADHD diagnosis and assess comorbid ODD or CD, parents were administered the Dutch version of the disruptive behaviour disorder section of the Diagnostic Interview Scale for Children (DISC-IV, Schaffer et al., 2000). The DISC-IV indicated that 13 children met ADHD combined type criteria, 8 children met criteria for ADHD inattentive type and one child met criteria for ADHD hyperactive/impulsive type. The DISC of one child was incomplete; therefore, the clinical ADHD diagnosis of that child was confirmed by the DBD only (see below). Seven children fulfilled additional

Table 5.1 || Age, IQ, Rating Scale Scores and Pairwise Group Comparisons.

Measure	Group							
	ADHD (*n* = 23)		CC (*n* = 21)		NC (*n* = 30)			
	M	*SD*	*M*	*SD*	*M*	*SD*	$F_{2,71}$	Group contrasts
Age in months	9.9	1.5	10.0	1.6	9.4	1.0	1.1	
IQ score	98.1	12.7	102.1	15.6	103.4	14.3	0.9	
DBD parents								
Inattention	16.8	6.7	15.2	5.8	2.3	2.7	62.9**	ADHD; CC>NC
Hyperactivity/Impulsivity	16.5	5.2	13.0	7.3	2.9	2.9	43.3**	ADHD>CC>NC
ODD	8.7	5.0	7.2	5.2	1.8	2.5	8.9**	ADHD; CC>NC
CD	2.2	2.5	1.6	2.4	0.3	0.7	6.1*	ADHD; CC>NC
DBD teacher								
Inattention	11.7	6.9	10.9	6.0	2.1	3.6	23.9**	ADHD; CC>NC
Hyperactivity/Impulsivity	11.0	7.3	8.8	7.6	1.6	2.5	18.1**	ADHD; CC>NC
ODD	5.9	5.7	5.0	5.2	0.6	1.7	11.7**	ADHD; CC>NC
CD	1.7	2.2	1.5	2.9	0.3	1.7	2.6**	
CSBQ Total Score	33.1	11.4	47.8	16.3	9.9	10.1	49.0**	CC>ADHD>NC

* $p < .01$, ** $p < .001$.

ADHD = Attention-Deficit/ Hyperactivity Disorder; CSBQ = Children's Social Behavior Questionnaire; CC = Clinical Controls; CD = Conduct Disorder; DBD = Disruptive Behavior Disorder rating scale; NC = Normal Controls, ODD = Oppositional Defiant Disorder.

criteria for comorbid ODD, one other child was comorbid for CD. Secondly, to ensure symptom pervasiveness, both the parent and teacher version of the Disruptive Behavior Disorder rating scale (DBD; Pelham et al., 1992) were administered. Children were required to score within the clinical problem range (95th to 100th percentile) on one of the ADHD scales of both parent and teacher rating scales. DBD teacher ratings of 4 children were missing (1 ADHD, 1 NC, 2 ASD). Table 5.1 shows that the scores of the ADHD group were significantly higher compared to the NC group on *all* scales of the parent and teacher DBD, except for teacher-rated CD. To confirm the diagnosis of the children in the ASD group (2 boys with Autism, 5 with Asperger Syndrome, and 14 boys with a Pervasive Developmental Disorder-Not Otherwise Specified, PDD-NOS) the Children's Social Behavior Questionnaire (CSBQ; Luteijn et al., 2002) was administered to parents. Children with ASD were required to score above the clinical cut-off (95th percentile) of the total CBSQ score (> 23). Table 5.1 shows that children with ASD scored significantly higher than children with ADHD and normal controls on the CBSQ. CBSQ scores of 8 children were missing (2 ADHD, 6 NC). Children in the NC group were required to score in the normal range (< 90th percentile) on all scales of the parent and teacher DBD.

Reinforcement-learning Task

In this task, children were required to match 4 pictures (simple clipart figures) with 2 response buttons (left/right) using visual performance feedback. The order of presentation of the pictures was random with the restriction that each of the 4 pictures was presented 4 times every 16 trials. Pictures (5 by 5 cm) were presented in the middle on the screen for 1000 ms (see Figure 5.1a) and disappeared, when children pressed the left or right button on a response box. Immediately following the response, feedback pictures (indicating correct or incorrect) appeared on the screen for 1500 ms. When the stimulus-response match was correct, children saw the word 'correct!' in the middle of the screen below a cartoon-figure that pointed a thumb upwards. Incorrect stimulus-response matches resulted in: 'unfortunately, incorrect' that was placed below a picture showing a thumb downwards. When children exceeded the response deadline of 2000 ms, they received negative feedback and the next trial began. The inter-trial interval was 1000 ms.

The task was administered under four reward conditions, in which both the frequency and magnitude of the rewards were manipulated in a 2 x 2 within-subject design. Depending on the condition, on average 12.5% (infrequent) or 50% (frequent) correct trials were rewarded with either 2 (small) or 8 cents (large), resulting in the conditions: Infrequent-Small, Frequent-Small, Infrequent-Large, or Frequent-Large (see

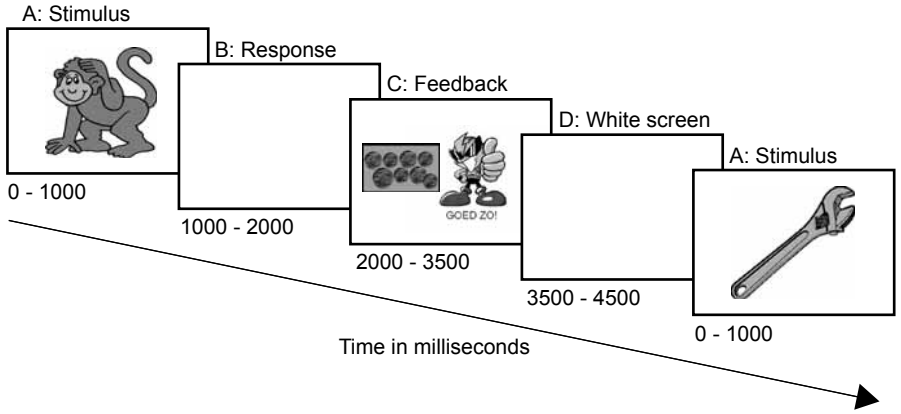


Figure 5.1a represents a correct trial (max 4500 ms) that is coupled with a large reward. (a) The stimulus was presented on the screen (1000 ms) and (b) is followed by a button-press (left or right). The response deadline was 2000 ms. (c) Feedback was presented (1500 ms) that was coupled to a reward (small/large) when applicable. (d) After 1000 ms, the next trial started.

Figure 5.1a || Time course of a stimulus-response learning trial and an overview of the reward conditions.

Frequentie / Magnitude	Infrequent (1 out of 8)	Frequent (1 out of 2)
Small (2 cents)	Infrequent-Small	Frequent-Small
Total reward	16 cents	70 cents
Large (8 cents)	Infrequent-Large	Frequent-Large
Total reward	70 cents	280 cents

This figure shows the (marginally significant) interaction between frequency and the ADHD and NC contrast.

Figure 5.1b || shows the percentage correct averaged over trials in the frequent and infrequent reward condition.

Figure 5.1b). The rewards consisted of a picture of either 2 or 8 eurocents that was presented simultaneously with the (positive) feedback information on the screen (see Figure 5.1a). Each of the four reward conditions contained five sets of four different pictures, resulting in a total of 20 picture sets. Pictures within a set came from different simple categories (e.g., vehicles/animals). In order to minimize the differences between two consecutive reward conditions, only one reward dimension changed in a successive condition, resulting in eight possible condition orders (e.g., the Infrequent-Small condition and Frequent-Large condition never followed each other). Children of all groups were allocated to one of the eight condition-orders of the task, depending on their subject number.

The amount of correctly identified pictures was controlled for, to ensure that every child was reinforced similarly. Children proceeded to the next picture set only after each of the four pictures within the set was correctly identified three times. Each set contained a minimum of 16 trials and, if children did not reach the target of three correctly identified pictures, the task continued until this was the case. In this way, within each reward condition, the total gain was kept (approximately) similar for each child (see Figure 5.1b). To investigate reinforcement-learning, the percentage correct and speed of responding were investigated during trial 1 to 16. The dependent variables were averaged over the five picture sets in each reward condition. To study the acquisition curves of stimulus-response learning over time, the 16 trials were divided into 4 bins of 4 trials each. In this way, each cell in the ANOVA contained 20 trials (4 trials x 5 picture sets).

In order to determine whether the task manipulation was successful, a visual-analogue scale (VAS) was administered after each reward condition (but before they were informed about their actual gain) on which children were asked how much they thought they had won. Children answered this question by drawing a vertical line through a 10 cm horizontal scale, which was anchored by a happy face to the right (very much), and a sad face to the left (nothing).

Procedure

This study was part of a multi-centre project on motivational modulation of cognitive control in children with developmental disorders. All parents completed a written informed consent prior to the study that was approved by the medical ethics committee. First, children were told that they played a memory game in which they had to match 4 pictures with two response buttons (left or right). A practice session of 12 trials familiarized children with the procedure, followed by a second practice session with new pictures. This session continued until all pictures were correctly identified 3 times. After this, children were told that correct responses were coupled with either a small or large reward (the reward pictures were shown on the screen) that could be delivered in a frequent or infrequent manner. Depending on the first reward condition, children were informed about the magnitude of reward of the present condition and the task started. Every new picture set was announced on the screen: 'new pictures!' At the end of each reward condition, there was a short break and children were told how much they had won; this amount was pre-set (see Figure 5.1b). The money was put into a savings box that was placed in front of them. Task duration including instructions and four short breaks (between conditions) was 30 minutes. At the end of the task, all children could exchange their money for a self-chosen present. To allow

complete washout, all children who were on medication discontinued use at least 24 hours before testing. The IQ score of each child was estimated by two subtests (Block Design and Vocabulary) of the Wechsler Intelligence Scale for Children (WISC-III). This composite score has satisfactory reliability (r = .91) and validity (r = .86; Sattler, 2001). Table 5.1 indicates that no group differences were revealed on estimated IQ.

Statistical Analyses

Percentage correct, speed of responding and the standard deviation of responding were compared using a 2 x 2 x 4 x 3 repeated measures ANOVA with frequency (low, high), magnitude (low, high) and trial bin (1-4) as within subject-factors and group (ADHD, CC, NC) as between-subject factor. Planned group contrasts were tested. Children with ADHD were compared to the NC group to investigate problems in reinforcement-learning and compared to the CC group to investigate the specificity of such problems. VAS scores were compared using an ANOVA.

Results

Subjective Experience of Total Gain

When children were asked how much they thought they had won, there was a significant difference between the conditions, $F_{3,68} = 18.9$, $p < .001$, demonstrating that children were aware of the reward manipulations. Children thought they had won the least in the Infrequent-Small condition, which differed significantly from the Frequent-Small ($p < .001$) and Infrequent-Large condition ($p < .001$). The Frequent-Small and Infrequent-Large condition did not differ from each other ($p = .38$), but both differed from the Frequent-Large condition ($p = .004$ and $p = .001$ respectively) in which the total perceived gain was largest. There were no significant group differences ($p = .36$) or interactions between group and condition ($p = .62$).

Table 5.2 || Statistical Results of the Analyses Investigating the Impact of Trial Bin, Reward Frequency and Magnitude on Performance in the Learning Task.

Factor / Measure	Group *df* 2,71	Trial Bin (bin 1 to 4) *df* 3,69	Frequency (low, high) *df* 1,71	Magnitude (low, high) *df* 1,71	Frequency x Trial Bin *df* 3,69	Magnitude x Trial Bin *df* 3,69
% Correct						
Main Effect	-	F= 122.1, p <.01, η_p^2 = .84	F = 3.7, p = .04, η_p^2 = .05	p = .74	p = .39	p = .49
Group Contrast						
ADHD, NC	F = 5.1, p = .03, η_p^2 = .09	p = .24	F = 2.0, p = .09, η_p^2 = .05	p = .64	p = .17	p = .72
ADHD, CC	p = .52	p = .47 (see Figure 5.2)	p = .35 (see Figure 5.3)	p = .71	p = .39	p = .51
Response Speed						
Main Effect	-	F = 8.1, p < .001, η_p^2 =.26	p = .29	p = .95	p = .46	p = .15
Group Contrast						
ADHD, NC	F = 2.7, p = .10, η_p^2 = .05	F = 3.0, p = .04, η_p^2 =.16	F = 4.3, p = .04, η_p^2 = .08	p = .12	F = 9.5, p = .07, η_p^2 = .05	p = .94
ADHD, CC	F = 3.0, p = .09, η_p^2 = .07	p = .23 (see Figure 5.4)	p = .31 (see Figure 5.4 and 5.5)	p = .27	p = .40 (see Figure 5.4)	p = .71

ADHD = attention-deficit/ hyperactivity disorder; CC = Clinical Control Group; DF = Degrees of Freedom of the main effect of the ANOVA; NC = normal controls.

Percentage Correct

Table 5.2 presents the statistical results of the group analyses regarding the impact of the reward frequency, reward magnitude and trial bin. A significant group contrast was found: Children with ADHD had a lower percentage correct than the NC group. Figure 5.2a illustrates that the association between the stimulus and response became stronger over time, as indicated by a significant effect of trial bin on percentage correct. The acquisition slope did not differ between groups; there was no significant interaction between trial bin and group.

The frequency effect was significant and this effect was qualified by a marginally significant group by frequency interaction on percentage correct trials, when the ADHD group was compared to the NC group. Figure 5.2b illustrates this interaction: The percentage correct of the ADHD group was similar in both frequency conditions (p = .87), while percentage correct of the NC group was larger in the infrequent compared to the frequent conditions (p = .005). No significant effect of reward magnitude was revealed. The reinforcement manipulations did not affect the acquisition slopes, since there was no significant interaction between trial bin and the reward conditions. No significant interactions between frequency and magnitude occurred (all p-values > .49), indicating that the total amount of reward did not influence the percentage correct trials or acquisition curves.

Figure 5.2b illustrates that the percentage correct of the CC group laid in-between the ADHD and NC group. The CC group did not differ from the ADHD group (see Table 5.2) and did not differ significantly from the NC group, $F_{1,49}$ = 2.9, p = .10, ηp^2 = .06. There were no interactions between group and the reinforcement conditions, when the ADHD group was compared to the CC group on either percentage correct or the change in percentage correct over trials. The interaction between group and frequency as observed in the ADHD and NC contrast (see Table 5.2), was not significant for the CC group compared to the NC group, $F_{1,49}$ = .55, p = .46, ηp^2 = .01. This suggests that the impact of reward frequency on children in the CC group lay in-between that of the ADHD and NC group. No significant interactions between group, trial bin and the reinforcement conditions were revealed, when the ADHD group was compared to the CC group.

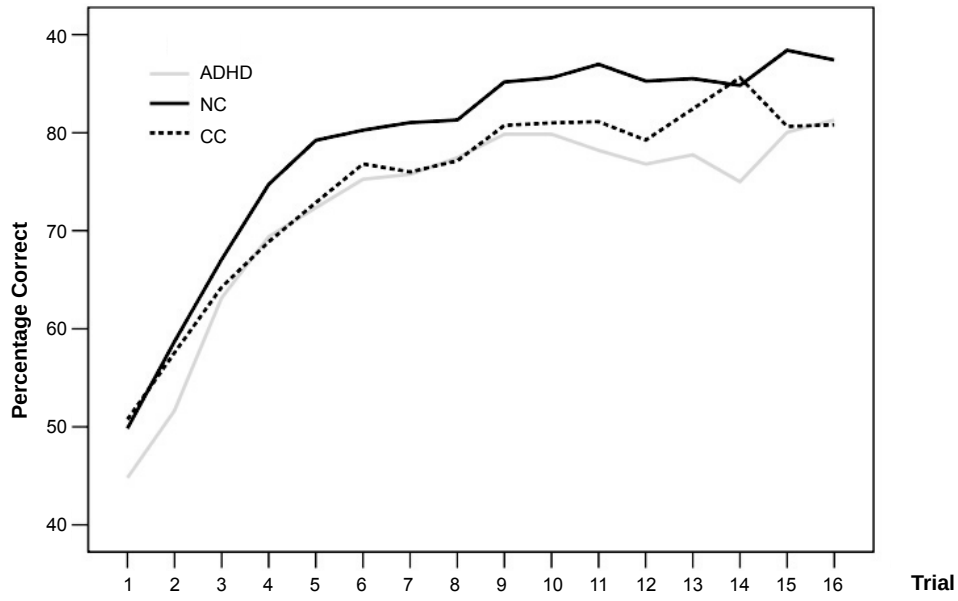
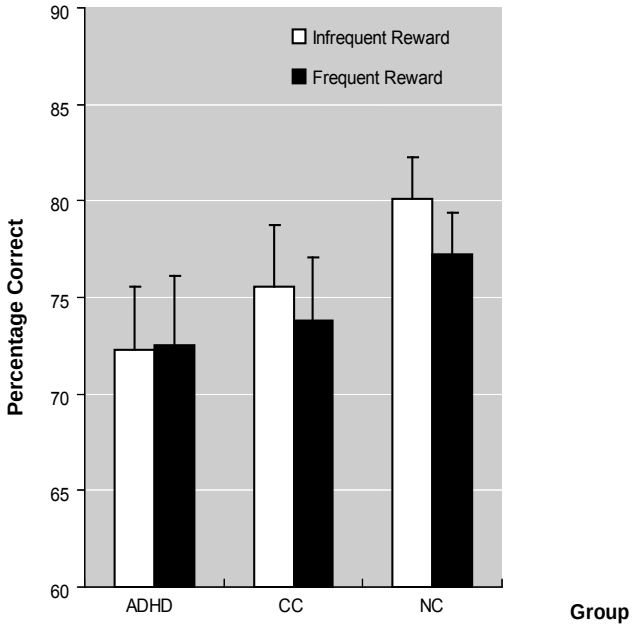


Figure shows the acquisition curves, collapsed over the reward conditions. For the trial bin analyses, the 16 trials were divided in four bins of consecutive trials, averaged over the picture sets.

Figure 5.2a || Percentage correct for children with attention-deficit/hyperactivity disorder (ADHD), normal controls (NC) and clinical controls (CC) during the stimulus-response learning task.



This figure shows the (marginally significant) interaction between frequency and the ADHD and NC contrast.

Figure 5.2b || Percentage correct averaged over trials in the frequent and infrequent reward condition.

Speed of Responding

Children with ADHD showed a trend towards slower responding than the NC group (see Figure 5.3a). During stimulus-response acquisition, the speed of responding changed significantly over trials. This effect of trial bin was qualified by a significant interaction between group and trial bin, when the ADHD and NC group were compared. Figure 5.3a illustrates this interaction: The ADHD group became slower during the first to the second trial bin ($p = .01$) and then maintained their speed ($p = .17$). NC children, in contrast, remained equally fast during the first and second trial bins ($p = .22$) and speeded up from the second to the final trial bin ($p < .001$).

The main effect for reward frequency was not significant. Group interacted significantly with reward frequency when children with ADHD were compared to the NC group. Figure 5.3a and 5.3b illustrates this interaction: Children with ADHD were equally fast in the frequent and infrequent reward condition ($p = .41$). In contrast, the NC children responded faster, when rewards were presented infrequently versus frequently ($p = .01$). No significant effects of reward magnitude were revealed on response speed. There was a (marginally significant) 3-way interaction between group, trial bin, and reward frequency (see Figure 5.3a), when children with ADHD were compared to the NC group. Post-hoc analyses showed that this interaction was due to the final three trial bins: Children with ADHD remained equally fast during trial bin two to four irrespective of the frequency of reward, while NC children speeded up in the frequent reward condition ($p = .001$), but less in the infrequent reward condition ($p = .02$). This indicates that the deteriorating impact of frequent reward on the speed of responding in the NC group was observed only during the early trials. There were no other significant interactions between trial bin and the reinforcement conditions. No interactions between group, frequency, and magnitude were revealed (all p-values $> .12$), indicating that the total amount of reward did not differentially influence the speed of responding of the three groups.

Children with ADHD showed a trend towards slower responding than the CC group (see Figure 5.3b). There were no significant group and reinforcement condition interactions, when the ADHD group was compared to the CC group. The significant interaction between group and frequency as observed in the ADHD and NC contrast, was not significant for the CC group compared to the NC group, $F_{1,49} = .69$, $p = .41$, $\eta p^2 = .01$. This suggests that infrequent compared to frequent reward positively affected the response speed in the NC group and to some extent in the CC group (see Figure 5.3b). In addition, the interactions between group, trial bin and the reinforcement conditions were not significant when children with ADHD were compared to the CC children.

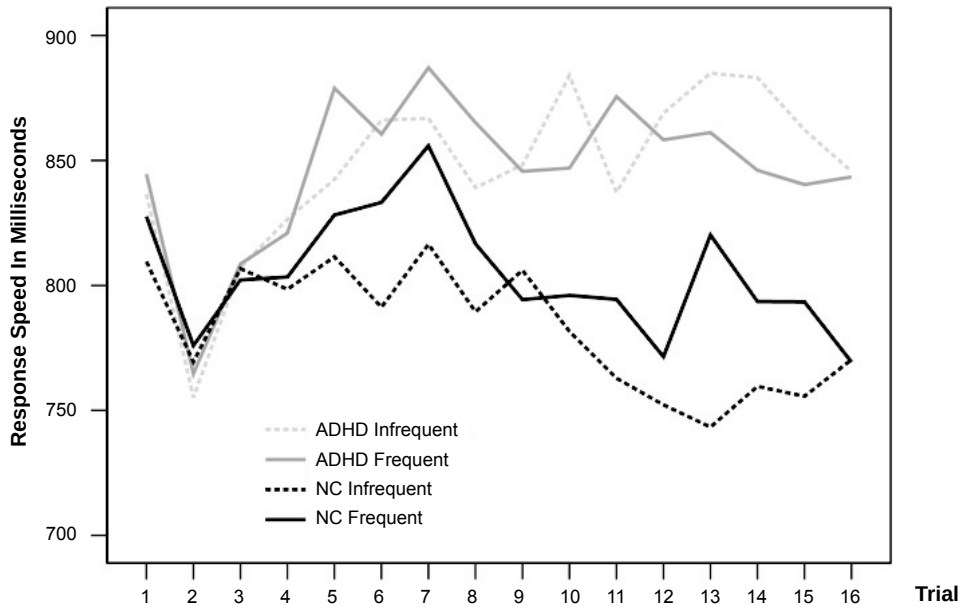
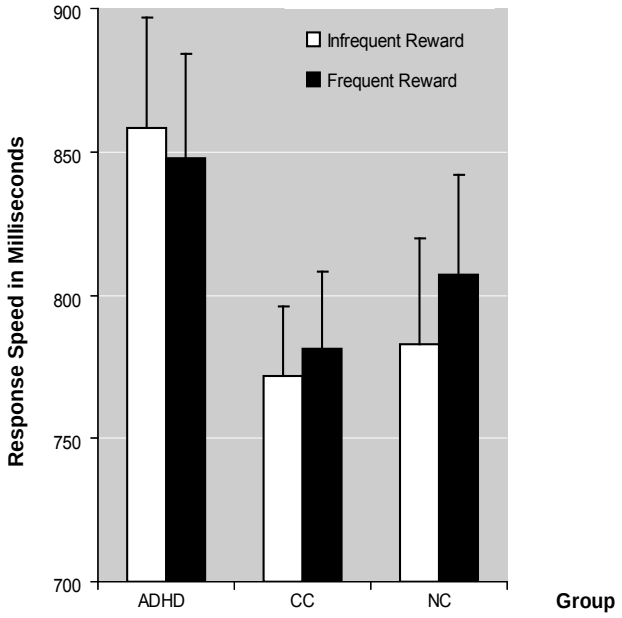


Figure 5.3a shows the acquisition curves plotted separately for the frequent and infrequent reward condition. For simplicity, the CC group is omitted from this graph. For the trial bin analyses, the 16 trials were divided in 4 bins of consecutive trials averaged over the picture sets. This figure illustrates the significant interaction between trial bin and group as well as the marginal significant interaction between trial bin, frequency, and group.

Figure 5.3a || Response speed for children with attention-deficit/hyperactivity disorder (ADHD) and normal controls (NC) and clinical controls (CC) during the stimulus-response learning task.



This figure illustrates the interaction between frequency and group when the ADHD and NC group were compared.

Figure 5.3b || Response speed averaged over trials in the frequent and infrequent reward condition.

Discussion

The current study investigated the impact of reward on reinforcement-learning in children with ADHD using a stimulus-response learning task. The effect of reward frequency and reward magnitude were independently examined. Such an independent investigation, to our knowledge, has not been conducted before in children with ADHD. The study was aimed to answer three questions: Firstly, is there evidence for problems with reinforcement-learning in children with ADHD? Secondly, is there a differential impact of frequency and/or magnitude of reinforcement on reinforcement-learning in children with ADHD compared to NC children? Thirdly, are reinforcement-learning problems specific to children with ADHD or are they also present in a clinical comparison group, in this case, children with ASD who showed comorbid ADHD symptoms.

Reinforcement-learning in ADHD

To our knowledge, this is the first study to investigate the rate of learning of arbitrary stimulus-response associations in children with ADHD, despite the theoretical suggestions of problems with feedback monitoring in many theoretical models (Douglas, 1989; Barkley, 1997; Sergeant et al., 1999). In the current study, children with ADHD performed less accurately than controls (lower percentage correct and slower responses). Impairments in reinforcement-learning suggest problems in storing the stimulus-response associations and updating the information regarding correct and incorrect responses. Among other functions, these abilities require working memory capacity, which is found impaired in the majority of studies in children with ADHD (Martinussen et al., 2005). Otherwise, impaired reinforcement-learning in the ADHD group may relate to their difficulties with more basic functions such as problems with motor output organisation (Rubia et al., 1999; Leth-Steensen, et al., 2001). Problems with motor output come to the fore in the current study as seen in the difference in response speed over trials between children with ADHD and normal controls: NC children speeded up as the association between the stimulus and response became stronger, children with ADHD maintained their (slower) response speed.

Although performance of children with ADHD remained inferior to that of NC children, children with ADHD were able to utilize feedback like the NC group as indicated by the shape of the learning curves which was comparable for both groups. This indicates that when children with ADHD receive consistent and immediate feedback, problems with feedback learning are minimized. This is in line with an earlier study (Sergeant & Van der Meere, 1988) showing that children with ADHD successfully

corrected their mistakes when explicitly instructed to do so. The fact that children with ADHD fail to achieve the same level of performance as control children, despite comparable learning rates, may suggest that the strength of the association between a stimulus and the associated response may be more susceptible to degradation in children with ADHD. Another explanation is that children with ADHD may fail to optimize the implementation of motor responses.

Impact of Reward Frequency and Magnitude on Reinforcement-learning

The second part of the study was aimed to separate the impact of reward magnitude from the impact of reward frequency on reinforcement-learning, based on the hypothesis that children with ADHD may need more intense (Haenlein & Caul, 1987) or more frequent reward to optimize their performance (Johansen et al., 2002; Sagvolden et al., 2005). Self-reports of the subjective experience of the amount of monetary gains indicated that the children were fully aware of the differences in contingencies between experimental conditions: Children thought they had gained the most during the Large-Frequent reward condition and the least in the Small-Infrequent condition. Contrary to prediction, neither frequent rewards nor intense rewards influenced reinforcement-learning of children with ADHD. A possible explanation for the absence of an impact of reward on the performance of children with ADHD may be that children with ADHD may have needed continuous reward (100%) instead of 50% reward in order to perform well. Sagvolden et al. (2005) hypothesized that the decay of reward is faster in ADHD children than in controls and, therefore, a 50% reward rate used here may have been too small to ensure optimal stimulus-response coupling. Otherwise, an infrequent reward of 2 cents may have already optimally motivated children with ADHD, which can explain why larger or more frequent rewards did not influence performance.

Remarkably, infrequent as opposed to frequent rewards significantly improved performance (percentage correct and response speed) in control children. In contrast, children with ADHD were insensitive to the frequency of reward. A negative impact of frequent rewards on response speed has been observed earlier (Douglas & Parry, 1994). We speculate that control children were already satiated by infrequent rewards, resulting in impaired performance in the frequent reward conditions, in line with the Yerkes-Dodson Law (1908). This law suggests that performance increases with cognitive arousal, but only to a certain point: When levels of arousal become too high, performance will deteriorate. The absence of such an effect in the ADHD group may be related to a limitation in physiological arousability as observed in psychophysiological studies (Barry et al., 2003). Studies into the impact of reinforcement frequency and

magnitude on psychophysiological responses in children with ADHD are needed to reject or confirm our hypothesis.

Specificity of Reinforcement-learning in ADHD

No difference in accuracy between the ADHD and CC group indicates that cognitive performance deficits may be common to various psychiatric groups. The response to the frequency of reward, however, differed between the ADHD and CC group. Children with ADHD were unaffected by reward frequency in terms of accuracy and response speed in contrast to the NC group, who responded in-between children with ADHD and NC children. This suggests that a possible limitation in arousability, as described above, may be more specific to children with ADHD than children with ASD who show comorbid ADHD symptoms.

There are some limitations that are worthy of note. First, the inclusion of performance feedback that was not coupled to reward would have enabled us to investigate whether 2 cents already optimally motivated children. Second, the diagnostic assessment of the ASD group is limited, although the CBSQ confirms the clinical diagnosis in this group. Fourth, the children with ASD showed many characteristics with ADHD that may explain the similarities in performance between the groups. Third, the small number of children of the different ADHD and ASD subtypes excludes the possibility to explore whether these subtypes differed in their response to the applied task. Larger sample sizes may have enabled us to explore performance in the subtypes of children with ADHD and children with ASD. As both clinical groups are known for its heterogeneity it could well be that there are large individual differences in the impact of reinforcement on performance.

Conclusion

The current study contrasted the impact of reward frequency against the impact of reward magnitude on reinforcement-learning in children with ADHD compared to a NC and CC group using a stimulus-response learning task. The task demonstrated difficulties with stimulus-response learning in children with ADHD: Children with ADHD differed from NC children in response accuracy and speed (although the latter effect was only of marginal significance). Children with ADHD were able to enhance their performance over time as NC children, although they remain less accurate. In contrast to previous studies, a high reward frequency (Johansen et al., 2002; Sagvolden et al., 2005) or high reward magnitude (Haenlein & Caul, 1987) did not improve reinforcement-learning of children with ADHD, although self-reports

showed that children with ADHD had an intact perception of the reward manipulations. Controls significantly improved in performance with infrequent as opposed to frequent reward. This indicates a relative insensitivity to the possible arousing impact of reward frequency in children with ADHD, suggesting limitation in physiological arousability (Zentall & Zentall, 1983; Sergeant et al., 1999). Stimulus-response learning problems were not specific to children with ADHD, although children with ADHD were dissociated from the clinical control group by their insensitivity to the frequency of reinforcement. Possibly, the weak performance of the ADHD group may relate to an impaired maintenance of the stimulus-response associations in working memory or problems with the organization of motor output.

Chapter 6

Heart Rate and Reinforcement Sensitivity in ADHD

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Abstract

Both theoretical and clinical accounts of ADHD implicate a dysfunctional reinforcement system. This study investigated heart rate parameters in response to feedback associated with reward and response cost in ADHD children and controls aged 8 to 12. Heart rate responses (HRRs) following feedback and heart rate variability (HRV) in the low frequency band (0.04 - 0.08 Hz), a measure of mental effort, were calculated during a time production paradigm. Performance was coupled to monetary gain, loss or only feedback in a cross-over design. Children with ADHD showed smaller HRRs to feedback compared to controls. HRV of children with ADHD decreased, when performance was coupled to reward or response cost compared to feedback-only. HRV of controls was similar across conditions. Children with ADHD were characterized by (a) possible abnormalities in feedback monitoring and (b) motivational deficits, when no external reinforcement is present.

Introduction

Attention Deficit Hyperactivity Disorder (ADHD) is characterized by inattention, impulsive behaviour and motor restlessness. One of the candidate endophenotypes of ADHD is a dysfunctional reinforcement system (Castellanos & Tannock, 2002; Doyle et al., 2005; Sagvolden, Johansen, Aase, & Russel, 2005; Sonuga-Barke, 2002) that is responsible for cognitive and motor limitations in ADHD. A review of 21 studies on the impact of reinforcement in ADHD revealed that the improvement in task performance by using appropriate reinforcement was somewhat larger in ADHD children than controls (Luman, Oosterlaan, & Sergeant, 2005). ADHD is considered a motivational problem whereby ADHD individuals are unable to show optimal performance by using intrinsic motivation (Douglas, 1989; Sergeant, Oosterlaan, & Van der Meere, 1999). Others stress dysfunctions in processing stimuli that are related to reward and extinction, caused by fronto-limbic abnormalities (Sagvolden et al., 2005; Sonuga-Barke, 2002). The goal of this study was to seek psychobiological evidence for an abnormal reinforcement sensitivity and motivational deficits in ADHD by measuring (a) the short-term change in heart rate following reinforcement feedback (heart rate response, HRR) and (b) heart rate variability (HRV) under different reinforcement conditions. These measures are both sensitive to reinforcement processing (Crone, Bunge, De Klerk, & Van der Molen, 2005; Suess, Newlin, & Porges, 1997).

Experimental studies of ADHD children have identified abnormalities in self-rated and observed motivation (Carlson, Booth, Shin, & Canu, 2002), in both cognitive (Slusarek, Velling, Bunk, & Eggers, 2001) and academic performance (Volkow et al., 2004). Otherwise, children with ADHD demonstrate dysfunctions in several aspects of (reinforcement) feedback processing such as: error detection (internal detection of whether a response was correct) (Liotti, Pliszka, Perez, Kothmann, & Woldorff, 2005), error appraisal (Wiersema, Van der Meere, & Roeyers, 2005), reinforcement processing (Van Meel, Oosterlaan, Heslenfeld, & Sergeant, 2005b) and error related compensatory responses such as post-error slowing (Schachar et al., 2004; Sergeant & Van der Meere, 1988). By adding reinforcement to feedback, performance of ADHD children may improve by shaping behaviour (Keitz, Martin-Soelch & Leenders, 2003; Schulz, 2000). Alternatively, performance may improve by an increase in motivation (Cameron & Pierce, 1994).

When humans receive feedback, heart rate is found to decelerate (Somsen, Van der Molen, Jennings, & Van Beek, 2000; Van der Veen, Van der Molen, Crone, & Jennings, 2004). This deceleration is larger following negative than positive feedback (Somsen et al., 2000). The degree of cardiac deceleration is dependent, firstly, on the

information value regarding performance and secondly, on the mismatch between the feedback expectation and the actual feedback (Somsen et al., 2000). When the mismatch between expected and actual feedback is large, heart rate decelerates. Crone et al., (2005) demonstrated that heart rate deceleration was larger, when the financial gain that was related to feedback increased.

Variability in heart rate (HRV) is considered an indicator of motivation, since tasks that demand cognitive effort or active attention evoke lower HRV (see for a review Jorna, 1992). Three cardiac rhythmicities have been identified (Hyde & Izard, 1997). The fastest rhythmicity (0.15 - 0.60 Hz) is the respiratory sinus arrhythmia (RSA), which reflects synchronization of the heart with the respiratory system. Higher RSA in children has been associated with attention to novel stimuli (Porges, 1991). The intermediate frequency (0.08 - 0.15 Hz), the Traube-Herring-Meyer (THM) wave reflects synchronization of the heart with blood pressure and the slowest rhythm (0.04 - 0.08 Hz), the angiotensin-renin vasomotor (ARV) rhythmicity, reflects synchronization of the heart with the peripheral vascular system. Diminished variability in the THM and more specifically variability in the ARV rhythm is associated with sustained mental effort in adults (Mulder & Mulder, 1981) and in children (Hyde & Izard 1997). Interestingly, experimental studies indicate that both motivation and reward reduce HRV (Pruyn, Aasman, & Weyers, 1985; Suess, Newlin, & Porges, 1997), while time-on-task (diminished allocation of effort) increases HRV.

Decreased HRRs to reinforcement feedback in ADHD have been reported (Crone, Jennings, & Van der Molen, 2003; Iaboni, Douglas, & Ditto, 1997). Both Iaboni et al. (1997) and Crone et al. (2003) demonstrated that the differential effects of positive and negative reinforcement were less pronounced for HRR in ADHD children than controls. Increased HRV within the middle frequency band (0.07 - 0.15 Hz) has been reported in ADHD children compared to controls, indicating motivational problems in ADHD children (Börger et al. 1999; Börger & Van der Meere, 2000). This finding is consistent with current theoretical frameworks claiming that ADHD children have difficulties maintaining an optimal intrinsic level of motivation (e.g., Sergeant et al., 1999).

We used three conditions to study the impact of reinforcement feedback on performance: (1) feedback-only, (2) reward for correct responses, (3) response cost for incorrect responses. Since there is evidence of diminished feedback processing in ADHD (Van Meel et al., 2005b), we expect the HRR to reinforcement feedback to be less pronounced in children with ADHD than controls. When both the reward and extinction systems are dysfunctional in ADHD (Sagvolden et al., 2005), an increase in HRR is

expected when reinforcement is added to feedback (Crone et al., 2005) which would be smaller in children with ADHD than controls. Children with ADHD are thought to suffer from motivational problems (Douglas, 1989; Sergeant et al., 1999), therefore, HRV is predicted to be larger (lower task engagement) in children with ADHD than in controls. In the reinforcement conditions compared to the feedback-only, the group difference in HRV is expected to be smaller, since reinforcement increases motivation (Cameron & Pierce, 1994) and lowers HRV (Suess, Newlin, & Porges, 1997).

Method

Participants

Eighteen children aged 8 to 12 (three girls; mean age 122 months) with a clinical diagnosis of ADHD were compared to 18 age matched normal control children (two girls, mean age 124 months). All parents completed a written informed consent prior to the experiment and the experiment was approved by the ethics committee of the Vrije Universiteit Amsterdam. Inclusion criteria were the following: (1) Intelligence quotient > 70, estimated by four subtests of the Revised Wechsler Intelligence Scale for Children: Block Design, Picture Arrangement, Arithmetic and Vocabulary (Groth-Marnat, 1997), (2) absence of any neurological disorders, learning disabilities, sensory or motor impairment, and (3) absence of all psychiatric disorders other than ODD or CD for children with ADHD, absence of all psychiatric disorders including ADHD, ODD or CD for normal controls. Background information of the participants is presented in Table 6.1.

The ADHD group was recruited via the Dutch ADHD parent association and had a clinical diagnosis of ADHD. A structured clinical interview (Diagnostic Interview Schedule for Children, based on the DSM-IV; DISC-IV) was administered to the parents of ADHD children to confirm the diagnosis (Shaffer, Fisher, Lucas, Dulcan, & Schwab-Stone, 2000). Sixteen children met DISC-IV criteria for ADHD combined subtype and two other children for the inattentive subtype. Eleven children met the criteria for an additional ODD diagnosis and two children were comorbid for CD. The Disruptive Behaviour Disorder rating scale (DBD, parent and teacher version), served to confirm the pervasiveness of ADHD symptoms (Pelham, Gnagy, Greenslade, & Milich, 1992). Children in the ADHD group were required to score within the clinical range (95^{th} to 100^{th} percentile) on both the parent and teacher DBD for either the Inattention or Hyperactivity/Impulsivity scale.

Table 6.1 || Background and Clinical Characteristics of the ADHD and Control Groups.

Measure	Group				
	ADHD (*n* = 18)		Normal Controls (*n* = 18)		
	M	*SD*	*M*	*SD*	$F_{1, 34}$
No. Of males	15	-	16	-	-
Age in months	122	14.7	124	15.6	ns
Estimated full scale IQ	93.4	14.1	112.3	12.4	14.3*
DBD parents					
Inattention	20.8 [a]	4.1	2.2	2.4	273.4**
Hyperactivity/Impulsivity	17.8 [a]	7.7	2.1	2.1	70.4**
ODD	9.7	5.5	1.4	1.5	36.2**
CD	2.7	2.1	0.1	0.2	82.4**
DBD teacher					
Inattention	16.3 [a]	5.6	1.8	3.9	71.6**
Hyperactivity/Impulsivity	14.9 [a]	5.3	1.7	2.8	82.2**
ODD	7.8	5.1	0.3	1.0	32.6**
CD	2.6	3.6	0.1	0.2	8.9*
FSSC-R (decile scores)	4.3	0.7	6.2	0.6	ns [b]

* $p < .01$, ** $p < .001$, ns = $p > .05$

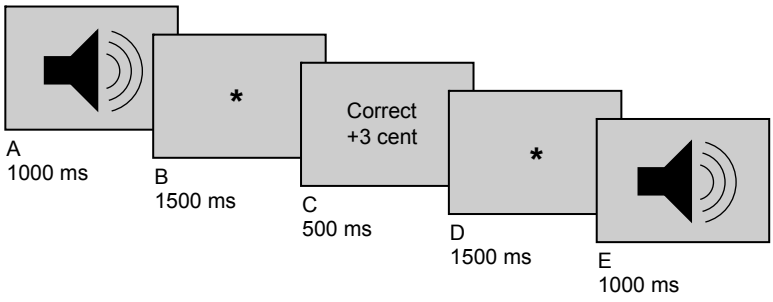
ADHD = Attention Deficit Hyperactivity Disorder, CD = Conduct Disorder, DBD = Disrupted Behavior Disorder Subscale, FSSCR = revised fear survey schedule for children, ODD = Oppositional Defiant Disorder. [a] = Clinical score (> 95th percentile), [b] Data of two children were missing (one ADHD, one control).

Table 6.1 shows that the scores of children in the ADHD group were significantly higher compared to normal controls on the parent and teacher DBD scales of Inattention, Hyperactivity/Impulsivity, ODD and CD. To assess the level of chronic anxiety in children, all children completed the Dutch version of the Fear Survey Schedule for Children-Revised (FSSC-R; Ollendick, 1983). As shown in Table 6.1, no group differences were revealed on scores of total anxiety for the FSSC-R. Fourteen children with ADHD were treated with methylphenidate and discontinued use at least 36 hours prior to testing.

Normal control children were recruited from different local community schools. Control children with scores were excluded above the 80th percentile on *any* subscale of the parent or teacher DBD.

Time Production Task

Figure 6.1 shows the stimulus sequence in the time production task. Each trial commenced with a tone (80 db, 50 ms) after which children pressed a response button with their right index finger, when they thought a 1-second interval had elapsed. A 1500 ms delay screen separated the button press from the feedback information (500 ms). The inter-trial-interval was 1500 ms. Accuracy feedback ('too short', 'too long' or 'correct') was provided using a staircase algorithm, which ensured similar levels of positive and negative feedback for each subject in each condition. The initial criterion for a response to be correct was a response between 500 and 1500 ms. Positive feedback was provided, when response latencies fell within the boundaries of the current time window. After positive feedback, the boundaries narrowed by 50 ms on both sides of the window. After negative feedback ('too short' or 'too long'), the boundaries widened by 50 ms. Children were required to produce a 1-second interval under three reinforcement conditions: (1) feedback-only, (2) response cost: feedback and a 3 cents loss when responses were incorrect and (3) reward: feedback and 3 cents gain when responses were correct. The conditions were presented in a pseudo-random order. Loss or gain ('+3 cent', '-3 cent') were presented on the screen.Stimuli were presented on a 17-inch computer screen, positioned 2.40 metres in front of the participant. To familiarize children with the one-second interval, a cartoon character appeared on the screen ten times for exactly one second. Children practiced the task in a 30-trial prac-



A) Children heard an auditory beep (50 ms) indicating the start of a 1-second interval, while looking at a fixation cross on the screen. Approximately 1000 ms later, children pressed the response button; B) 1500 ms after pressing the button, C) feedback (correct, too short, too long) appeared on the screen for 500 ms. D) The screen goes blank for 1500 ms prior to the next trial.

Figure 6.1 || The stimulus sequence in the time production task (this example represents a reward trial).

tice session. Standardized task instructions were provided by the experimenter and the task commenced. Each condition consisted of 160 trials divided in two blocks. In the feedback-only condition, children were told to perform as accurate as possible. In the reward condition, similar instructions were provided and children were told to gain as much money as possible, which was put into a savings box in front of the children after each block. To make the task realistic, all children gained 80 cents after the first block and another 100 cents following the second block. In the response cost condition children received 350 cent at the start and they were told to loose as little as possible. From this, children lost 100 cents following the first block and 80 cents following the second block. The total gain after three reinforcement conditions was thus 350 cents. Heart rate was measured during the task.

ECG Measurements

ECG was registered with two Ag/AgCl electrodes, attached between the collarbones over the jugular notch of the sternum and at the right lateral side between the lower two ribs. The continuous signals were amplified and sampled at 500 Hz. R-peak occurrences were detected by using peak detection software and stored off-line. To include all validly recorded inter-beat-intervals (IBIs) and exclude noise in the heart rate data, IBIs that were larger than 1500 ms and smaller than 400 ms were excluded. IBIs were extracted around the feedback moment. The interval in which the feedback took place was IBI0. IBI+1, IBI+2 and IBI+3 followed feedback, and the intervals preceding feedback were IBI-1, IBI-2, and IBI-3. Time production trials over 3 s and under 200 ms were excluded as being non-informative for our heart beat data (e.g., due to omissions and premature responses). This was 0.7% of the trials across groups.

Heart Rate Response

In order to investigate HRRs to reinforcement feedback, we explored the change in interval between successive IBIs following feedback. The effect of feedback on heart rate is found to be the most robust between IBI0 to IBI+2 following feedback (approximately 1800 ms; Crone et al., 2005; Somsen et al., 2000). IBIs were compared to a baseline IBI prior to the start of the trial. The baseline was a single value, that was subtracted from the IBIs of interest in each individual trial. There were no main or interaction effects of group, condition or feedback that could influence the results for this IBI. The IBIs were submitted to an ANOVA with condition (feedback-only, response cost, reward), feedback (positive, negative) and sequential IBI (IBI0, IBI+1, IBI+2) as repeated measures and group (ADHD, normal controls) as between subject factor.

Heart Rate Variability

IBI files were converted from the event domain (the IBI values), to the time domain (evenly spaced time points). HRV was measured using Fast Fourier Transform as calculated using a custom software program. The area under the curve for each subject was calculated for the low (0.04 - 0.08 Hz) and middle (0.09 – 0.15 Hz) frequency bands in the power spectrum, since these frequency bands are most sensitive to manipulations of task engagement (see Hyde & Izard, 1997). Concerning both blocks of the two reinforcement conditions, the last 340 seconds of data were analyzed (represented as a time series of 512 data points sampled every 664 ms) to minimize practice effects. The spectral power index was expressed in deviations relative to the mean value of the time series of each block (squared modulation index). The time series were detrended with sequential cubic spines (see Hyde & Izard, 1997) to remove low frequency noise (e.g., movement artefacts).

In order to investigate task engagement in the reinforcement conditions, HRV was compared in an ANOVA with condition (feedback-only, response cost, reward) as repeated measures and group (ADHD, controls) as between subject factor. When sphericity assumptions were violated, Greenhousse Geisser adjusted *F*-values and *p*-values are reported in parentheses for all dependent variables.

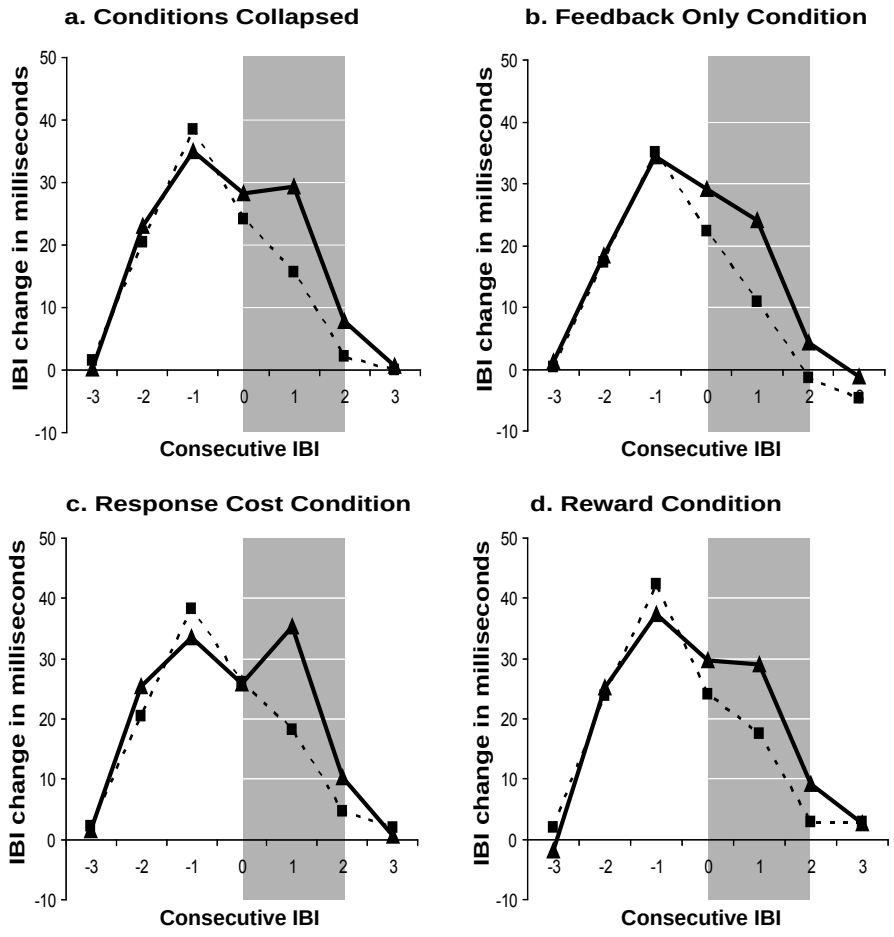
Results

Heart Rate Response to Reinforcement Feedback

Figure 6.2 shows baseline corrected HRRs for children with ADHD and controls in the reinforcement conditions. Note that heart rate decreased between IBI-3 to IBI-1. This is a well known phenomenon and associated with preparatory motor responses (e.g., Jennings, Van der Molen, Brock, & Somsen, 1991) and is followed by heart rate recovery.

The planned analysis for IBI0 to IBI+2 following feedback revealed no significant main effect of group or condition (*p* values > .05). Negative feedback resulted in a lower heart rate compared to positive feedback, $F_{1,34} = 16.3$, $p < .001$, $\eta_p^2 = .32$. This effect did not differ between groups (p > .05). There was a main effect of sequential IBI, $F_{2,33} = 27.8$, $p < .001$, $\eta_p^2 = .63$, and an interaction between sequential IBI and group, $F_{2,33} = 3.3$, $p = .049$, $\eta_p^2 = .17$. Post-hoc analyses showed that controls exhibited a delay in heart rate recovery between IBI0 and IBI+1 (no difference, $p > .05$), while

their heart rate accelerated between IBI+1 (29.4 ms) and IBI+2 (7.9 ms), $F_{1,17} = 53.3$, $p < .001$, $\eta p^2 = .76$. In contrast, children with ADHD showed a linear increase in heart rate from IBI0 (24.1 ms) to IBI+1 (15.6 ms), $F_{1,17} = 6.6$, $p = .030$, $\eta p^2 = .25$, to IBI+2 (2.1 ms), $F_{1,17} = 19.3$, $p < .001$, $\eta p^2 = .53$. Other higher-order interactions involving group were not significant (p values > .05). Consequently, children with ADHD exhibited smaller HRRs than controls, irrespective of the reinforcement condition.

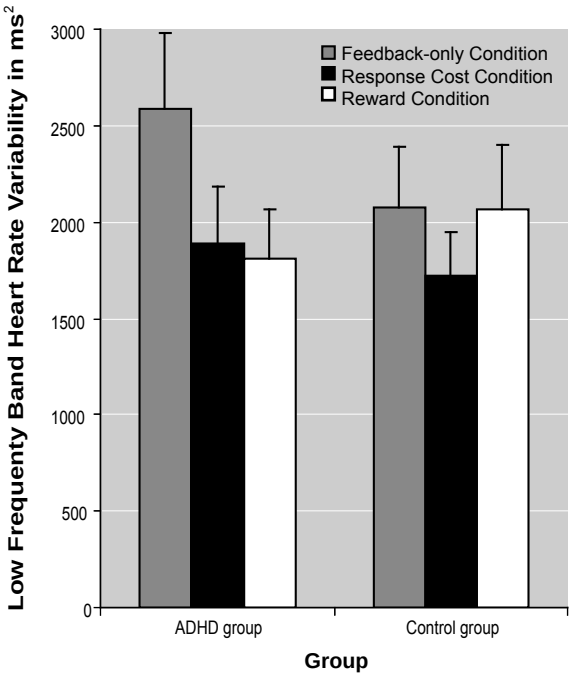


Positive and negative feedback are collapsed. IBI0 indicates the interval in which the feedback was presented. IBI = Inter-Beat-Interval

Figure 6.2 || Heart rate responses following feedback for IBI0 to IBI+2 (gray area) collapsed across reinforcement conditions (6.2a) and in the reinforcement conditions (6.2b, c, d) of the time production task for children with ADHD (dotted lines) and controls (solid lines).

Heart Rate Variability

The effects of group, condition and the interaction between group and condition were not significant for HRV in the middle frequency band (p values > .05). In the low frequency band group interacted with condition (see Figure 6.3), $F_{2,33} = 4.3$, $p = .015$, $\eta p^2 = .22$ (Greenhouse Geisser $F_{2,33} = 3.5$, $p = .045$, $\eta p^2 = .09$). Post-hoc analyses revealed that controls exhibited no difference in HRV between conditions ($p > .05$). In contrast, children with ADHD showed HRV suppression in the response cost, $F_{1,17} = 17.3$, $p = .001$, $\eta p^2 = .51$, and reward conditions, $F_{1,17} = 8.6$, $p = .009$, $\eta p^2 = .34$, compared to the feedback-only condition. There were no main effects of group or condition ($p > .05$) for HRV in the low frequency band. Taken together, the results suggest that children with ADHD show a lack of task engagement, when performance is not tightly coupled with incentives.



Lower values indicate less HRV and increased task engagement.

Figure 6.3 || Task engagement in three reinforcement conditions of the time production task for children with ADHD and controls. Bars show the area under the curve (and standar errors) of power calculations in the low frequency band (.04–.08) of inter-beat-interv data.

Discussion

This is the first study that has employed HRRs and HRV to investigate the neurobiological processing of reinforcement feedback processing in ADHD. In a time production paradigm, participants received positive and negative feedback under three reinforcement conditions: feedback-only, response cost and reward. We tested (a) whether children with ADHD show disturbed reinforcement feedback processing by measuring HRR to reinforcement feedback, and (b) whether children with ADHD show motivational deficits (lack in task engagement) as measured by HRV. Our findings indicate that ADHD children have problems in processing feedback. Second, ADHD participants have poor task engagement, when performance was not reinforced.

Reinforcement Feedback Processing

In both children with ADHD and controls, heart rate decelerated in preparation to making a response, and was followed by heart rate recovery after the response. ADHD children showed smaller HRRs to feedback compared to controls as demonstrated by the interaction between group and sequential IBI. Controls initially showed delayed heart rate recovery following feedback (IBI0 to IBI+1), after which heart rate accelerated (IBI+1 to IBI+2). ADHD children, in contrast, showed immediate heart recovery following the button press in all reinforcement conditions. From the literature, there are several interpretations on impaired HRRs to feedback which are related to problems with: (a) feedback processing with the purpose of adjusting future performance (Crone et al., 2005), (b) motivational evaluation of feedback (Van der Veen et al., 2004), and (c) performance monitoring and feedback expectancy (Somsen et al., 2000). Performance data of our study indicated that timing adjustment on the trials following negative feedback ('too short' or 'too long') did not differ between children with ADHD and controls ($p > .05$), which argues against the first hypothesis (a). Processing of the motivation related features of feedback (hypothesis b) seems intact in children with ADHD, since the discrimination between positive and negative feedback did not differ between groups and there was no condition by group interaction. Therefore, the interpretation that feedback expectancy is impaired in children with ADHD seems most plausible (hypothesis c). HRRs to feedback are suggested to be larger when the difference between the 'expected' and 'actual' feedback is larger (Somsen et al., 2000) and due the dynamic tracking algorithm, feedback expectancy is not dependent on performance monitoring only. In control children, 50% positive feedback may have been worse than expected in terms of performance, which resulted in a sharpened HRR to feedback. In ADHD, due to a learned history of blunted performance, they demonstrate abnormal performance expectancies which resulted

in smaller HRRs to feedback as compared to controls. An unexpected event may trigger an attention response (Jennings et al., 1991) and impaired allocation of attention following feedback in children with ADHD may explain the findings of response timing problems in ADHD in the current study.

Task Engagement

The increased low frequency HRV (ARV band) in the absence of reinforcement contingencies suggests a lack of task engagement in children with ADHD, when reinforcement is not available. This is in line with the suggestion that children with ADHD suffer from a motivation deficit and cannot keep up with task demands due to a non-optimal energetic state (Sergeant et al., 1999). They dependent on external motivators such as reward and response cost in order to in crease there motivation and perform well. Lower ARV rhythmicity is associated with a changes in the bloodflow that regulates the local cerebral metabolic demands, for example, during task performance (Akselrod et al., 1985). Whereas two previous studies showed group differences in HRV between ADHD children and controls during a cognitive task (Börger et al., 1999; Börger & Van der Meere, 2000), the current findings demonstrate that these differences can be modified by reinforcement contingencies. The findings are in line with suggestions that the pathogenesis of ADHD should be conceptualized from a perspective other than a purely cognitive one (Castellanos & Tannock, 2002; Sonuga-Barke, 2002; Sergeant et al., 1999). Sonuga-Barke (2002) proposed two dysfunctional brain pathways that reciprocally interact in explaining the pathogenesis of ADHD. The pathways are responsible for cognitive deficits on the one hand and motivational deficits on the other. The motivation deficits are explained by a shortage in extracellular dopamine in the striatum that reduces the impact of reinforcement onto behaviour (Sagvolden et al., 2005).

An alternative theoretical focus is to classify increased HRV as being part of variability in several domains of functioning. Besides greater variability in heart rate (Börger et al., 1999), children with ADHD are characterized by an enhanced levels of symptom variability (Castellanos & Tannock, 2002) and behavioural variability: more variable response times (Leth-Steensen, Elbaz, & Douglas, 2000), time estimation (e.g., Van Meel et al., 2005a), and increased variability in the P300 following feedback (Lazarro et al., 1997). Castellanos et al. (2005) speculated that children with ADHD show a deficiency in reducing low frequency fluctuations in neuronal activity that causes lapses of attention and which is responsible for attention problems, forgetfulness, and unexpected errors. There is evidence of decreased response variability in ADHD when performance is reinforced (Van Meel et al., 2005a), however, future studies

need to investigate whether the impact of motivation on response variability and psychophysiological variability are associated.

Heart Rate and Performance

Behavioural data of this study (Van Meel, et al., 2005a) showed that children with ADHD improved their performance under conditions of reinforcement. However, despite normal psychophysiological task engagement under reinforcement, children with ADHD were less accurate in time production than controls. This suggests, firstly, that ADHD children may need to compensate for deficits other than solely a reinforcement dysfunction (in this case timing dysfunctions). Compensation mechanisms in ADHD have been reported in the neuro-imaging literature (Bush et al., 1999; Johnstone & Barry, 1996), whereby children with ADHD showed increased brain activation in other areas than in controls (Fassbender & Schweitzer, 2006). A second possibility is that the reinforcers were not sufficiently salient for children with ADHD. Children with ADHD may need larger reinforcement in order to perform as well as controls (Slusarek et al., 2001). A third possibility is that the neurobiological sensitivity may differ between children with ADHD and controls (Fassbender & Schweitzer, 2006), for example, due to deviation in brain development. This suggests that the psychophysiological activity that correlates with behaviour may differ between children with ADHD and controls.

Heart rate variables in our study suggest that children with ADHD suffer from difficulties to motivate themselves and perform well when reinforcement is not available. If children with ADHD show impaired feedback monitoring as compared to controls, this may have triggered less 'attention' to the task. Children with ADHD may need reinforcement in addition to feedback for (a) more efficient shaping of behaviour, for example, by controlling their responses and hence becoming less variable, or (b) increase the subjective value of feedback in order to boost their motivation.

Limitations

Firstly, the small sample size demands verification of our findings in a larger sample. Secondly, children with ADHD had lower IQ scores than controls. Kuntsi et al. (2004) demonstrated that correlations between ADHD and IQ are due to a genetic component. The relation between IQ and HRR or HRV is unknown; in our study we found no meaningful correlations between IQ and the dependent variables (all p values > .05), suggesting no confounding effects of IQ. The third issue is the presence of oppositional and aggressive behaviour in the ADHD sample, as indicated by scores

on the DISC and DBD. There is substantial overlap between ADHD and ODD/CD, and with ADHD and anxiety disorders (Angold, Castello, & Erkanli, 1999). Studies have found diminished sensitivity to punishment in ODD/CD groups as measured by both behavioural and psychophysiological recordings (Herpertz et al., 2001; Newman, Wallace, Schmitt, & Arnett, 1997). There are indications of increased heart rate responses to feedback in anxious individuals (Crone et al., 2005). We examined the potential contribution of DBD parent and teacher reported ODD and CD symptoms and the self-report measure of anxiety to our dependent variables, and no meaningful correlations were revealed (all p values > .05).

Conclusion

The present study demonstrated that heart rate variables can provide insight into processes that are not easily detectable using performance measures: ADHD is characterized by impaired monitoring of feedback and reduced task engagement. Motivational deficits at a psychophysiological level have been identified earlier in ADHD using fMRI (Scheres, Milham, Knutson, & Castellonos, 2005). If replicated, the current findings open up a window for research into the practical consequences of reinforcement feedback in ADHD. Issues to be studied include whether possible abnormal motivation and impaired monitoring of feedback affects academic performance in children with ADHD, whether the enhanced impact of reinforcement using pharmacological treatment influences performance, and whether such findings influence the psychosocial management of children with ADHD. From a clinical perspective, feedback is a crucial concept in behavioural therapy (Milne & James, 2000). Hence, analysis of feedback and its biological underpinning can potentially assist in developing therapeutic procedures. Interventions for ADHD need to be designed that take account of diminished monitoring of feedback a lack in task engagement by, for example, making feedback more salient or systematically changing the subjective value of reinforcement.

Chapter 7

General Discussion: Limitations of a Motivational Explanation of ADHD

There is evidence that children with attention-deficit/hyperactivity disorder (ADHD) show motivational problems in terms of an abnormal response to reinforcement contingencies (e.g., Sonuga-Barke, Taylor, Sembi, & Smith, 1992; Tripp & Alsop, 1999), however, the nature of this problem is not well understood. The studies presented in this thesis aimed to extend the knowledge on the role of reinforcement in ADHD by studying neurocognitive as well as autonomic functions of children with ADHD and typically developing children. Three questions were investigated. Firstly, are neurocognitive dysfunctions in ADHD secondary to a motivational deficit such as an abnormal sensitivity to reinforcement? Secondly, are children with ADHD sensitive to specific aspects of reinforcement that can explain the underlying mechanisms of a reinforcement deficit? Thirdly, is an abnormal sensitivity to reinforcement accompanied by aberrant autonomic responses to reward and penalty?

ADHD: Can Reinforcement Resolve the Problem?

The first issue addressed in the current thesis was whether children with ADHD suffer from a reinforcement sensitivity problem that may interfere with their neurocognitive abilities. The majority of studies reviewed in Chapter 2 indicate that both reward and penalty positively influenced task performance as well as self-rated motivation in all children. Five out of ten studies, however, demonstrated a disproportional improvement in children with ADHD under contingency conditions (either reward or penalty) compared to a neutral condition. This suggests that the improvement in

performance, when coupled with reward or penalty was somewhat more prominent for children with ADHD than for typically developing children. No group differences were observed in increases in self-rated motivation, indicating that self-rated and observed motivation (improvements in task performance) did not tap the same concept. The experimental studies (Chapter 3, 4, 5 and 6) of this thesis confirmed that performance deficits in ADHD partly represent a motivational problem, as observed by an abnormal sensitivity to reinforcement. Thus, observed impairments of children with ADHD in cognitive control (response inhibition, decision making; Chapters 2 and 4), temporal information processing (Chapter 2 and 3), mathematics and visual matching (Chapter 2) diminished, when performance was reinforced immediately and frequently. Importantly, the abovementioned impairments of children with ADHD were not completely ameliorated by reinforcement contingencies: In most studies, performance of ADHD children remained inferior to that of controls (Chapters 2, 3, 5 and 6). Some performance deficits such as stimulus-response learning in ADHD (Chapter 5) may be insensitive to the reinforcement conditions. Thus, neurocognitive deficits in children with ADHD were partly explained by a motivational problem.

Motivational Modulation of Cognitive Control

In Chapter 2, children with ADHD compared to a typically developing group displayed a disproportional improvement in performance (collapsed over a range of cognitive tasks) in the face of reinforcement contingencies. Due to the heterogeneity in cognitive processes explored in Chapter 2, it was not possible to study the impact of reinforcement on specific neurocognitive deficits in ADHD. However, the inclusion of more recent studies on reinforcement and performance in ADHD allows investigation of the impact of reinforcement on response inhibition, an often reported cognitive control deficit in ADHD (e.g., Doyle et al., 2005; Willcut, Doyle, Nigg, Faraone, & Pennington, 2005). Two out of six studies on response inhibition indicated an abnormal reinforcement sensitivity in ADHD (Konrad, Gauggel, Manz, & Scholl, 2000; Slusarek, Velling, Bunk, & Eggers, 2001). In these two studies, reinforcement contingencies 'normalized' performance of children with ADHD to a level comparable to that of typically developing controls. The other studies, however, indicated that response inhibition problems in children with ADHD were independent of the reinforcement conditions (Crone, Jennings, & Van der Molen, 2003; Desman, et al., 2006; Scheres, Oosterlaan, & Sergeant, 2001; Wodka et al., 2007). Thus, the majority of studies demonstrated that inhibition problems in children with ADHD represented a stable deficit that was independent of motivational manipulations.

Motivational Modulation of Temporal Information Processing

Chapter 3 addressed whether temporal information processing deficiencies in ADHD were secondary to a motivational deficit. Children with ADHD persistently produced shorter, as well as more variable time intervals than typical developing controls, confirming earlier findings (Toplak, Dockstader, & Tannock, 2006). Systematic over- or underproduction of time is thought to indicate defect internal clock functioning (Harrington, Haaland, & Hermanowicz, 1998; Ivry, 1996). A fast internal clock in ADHD (systematic production of shorter time intervals) implies that time intervals subjectively 'lasts longer' for children with ADHD than for control children, which may explain the persistent problems with waiting (Sonuga-Barke, 2002; Sonuga-Barke et al., 1992) and disinhibited behaviour such as blurting out answers before a question has been completed. The internal clock dysfunction in the ADHD group was insensitive to motivational modulations, similarly to what has been reported by others (Van Meel, Oosterlaan, Heslenfeld, & Sergeant, 2005a). More variable time intervals in ADHD as observed in Chapter 3 would point towards impaired response organization. In contrast to internal clock functioning, timing variability in ADHD children reduced compared to controls, when performance was coupled to monetary consequences compared to feedback only (Chapter 3). This indicates that time production difficulties in ADHD partly represent a motivational problem. Bellgrove, Hester, and Garavan (2004) reported that greater response variability was associated with impaired performance on a go/no-go task, indicating that variability in responding may impair cognitive control functions such as response inhibition. In addition, there is evidence that controlling for 'basic' abilities (such as response variability) ameliorates differences in cognitive control between children with ADHD and typically developing children (Rhodes, Coghill, & Matthews, 2005; Marks, et al., 2005). Since enhanced variability in responding is reported often in ADHD (e.g., Leth-Steensen, Elbaz, & Douglas, 2001), our findings increase the understanding of the role of reinforcement in more complex neurocognitive deficiencies in ADHD. Therefore, future studies should include measures of more 'basic' functions, such as response variability, when studying the role of reinforcement in ADHD.

Thus, the first main question in this thesis, whether neurocognitive dysfunctions in ADHD are secondary to a motivational deficit such as aberrant reinforcement sensitivity, cannot be confirmed. The findings indicate that only some (aspects of) neurocognitive abilities in ADHD are sensitive to reinforcement contingencies. Performance deficits in children with ADHD cannot be fully attributed to a motivational deficit. This agrees with the suggestion that there are multiple distinct endophenotypes of ADHD, among which, an aberrant sensitivity to reinforcement (Doyle et al., 2005; Castellanos & Tannock, 2002; Nigg, 2005; Sonuga-Barke, 2002).

Sensitivity to Specific Aspects of Reinforcement: Towards a Clearer Definition of ADHD?

The second question in this thesis was whether children with ADHD may be sensitive to specific aspect of reinforcement such as suggested by several theoretical models (Barkley, 1997; Douglas, 1989; Haenlein & Caul, 1987; Quay, 1988a; Sagvolden, Johansen, Aase, & Russell, 2005; Sergeant, Oosterlaan, & Van der Meere, 1999; Sonuga-Barke, 2002). There was investigated whether children with ADHD compared to typical developing children displayed an abnormal sensitivity to: reinforcement compared to feedback only (Chapters 2, 3, and 6), the valence of reinforcement (Chapters 2, 3, and 6), the frequency of reinforcement (Chapters 4 and 5) or the magnitude of reinforcement (Chapters 3, 4 and 5).

Compared to controls, children with ADHD seem somewhat more sensitive to monetary reinforcement than controls (as described in the section above). No evidence was revealed for an abnormal sensitivity in children with ADHD to the valence of reinforcement (Chapters 2, 3, and 6). One exception was that, compared to typical developing controls, children with ADHD exhibited a decreased sensitivity to behavioural choices that were ultimately disadvantageous (Chapter 4). In this study, children had to choose between three alternatives: A favourable alternative that carried small gains and small losses, and two unfavourable alternatives that both carried large losses, but were dissociated by the size of their gain, being either small or large. By choosing repeatedly between the alternatives, children had to find out that the favourable alternative resulted in the largest net gain (gains larger than losses). In other words, children had to remember the reinforcement history of the alternatives. Since it was too difficult to calculate the exact net gain of the alternatives, children had to use their 'gut-feeling' to experience what alternative was ultimately favourable (Damasio, 1996). Children with ADHD showed a maladaptive response strategy by choosing less often for the advantageous alternative and more often for the disadvantageous alternatives. This was independent of whether the gain in the disadvantage alternative was large or small. These findings suggest that children with ADHD were less sensitive than controls to future negative consequences, rather than focussing on immediate gains (e.g., Newman, 1987). This indicates that children with ADHD displayed difficulties keeping track of the reinforcement history of the task. Possibly, the decay of the impact of aversive stimuli was faster in children with ADHD than in typically developing children. This was emphasized by the findings in Chapter 4 that decision-making problems in ADHD diminished, when penalty (carried by the unfavourable alternatives) was delivered more frequently, thus less distant in time. A possible faster decay of reinforcement in ADHD has been suggested earlier with re-

spect to reward processing; children with ADHD would suffer from a faster decay of reward as the result of a dysfunction in dopamine transmission in the limbic system (Johansen, Aase, Meyer, & Sagvolden, 2002). This diminished sensitivity to aversive behavioural consequences may be regulated by the neurotransmitter serotonin and noradrenalin (Quay, 1988a; 1988b; 1988c; 1997). According to Quay, due to this neurochemical imbalance, children with ADHD suffer from a decreased control over behaviour by signals of non-reward or punishment and show increased disinhibited behaviour (Gray, 1982; 1987). The results of this thesis suggest that children with ADHD were sensitive to penalty like controls, when penalty was delivered immediately and consistently (Chapter 3, 4, and 6), in line with other studies (Daugherty & Quay, 1991; Fischer, Barkley, Smallish, & Fletcher, 2005).

Children with ADHD and typical developing children were differentiated by their sensitivity to the frequency of reinforcement (Chapters 4 and 5). In the decision making study (Chapter 4) performance of children with ADHD improved to a level similar to that of controls when reinforcement (penalty) was delivered frequently versus infrequently, suggesting a diminished sensitivity to low frequency reinforcement. In contrast, in the reinforcement learning task (Chapter 5) infrequent compared to frequent rewards improved performance of typically developing children, while this was not seen in children with ADHD. It was speculated that, in line with earlier suggestions (Sergeant et al., 1999; Van der Meere, 2002), that children with ADHD were hypo-aroused and less sensitive to the possible (over)arousing impact of frequent rewards (see discussion of Chapter 5).

Children with ADHD do not seem to profit like typically developing children from a large compared to a small magnitude of reinforcement (Chapters 3, 4 and 5). These findings question the assumptions of an elevated reward threshold in ADHD (Haenlein & Caul, 1987).

Thus, the second question of this thesis, whether children with ADHD and typical developing children differed in their sensitivity to specific aspects of reinforcement was confirmed: Children with ADHD were differentiated from controls by an aberrant sensitivity to reinforcement versus feedback-only and an aberrant sensitivity to the frequency (or immediacy) of reinforcement. When delivered frequently and immediately, both reward and penalty seemed effective in decreasing performance deficits in children with ADHD to a level similar to that of typical developing controls (Chapters 2, 3, and 6). This suggests that children with ADHD may suffer from a motivational deficiency when reinforcement is not available (Barkley, 1997; Douglas, 1989; Sergeant et al., 1999). This would result in a disability to adjust their behav-

ioural strategy and increase the allocation of attention that is necessary to keep up with the demands of the task (Sergeant et al., 1999; Van der Meere, 2002). In face of external stimulation, such as monetary gain and loss, children with ADHD seem able to improve their performance similarly to typically developing children. A recent study (Geurts, Luman & Van Meel, unpublished) demonstrated that not only monetary reinforcement but also social motivators (playing a game against other children) can ameliorate performance deficits of children with ADHD in a task that measured interference control.

Autonomic Response to Reinforcement Contingencies

The third question here was to investigate whether an abnormal sensitivity to reinforcement in children with ADHD may be linked to abnormalities in the autonomic nervous system (ANS). The studies in this thesis revealed heterogeneous results.

The studies showed some evidence of abnormal sympathetic nervous system (SNS) activity to feedback stimuli in children with ADHD compared to typical developing controls, when their performance was not reinforced (Chapter 3, 4, and 6). The autonomic response to feedback in children with ADHD 'normalized' when performance was coupled to monetary contingencies. Interestingly, normalization of autonomic responses in the ADHD group was accompanied by a normalization of their performance. In the timing study (Chapter 3), both skin conductance responses (to feedback) as well as timing variability of ADHD children normalized to a level similar to controls when reinforcement was added to feedback. In the decision-making study (Chapter 4), skin conductance responses following unfavourable choices as well as performance of children with ADHD normalized compared to typically developing controls, when penalties were delivered frequently versus infrequently. Increased skin conductance responses in children with ADHD as observed in the reinforcement conditions might be related to an increase in the awareness of the consequences of feedback (see discussion of Chapter 3). This could explain the disproportional increase in performance in children with ADHD when feedback was coupled to reinforcement. Decreases in low frequency heart rate variability (associated with an increase in task engagement, Chapter 6), when reinforcement was added to feedback, were found to be larger in children with ADHD than in controls (Chapter 6). Changes in low frequency heart rate variability have been associated with activity in the vascular system that initiates changes in blood flow that are necessary for local metabolic demands (Akselrod et al., 1985). These findings suggest that monetary reinforcers increase the allocation of attention in children with ADHD, which improves performance.

And although performance of children with ADHD improved, when reinforcement was added to feedback, it remained inferior to that of controls (Chapter 6). Possibly, children with ADHD had to compensate for deficits that are not solely a motivational dysfunction (in this case timing performance, see Chapter 3).

Some evidence was found for smaller (phasic) heart rate and skin conductance responses to reinforcement in children with ADHD compared to in typically developing controls, suggesting stronger parasympathetic than sympathetic activity in ADHD (Chapter 2: Crone, Jennings, & Van der Molen, 2003; Iaboni, Douglas, & Ditto, 1997). These findings are in line with a more recent study that showed smaller cardiac activity to reward in children with ADHD compared to typically developing children (Crowell et al., 2006). The experimental chapters in this thesis, however, did not report on abnormal autonomic responses to reinforcement contingencies in ADHD (Chapter 3, 4, and 6), with the exception of one study that found enlarged HR responses to reward in the ADHD group (Chapter 4). Thus, children with ADHD exhibited abnormal cardiac responses to reward, showing either a blunted or increased response compared to typically developing children.

Moreover, the studies in this thesis show some evidence for an aberrant autonomic response in children with ADHD to reinforcement contingencies, confirming the third research question of this thesis. Children with ADHD were differentiated from controls in their autonomic response to reinforcement compared to feedback only (Chapter, 2, 3, 4, and 6) and the frequency of reinforcement (Chapter 4). There were some indications of an abnormal cardiac response to reward stimuli in ADHD; no strong evidence was found for an abnormal response to penalty. The exact relation between performance problems and autonomic responses remains unclear, since the correlations between the two levels of measurement were weak.

Limitations

Before conclusions are drawn regarding the role of reinforcement in ADHD, some limitations are worth noting. A first limitation is the comorbidity in ADHD with other developmental disorders that may influence the sensitivity to reinforcement. For example, all ADHD groups described in the current thesis show comorbid antisocial behaviour, such as observed in oppositional defiant disorder (ODD) or conduct disorder (CD). The presence of comorbid ODD and CD in our group samples is in line with observations in large community samples (Angold, Costello, & Erkanli, 1999). Anti-social behaviour has been related to poor self-regulation in face of reinforcement

(Newman & Wallace, 1993; Raine, 1993): Raine proposed that a lack of fear in antisocial children decreases the attention to threat related stimuli such as punishment, and prevents passive avoidance learning. There are several studies that support this suggestion (Daugherty & Quay, 1991; Fonseca & Yule, 1995; Matthys, Van Goozen, De Vries, Cohen-Kettenis, & Van Engeland, 1998; Shapiro, Quay, Hogan, & Schwartz, 1988). Internalizing behaviour problems (high fear levels) ameliorated impaired performance of antisocial children on reinforcement tasks (O'Brien & Frick, 1996) and may possibly do the same in children with ADHD, in line with a recent decision making study in ADHD (Garon, Moore, & Waschbusch, 2006). Otherwise, children with autism spectrum disorder (ASD) may show overlap with ADHD children in their response to reinforcement contingencies (see Chapter 5). The impact of reinforcement on children with learning problems (highly comorbid in ADHD), for example, has not been investigated thus far. To minimize the impact of comorbid symptoms in the studies described in this thesis, children with a clinical diagnosis other than ADHD, ODD or CD were excluded from the ADHD group, such as anxiety disorder, depression disorder, or ASD. In the experimental studies of this thesis, the contribution of the ODD and CD symptoms to the impact of reinforcement on performance in ADHD was statistically non-significant (Chapter 3, 4 and 6). Clearly, future studies with large sample sizes are needed that focus on the specificity of motivational problems in ADHD.

A second issue is that motivation in the current thesis was manipulated using monetary reinforcers. There was no control over other possible motivating factors, such as the impact of computerized tasks, exiting test stimuli, the individualized test situation, and the fact that most children were free from school to come over to the university test lab. Possibly, these background factors may have increased the motivational drive to perform well during the experiments, which may have overestimated the performance of children with ADHD. Otherwise, some tasks may have been extremely boring for children to perform, resulting in impaired performance in the ADHD group. Systematic investigation of impact of reinforcement on performance outside the lab requires longitudinal observation studies and large sample sizes. In the current thesis, the impact of background factors that could influence the level of motivation was minimized by manipulating various reinforcement conditions within each subject.

Third, the absence of strong correlations between the autonomic responses and performance in face of reinforcement contingencies in ADHD may weaken our speculations on the relation between psychophysiological processes and performance. Possibly, an abnormal sensitivity to reinforcement in ADHD in terms of performance and autonomic responses are caused by similar deficiencies in the brain, but share no

causal relation. Several brain structures that are associated with autonomic responses to affective stimuli are also associated with neurocognitive functioning, such as the anterior cingulate cortex (ACC), the ventromedial prefrontal cortex (VMedPFC), the ventral striatum and the amygdala (Anderson et al., 2003; Bechara, Damasio, Damasio, & Anderson, 1994; Bechara, Damasio, Damasio, & Lee, 1999; Beauchaine, 2001; Bush, Luu & Posner, 2000; Critchley, Matthias, & Dolan, 2001; Critchley et al., 2003). These brain structures have been found to function abnormally in ADHD (Bush et al., 1999; Ernst et al., 2003; Fallgatter et al., 2004; Plessen et al., 2006; Scheres et al., 2007). Low correlations between different levels of investigations have been observed more often in ADHD (e.g., Van Meel et al., 2005a; Van Meel et al., 2005b). Therefore, future multi-level projects are needed to resolve the discrepancies between the various levels of research (e.g., performance, psychophysiology, neuroanatomy, genetics, animal and computational models). Such integrated projects, however, cope with difficulties in the recruitment of children, and may result in biased samples.

General Conclusions and Future Directions

Children with ADHD showed a disproportional improvement in neurocognitive functioning compared to typically developing children, when performance was coupled to immediate and consistent monetary consequences. These findings suggest that children with ADHD suffer from a motivational deficit (Barkley, 1997; Douglas, 1989; Sergeant et al., 1999). Children with ADHD exhibited a disability to adjust their behavioural strategy and increase the attentional effort that is necessary to keep up with environmental demands without the help of external reinforcement (e.g., Chapter 3, Konrad et al., 2000; Slusarek et al., 2001). Although performance of ADHD children improved to a larger extent than that of controls, when reinforcement was available, in most studies it remained inferior to that of typically developing children. This indicates that neurocognitive deficits in ADHD are not secondary to a motivational deficit, *rejecting our first research question*. Performance in ADHD seemed impaired by several neurocognitive dysfunctions such as difficulties in reinforcement processing, cognitive control (Chapters 2, 4 and 5) and temporal information processing (Chapter 3). These dysfunctions may represent distinct, but interrelated, developmental pathways to ADHD, as described in the introductory chapter (Castellanos & Tannock, 2002; Nigg, 2005; Sonuga-Barke, 2002).

Interestingly, some evidence was found that basic abilities in ADHD such as timing variability are susceptible to disproportional improvement when coupled to monetary contingencies (Chapter 3). Since these basic abilities play a major role in performance

on more complex tasks (Bellgrove, Hester, & Garavan, 2004), more insight into how reinforcement influences these basic abilities is essential. Time production involves the activation of subcortical structures such as the cerebellum (Harrington et al., 1998; Ivry et al., 2002), which is found to correlate positively with the persistency of ADHD symptoms (Mackie et al., 2007) and may be characteristic for ADHD (Durston et al., 2004). Future studies should therefore systematically explore the impact of reinforcement on basic as well as more complex neurocognitive functions.

The results regarding *the second question of this thesis*, whether children with ADHD were sensitive to specific aspects of reinforcement, demonstrate that ADHD children were differentiated from controls by their sensitivity to reinforcement versus feedback-only and by their sensitivity to reinforcement frequency. No evidence was revealed that children with ADHD profited more than typically developing children from changes in the magnitude of reinforcement, arguing against the suggestion that children with ADHD suffer from an elevated reward threshold (Haenlein & Caul, 1987). Some evidence was found that children with ADHD compared to typically developing children are less sensitive to aversive consequences of behaviour, specifically when penalty was delivered infrequently compared to frequently (Chapter 4). Possibly, the decay of penalty is faster in ADHD compared to typically developing children. According to Sagvolden et al. (2005) the behaviour that characterizes ADHD can be explained by a hypo-dopaminergic functioning in the fronto-striatal pathway that is responsible for a faster decay of the impact of anticipated rewards. A recent imaging study demonstrated that children with ADHD compared to controls showed less ventral striatum activation during reward anticipation (Scheres et al., 2007), supporting the suggestion that the saliency of anticipated rewards is diminished (Johansen et al., 2002; Volkow et al., 2004). This may explain the finding that children with ADHD are more influenced by the last reward received than by the reinforcement history (Tripp & Alsop, 1999). Clearly, more studies are needed to confirm that children with ADHD are less sensitive to the reinforcement history of penalty, similarly to reward (Rapport, Tucker, DuPaul, Merlo, & Stoner, 1986; Sonuga-Barke et al., 1992; Tripp & Alsop, 1999). If a decreased sensitivity to aversive consequences is related to a weak behavioural inhibition system (e.g., Quay, 1988a) future studies need to determine whether inhibition problems in ADHD correlate with a decreased sensitivity to memorable signals of punishment. In contrast, when delivered immediately and consistently, children with ADHD were sensitive to reward and penalty, similarly to controls.

Reinforcement deficiencies in the dopamine system of the limbic system, such as suggested in ADHD (Johansen et al., 2002), have been related to addictive behaviours

including drinking, drug abuse, and gambling (Blum et al., 2000). People with addiction problems are suggested to require more dopamine than persons without this reward deficiency, which leads to reward-seeking behaviour (Goudriaan, 2005). Dopamine receptor abnormalities have been associated with reward searching behaviours (Blum et al., 1996; Comings & Blum, 2000) as well as aggression problems (Chen et al., 2007) and possibly, the same genes are associated with ADHD (Waldman & Gizer, 2006). The risk of children with ADHD to develop aggressive and addictive behaviour during adolescence and adulthood is considerable (Biederman, Monuteaux et al., 2006; Sood, Pallanti, & Hollander, 2003). Therefore, future longitudinal approaches are needed that focus on the behavioural consequences of an abnormal sensitivity to reinforcement in children with ADHD, as observed in the current thesis.

The third research question, whether there is a physiological basis of motivational problems in children with ADHD, *could not be confirmed or rejected*. There is some evidence that children with ADHD show abnormal cardiac activity to reward, pointing to abnormal SNS activity. No strong evidence was found for the suggestion that children with ADHD show attenuated autonomic activity to aversive stimuli that may explain disinhibition problems in ADHD (Newman, 1987; Patterson & Newman, 1993; Quay; 1988a; 1988b; 1988c; 1997; Wallace & Newman, 1990). Abnormal autonomic activity (increased heart rate variability and lower skin conductance responses) as well as low performance of children with ADHD 'normalized' when reinforcement was added to performance feedback (Chapters 3, 4 and 6). When reinforcement is not available, children with ADHD seem to suffer from a defect to activate efficiently the autonomic system, in response to changing environmental demands or internal goals. An increases in awareness of the consequences of behaviour (Chapter 3 and 4) and an increases in the motivation to perform well when reinforcement is available (Chapter 6), may explain the dependence of children with ADHD on contingencies to optimize their performance (Chapters 2, 3, and 4).

If the impact of reinforcement in children with ADHD decays faster than in controls, future studies should track the physiological response to reinforcement over time. The relatively slow changes in SNS activity in terms of skin conductance (around 0.2 Hz) or heart rate variability (around 0.06 Hz) are inadequate to detect such decay. In a recent electroencephalographic (EEG) study, children with ADHD displayed larger ERPs to penalty than controls in an early processing phase, while showing smaller ERPs to penalty in a later phase that is related to the affective evaluation of stimuli (Van Meel et al., 2005b). Thus, future ERP studies are needed to confirm the possibility that children with ADHD profit optimally from reinforcement when it is delivered immediately and frequently.

Motivational modulation of performance in children with ADHD as demonstrated in this thesis emphasizes the importance of behavioural interventions that make use of reinforcement contingencies. Contingency programmes that involve the direct application of both positive reinforcement and response cost (or time-out) are found to be effective in decreasing 'off-task' (or task irrelevant) behaviour in children with ADHD (DuPaul, Guevremont & Barkley, 1992; McGoey & DuPaul, 2000; Rapport, Murphy & Bailey, 1982). If children with ADHD are able to meet increasing task demands, when they are motivated by external reinforcement, studies are needed to explore which environmental conditions may optimize their abilities. The results of this thesis suggest that, when reinforcement is delivered immediately (Chapters 2, 3, and 6) and frequently (Chapter 4), both reward and penalty may improve (motor) behaviour and cognitive abilities of children with ADHD. However, future clinical studies are needed to confirm these suggestions.

Children with ADHD may be extremely vulnerable to exhibit an abnormal response to contingencies due to their learning history of the motivation to perform well (Chang & Burns, 2005). During development, children with ADHD are confronted with their cognitive and motor disabilities and children with ADHD may suffer from social rejection as a result of their uncontrolled behaviour (De Boo & Prins, 2007). These experiences may have decreased their motivation to perform well in school or behave well at home. No studies have investigated the impact of these social factors on motivational problems in ADHD. The prefrontal cortex of humans is developing until late adolescence (e.g., Segalowitz & Davies, 2004) and future studies may focus on the impact of early life events on the prefrontal cortex that may influence the development of motivational problems in ADHD.

To Conclude, This Thesis Suggests That:

- Immediate and frequent monetary reinforcement may normalize performance of children with ADHD. However, more replication studies are needed that systematically investigate the impact of reinforcement on neurocognitive functioning in ADHD. Some neurocognitive difficulties of ADHD children seem sensitive to motivational modulation, while others seem more stable. If replicated, such findings would have important therapeutic implications.

- Multi-level studies into ADHD are needed that explore relation between physiological and performance deficits in order to understand the underlying mechanisms of an abnormal sensitivity to reinforcement. The autonomic abnormalities in ADHD suggest an impaired awareness of the affective consequences of behaviour. This may explain the need for external (monetary) stimulation to perform optimally. If replicated, heart rate and skin conductance measures should be explored as diagnostic tools.

- If children with ADHD are less sensitive to reinforcers that are more distant in time, they need to be reinforced immediately and frequently for their behaviour, rather than more intensely. Future studies are needed to investigate the impact of more distant reinforcement on the performance of children with ADHD. In addition, psychophysiological studies are needed that track the physiological response of children with ADHD to reinforcement over time.

- Future studies should focus on the clinical specificity of an abnormal reinforcement sensitivity in ADHD, since this thesis shows evidence of such problems in comorbid groups of ADHD. More knowledge on the impact of reinforcement on different comorbid groups of ADHD would increase the specificity of interventions (such as contingency training) for these various clinical subgroups.

- More knowledge on the development of an abnormal sensitivity to reinforcement in ADHD is required. Studies are needed that investigate whether early intervention can ameliorate the development of an abnormal reinforcement sensitivity in ADHD. This may help to prevent the development of behavioural problems in adolescence and adulthood.

Nederlandse samenvatting (Summary in Dutch)

De Rol van Contingenties bij Kinderen met Attention-deficit/ hyperactivity Disorder (ADHD)

De studies in dit proefschrift hebben als doel een bijdrage te leveren aan de huidige literatuur over de rol van contingenties als straf en beloning bij kinderen met ADHD. De gevoeligheid voor contingenties wordt onderzocht door de prestatie op verschillende taken te koppelen aan contingenties als het winnen en verliezen van geld. Hierbij wordt ervan uitgegaan dat mensen werken voor een beloning, terwijl men probeert om negatieve stimuli zoals straf te vermijden. Een overzichtsartikel naar de invloed van contingenties op gedrag laat zien dat beloning een impact heeft op drie psychologische factoren: (a) motivatie (willen), (b) emotie/affect (leuk vinden), en (c) leergedrag. Een beloning kan de motivatie verhogen waarbij het verlangen om iets te willen of doen toeneemt. Dit kan in grote mate ons gedrag beïnvloeden en hoeft niet altijd bewust te verlopen. Dit proces kan los gezien worden van het meer bewuste, emotioneel/affectieve component waarbij positieve emoties worden opgewekt door een beloning. Als derde kan een beloning leergedrag beïnvloeden, omdat een beloning de kans verhoogt dat bepaald gedrag herhaald wordt. Dit proefschrift richt zich vooral op de (onbewuste) invloed van beloning op de motivatie en prestaties van kinderen met ADHD (Hoofdstukken 2, 3, 4, 5, en 6) en op de invloed van beloning op de leersnelheid (Hoofdstukken 5 en 6). De prestatieveranderingen van kinderen met ADHD worden vergeleken met die van zich normaal ontwikkelende kinderen (een gezonde controle groep). Daarbij wordt de psychofysiologische respons (hartslagfrequentie en huidgeleiding) op de verschillende contingenties gemeten om de onderliggende processen van een mogelijke afwijkende gevoeligheid voor straf en beloning in kaart te brengen. Tweehonderd kinderen tussen de 8 en 12 jaar hebben meegedaan aan de experimenten die beschreven zijn in dit proefschrift.

Hoofdstuk 2 geeft een overzicht van de literatuur met betrekking tot ADHD en gevoeligheid voor contingenties. Vijf theoretische modellen en 22 experimentele studies worden besproken waarin de invloed van contingenties op taakprestatie, motivatieniveau en psychofysiologische maten (hartslagfrequentie en huidgeleiding) bij kinderen met ADHD is onderzocht. In **Hoofdstuk 3** wordt de invloed van contingenties op

motorische timing onderzocht. Motorische timing is een basale vaardigheid waarbij temporele informatieverwerking een belangrijke rol speelt; deze vaardigheid is verstoord bij kinderen met ADHD. **Hoofdstuk 4** bestudeert beslisgedrag van kinderen met ADHD. Kinderen moesten kiezen tussen drie alternatieven. Er was één voordelig alternatief (A) waarbij kinderen kleine bedragen konden winnen en soms een klein bedrag verloren – uiteindelijk leverde dit alternatief winst op. Er waren daarnaast twee onvoordelige alternatieven waarbij kinderen ofwel een klein bedrag (B), ofwel een groot bedrag (C) konden winnen, maar ook grote bedragen konden verliezen. Kinderen moesten zelf uitvinden welk alternatief het meest gunstig was. Er werd onderzocht of kinderen met ADHD een voorkeur hadden voor een hoge beloning en ongevoelig leken voor de bijbehorende hoge verliezen (alternatief C). **Hoofdstuk 5** beschrijft of kinderen met ADHD afwijkingen laten zien in het leren van contingenties zoals straf of beloning. Kinderen met ADHD werden vergeleken met een gezonde controlegroep evenals een klinische controlegroep om zo een uitspraak te kunnen doen over de specificiteit van een afwijkende gevoeligheid voor contingenties. In **Hoofdstuk 6** wordt verslag gedaan van een studie naar de hartslag respons op contingenties bij kinderen met ADHD. Zowel snelle als tragere veranderingen in hartslagfrequentie worden in dit hoofdstuk bestudeerd. **Hoofdstuk 7** bestaat uit een algemene discussie, de klinische implicaties van de bevindingen, aanwijzingen voor toekomstig onderzoek en de conclusie.

Etiologie van ADHD

Attention-deficit/hyperactivity disorder (ADHD) is een ontwikkelingsstoornis met symptomen van aandachtsproblemen, hyperactiviteit en impulsiviteit. ADHD laat drie subtypen zien: het aandachtsgestoorde subtype, het hyperactieve/impulsieve subtype en het gecombineerde subtype. Aandachtsproblemen worden gekenmerkt door onder andere: concentratieproblemen, moeite met het afmaken van taken, moeite met organiseren, verhoogde afleidbaarheid en vergeetachtigheid. Hyperactiviteit manifesteert zich onder ander in rusteloosheid, overbewegelijkheid, rondrennen en veel praten. Impulsiviteit uit zich in ongeduldig gedrag, moeite met wachten en het onderbreken van anderen. ADHD ontstaat in de kindertijd voor het 7^{e} levensjaar waarbij de symptomen zichtbaar worden in verschillende situaties (bijvoorbeeld thuis en op school). ADHD gaat samen met een verstoorde ontwikkeling van sociale vaardigheden en een achterblijvende academische ontwikkeling. De gemiddelde wereldwijde prevalentie is 5.3%, waarbij de stoornis vaker voorkomt bij jongens dan bij meisjes in de verhouding 4:1.

Er is steeds meer evidentie dat de ontwikkeling van ADHD bepaald wordt door zowel neurobiologische als sociale factoren. Kinderen met ADHD laten verschillende cognitieve disfuncties zien, welke bijdragen aan de ontwikkeling van ADHD. Het blijkt dat kinderen met ADHD vooral een verstoring laten zien in drie gebieden: *cognitieve controle, temporele informatieverwerking* en de *gevoeligheid voor contingenties*. Cognitieve controle wordt gezien als de capaciteit om je flexibel aan te passen aan de continu veranderende eisen van de omgeving, in relatie tot interne doelen en intenties. Een verstoorde cognitieve controle bij kinderen met ADHD is zichtbaar in problemen met het werkgeheugen, inhibitie, planning, interferentie controle en het het maken van onderscheid tussen goed en fout. Temporele informatie verwerking betreft de capaciteit om informatie sequentieel te ordenen en het vermogen om ritmes te creëren. Deze capaciteit is van groot belang voor de planning van gedrag, maar ook voor de uitvoering van motorische handelingen. Kinderen met ADHD laten problemen zien in het onderscheiden van tijdsintervallen, het (re)produceren van tijdsintervallen en de organisatie van hun motoriek. Een afwijkende gevoeligheid voor contingenties bij kinderen met ADHD is zichtbaar in de geobserveerde voorkeur van kinderen met ADHD voor een onmiddellijke boven een uitgestelde beloning en een mogelijke verminderde motivatie wanneer zij niet geprikkeld worden door de omgeving. Dit proefschrift richt zich op de afwijkende gevoeligheid voor contingenties bij kinderen met ADHD en de mogelijke interacties met cognitieve controle en temporele informatie verwerking.

Motivationele Problemen bij Kinderen met ADHD

Opmerkelijk is dat de ernst van de gedragsproblemen (aandachtstekort, hyperactiviteit en impulsiviteit) van kinderen met ADHD zeer variabel is en afhankelijk lijkt van omgevingsfactoren. Een studie naar de aandachtsspanne van hyperactieve kinderen liet zien dat kinderen met ADHD een kortere aandachtsspanne hadden wanneer zij een taak alléén uitvoerden, vergeleken met een situatie waarbij de proefleider aanwezig was. Uit een ander onderzoek kwam naar voren dat het hyperactieve gedrag van kinderen met ADHD tijdens het wachten op een proefleider afnam wanneer zij werden afgeleid door een tekenfilm vergeleken met een neutrale (natuur) film. Deze bevindingen zijn in lijn met studies die laten zien dat de prestatie van kinderen met ADHD, meer dan dat van gezonde kinderen, omhoog gaat waneer een taak nieuw is, opvallend is, of leuk gevonden wordt. Deze abnormale interactie tussen gedrag en omgeving wordt ook geobserveerd in studies die afwijkende reacties van kinderen met ADHD laten zien op contingenties als straf en beloning (zie Hoofdstuk 2). Uit bovenstaande studies blijkt dat kinderen met ADHD externe prikkels als straf en

beloning nodig hebben om goed te kunnen presteren en minder gedragsproblemen te laten zien. Dit duidt op mogelijke problemen om zich intrinsiek (vanuit zichzelf) te motiveren, wat de bevinding kan verklaren dat kinderen met ADHD een voorkeur laten zien voor gemakkelijke werkjes vergeleken met gezonde kinderen, minder plezier ondervinden om dingen te leren en meer afhankelijk zijn van externe feedback om hun gedrag te beoordelen.

In meerdere theoretische modellen van ADHD staat een afwijkende gevoeligheid voor contingenties centraal, hoewel de rol van contingenties binnen deze modellen zeer uiteenlopend is. Een aantal modellen gaat er vanuit dat kinderen met ADHD *minder gevoelig zijn voor straf en beloning* vergeleken met gezonde kinderen. Kinderen met ADHD zouden een verhoogde beloningsdrempel hebben, waardoor ze meer beloning nodig hebben dan gezonde kinderen om hiervan te kunnen profiteren. Een neurobiologisch model van ADHD laat zien dat dit veroorzaakt wordt door een disfunctie in de dopamine transmissie in het frontale deel van het brein, waardoor het effect van een beloning sneller uitdooft. In andere modellen staat centraal dat kinderen met ADHD vooral ongevoelig zijn voor straf (of uitblijven van beloning). Naast de modellen die suggereren dat kinderen met ADHD minder gevoelig zijn, wordt er ook wel beweerd dat kinderen met ADHD juist *méér gevoelig zijn voor contingenties*. Kinderen met ADHD zouden meer gefrustreerd zijn dan gezonde kinderen wanneer zij geen beloning krijgen. Als laatste zijn er theoretische raamwerken waarin bij ADHD een *verhoogde afhankelijkheid van externe prikkels* zoals een beloning centraal staat, wat verklaart waarom kinderen met ADHD vergeleken met gezonde kinderen moeite hebben om zichzelf optimaal te motiveren waardoor hun prestatie suboptimaal blijft. Omdat de modellen zeer heterogeen zijn is het binnen het onderzoek naar de rol van contingenties bij kinderen met ADHD belangrijk om verschillende aspecten te toetsen om een afwijkende gevoeligheid voor straf en beloning in kaart te brengen: het effect van de contingentie ten opzichte van geen contingentie, evenals de valentie (beloning versus straf), de hoogte, en de frequentie hiervan. Deze vier variabelen zijn onderzocht in de studies die besproken worden in dit proefschrift.

Psychofysiologische Markers

De invloed van contingenties op ons gedrag (en emoties) wordt onder andere bepaald door veranderingen die de contingenties te weeg brengen in het autonome zenuwstelsel. Het autonome zenuwstelsel zorgt ervoor dat ons systeem klaar gemaakt wordt voor een gepaste respons op een externe prikkel, waarbij er (onder andere) veranderingen plaats vinden in de hartslagfrequentie en de galvanische huidgelei-

dingsrespons. Het bestuderen van het autonome systeem bij kinderen met ADHD kan daarom meer inzicht geven in de processen die ten grondslag liggen aan een afwijkende gevoeligheid voor contingenties bij kinderen met ADHD.

Een gangbaar model dat verklaart hoe ons gedrag wordt beïnvloed door motivationele factoren is het BIS/BAS model. Volgens dit model spelen twee onafhankelijke hersensystemen die nauw in balans zijn een belangrijke rol. Het 'behavioral activation system' (BAS) zorgt voor de initiatie van gedrag en het 'behavioral inhibiton system' (BIS) zou gedrag juist remmen. Het BAS wordt geactiveerd door positieve prikkels zoals een beloning (of het uitblijven van straf), terwijl het BIS wordt geactiveerd door negatieve prikkels zoals straf (of het uitblijven van beloning). Het BIS is dan ook gerelateerd aan gevoelens van angst. Psychofysiologische studies laten zien dat activatie van het BAS gepaard gaat met een toename in de hartslagfrequentie, terwijl activatie van het BIS gepaard gaat met een verhoogde huidgeleidingsrespons. ADHD symptomen (aandachtstekort, hyperactiviteit en impulsiviteit) zouden het resultaat zijn van een slechte balans tussen het BIS en het BAS. Kinderen met ADHD zouden een zwak BIS hebben, waardoor zij minder gevoelig zijn voor straf wat als gevolg heeft dat minder gedrag geremd wordt. Veranderingen in hartslagfrequentie en huidgeleidingsrespons op straf en beloning (winnen en verliezen van geld) bij kinderen met ADHD worden onderzocht in de Hoofdstukken 2, 3, 4, en 6

Om een optimale prestatie te kunnen leveren is de controle over de toewijzing van aandacht van groot belang. Taken die lastiger zijn om uit te voeren vergen immers meer aandacht dan gemakkelijke taken. Bij de toewijzing van aandacht speelt het autonome systeem een belangrijke rol; verschillend onderzoek laat zien dat een toename in aandachtsallocatie samen gaat met een verandering in de variabiliteit van de hartslag. De variabiliteit in hartslag is de fluctuatie in de tijd tussen de hartslagen over een bepaalde periode. Niet alleen wanneer een taak moeilijker is, maar ook wanneer een taak leuker is wordt er meer aandacht besteed aan een taak. Wanneer de motivatie om een taak uit te voeren hoger is, blijkt de variabiliteit in de lage en intermediaire hartslagfrequentie (.04 - .15 Hz) omlaag te gaan. Deze afname in hartslagvariabiliteit wordt geassocieerd met veranderingen in de metabolisme in het brein. Tijdens het uitvoeren van een taak blijkt dat kinderen met ADHD een hogere variabiliteit in hartslag zien dan gezonde kinderen dat aangeeft dat zij meer moeite hebben met het sturen van hun aandacht. Indien kinderen met ADHD externe prikkels zoals beloning en straf nodig hebben om hun aandacht te verhogen, zou dat zichtbaar moeten zijn in een afname in hartslagfrequentie als zij een beloning ontvangen. Dit wordt onderzocht in Hoofdstuk 6.

Bevindingen

Dit proefschrift beoogt drie vragen te beantwoorden: (1) Zijn neurocognitieve disfuncties bij ADHD, zoals verstoringen in de cognitieve controle en temporele informatieverwerking, secundair aan een afwijkende gevoeligheid voor contingenties? (2) Zijn kinderen met ADHD gevoelig voor specifieke aspecten van contingenties? (3) Kan een afwijkende gevoeligheid voor contingenties bij kinderen met ADHD verklaard worden door een afwijkende autonome respons op straf en beloning?

Neurocognitieve Disfuncties bij ADHD Secundair aan een Motivationeel Probleem?
Er wordt in dit proefschrift geen evidentie gevonden voor de suggestie dat neurocognitieve problemen van kinderen met ADHD secundair zijn aan een motivationele disfunctie als een afwijkende gevoeligheid voor contingenties. Het overgrote deel van de studies die besproken zijn in het overzichtsartikel (Hoofdstuk 2) laten zien dat zowel straf als beloning een positieve invloed had op de prestatie en zelfgerapporteerde motivatie van alle kinderen. Wanneer de prestatie gekoppeld werd aan contingenties, lieten kinderen met ADHD in vijf van de tien studies een grotere prestatieverbetering zien dan gezonde kinderen. Dit suggereert dat kinderen met ADHD, iets meer dan gezonde kinderen, profiteren van contingenties. Er werden geen groepsverschillen gevonden in motivatie wat aangeeft dat prestatieverbeteringen niet direct gekoppeld zijn aan een toename in zelfgerapporteerde motivatie.

De experimentele studies in dit proefschrift (Hoofdstukken 3, 4, 5 en 6) laten, net als Hoofdstuk 2, zien dat kinderen met ADHD een afwijkende gevoeligheid voor contingenties hebben. Er wordt evidentie gevonden voor een disfunctie bij kinderen met ADHD in cognitieve controle functies (inhibitie, en onderscheid tussen goed en fout, hoofdstuk 4), temporele informatie verwerking (Hoofdstuk 2 en 3), maar ook visuele associaties, en rekenen (beide Hoofdstuk 2), waarbij de prestatie verschillen tussen ADHD en de controle groep afnemen wanneer de prestatie onmiddellijk en regelmatig bekrachtigd wordt. In veel studies bleek echter dat de prestatie van kinderen met ADHD inferieur bleef aan dat van gezonde kinderen (Hoofdstukken 2, 3, 5 en 6).

Niet alle disfuncties bij kinderen met ADHD verminderen met de aanwezigheid van contingenties. Kinderen met ADHD lieten een verstoorde temporele informatieverwerking zien (Hoofdstuk 3), doordat zij tijdsintervallen systematisch onderschatten en een grotere variabiliteit in schattingen lieten zien. De onderschatting van tijd wordt in verband gebracht met een te snelle interne klok, waardoor tijdsintervallen 'langer lijken te duren' voor kinderen met ADHD dan voor gezonde kinderen. De variabiliteit in tijdschatting geeft aan dat kinderen met ADHD moeite hebben met de organisa-

tie van hun (motorische) output. De verstoring van de interne klok in ADHD bleek onafhankelijk van de contingentie manipulatie, terwijl het verschil in variabiliteit van tijdschattingen tussen kinderen met ADHD en gezonde kinderen verdween wanneer kinderen beloond werden voor hun prestatie. Omdat de variabiliteit van motorische output van invloed is op een verscheidenheid aan neurocognitieve taken, geven deze bevindingen inzicht in de interactie tussen motivatie en prestatie van kinderen met ADHD.

Gevoeligheid voor Specifieke Aspecten van Contingenties

Vergeleken met gezonde kinderen, lieten kinderen met ADHD een vergrootte respons op contingenties zien (een grotere prestatieverbetering dan controle kinderen). Daarnaast bleken kinderen met ADHD anders gevoelig voor de frequentie van aanbieding vergeleken met controle kinderen, hoewel de richting van dit effect niet eenduidig was. In de beslistaak waren kinderen met ADHD vergeleken met gezonde kinderen minder gevoelig voor negatieve consequenties wanneer deze niet frequent werden aangeboden (Hoofdstuk 4). De groepen was even gevoelig voor negatieve consequenties wanneer deze frequent werden aangeboden. In de contingentie-leertaak (Hoofdstuk 5) waarbij kinderen een plaatje aan een responsknop moesten koppelen en daarvoor beloond werden, waren kinderen met ADHD ongevoelig voor veranderingen in de frequentie van beloning, terwijl de gezonde controle groep beter presteerde bij een laag- dan hoogfrequente beloning.

Er is geen evidentie gevonden voor een specifieke gevoeligheid voor de valentie (straf versus beloning) van continenties; bij zowel straf als beloning verbeterde de prestatie van kinderen met ADHD in eenzelfde mate. Als laatste bleek dat kinderen met ADHD niet méér dan gezonde kinderen profiteerden van een grote hoeveelheid beloning, wat pleit tegen de hypothese dat kinderen met ADHD een hogere drempel hebben om een beloning waar te kunnen nemen.

Fysiologische Respons op Contingenties

In dit proefschrift wordt evidentie gevonden voor een afwijkende autonome respons op contingenties bij kinderen met ADHD. De resultaten zijn echter niet eenduidig. Uit Hoofdstuk 2 blijkt dat kinderen met ADHD een verkleinde autonome reactie (hartslagfrequentie en huidgeleidingsrespons) laten zien op zowel straf als beloning. Dit suggereert dat kinderen met ADHD een afwijking laten zien in de activatie van het sympathische zenuwstelsel in respons op motivationele informatie. De experimentele studies in dit proefschrift (Hoofdstukken 3, 4, en 6) laten echter geen bewijs zien voor een verkleinde autonome respons bij kinderen met ADHD. In Hoofdstuk 4 bleek de hartslag respons op het ontvangen van een beloning van kinderen met ADHD vergeleken met een controle groep zelfs vergroot.

Daarnaast lieten kinderen met ADHD vergeleken met een gezonde controle groep een abnormale autonome reactie (hartslagvariabiliteit en huidgeleidingsrespons) zien na het ontvangen van feedback over hun prestatie (Hoofdstukken 3, 4, en 6). Deze abnormale fysiologische respons bleek echter te verdwijnen wanneer de feedback was gekoppeld aan contingenties zoals straf of een beloning. Interessant genoeg bleken naast de 'normalisatie' van de fysiologische respons, de prestatieverschillen van kinderen met ADHD en gezonde kinderen te verdwijnen. In de timing studie (Hoofdstuk 3), lieten kinderen met ADHD in de neutrale conditie een kleinere huidgeleidingsrespons zien in reactie op feedback vergeleken met controlekinderen. In de contingentiecondities was dit verschil echter verdwenen, evenals de prestatieverschillen in respons variabiliteit. In de beslisstudie (Hoofdstuk 4) was de huidgeleidingsrespons na een ongunstige keuze kleiner dan die van controlekinderen wanneer de frequentie van de verliezen laag was. Deze afwijkende huidgeleidingsrespons kwam overeen met het ongunstige keuzegedrag dat kinderen met ADHD lieten zien ten opzichte van de controlegroep. Wanneer de frequentie van verliezen echter hoog waren, verdwenen de groepsverschillen in huidgeleidingsrespons en in beslisgedrag. De bevindingen suggereren dat de huidgeleidingsrespons gerelateerd is aan een de bewustwording van de consequenties van feedback (zie Discussie van Hoofdstuk 3).

Hoofdstuk 6 laat zien dat kinderen met ADHD, in tegenstelling tot de controlegroep, een afname in de hartslagvariabiliteit lieten zien (geassocieerd met een toename in de toewijzing van aandacht) wanneer feedback werd gekoppeld aan contingenties. Deze bevindingen suggereren dat een toename in motivatie door de koppeling van een consequentie aan de prestatie (winnen en verliezen van geld) resulteert in een toename in de controle over de aandachtstoewijzing bij kinderen met ADHD, waardoor de prestatie disproportioneel verbetert.

Conclusies

Dit proefschrift laat zien dat de prestatie van kinderen met ADHD op cognitieve taken verbetert ten opzichte van gezonde kinderen wanneer de prestatie onmiddellijk en consistent bekrachtigd wordt. Deze bevinding wijst erop dat kinderen met ADHD moeite hebben om optimaal te presteren als er geen contingenties aanwezig zijn. Ondanks de verbetering in taakprestatie, bleef de prestatie in veel studies echter inferieur aan dat van gezonde controlekinderen. Dit geeft aan dat een verstoorde cognitieve controle of temporele informatieverwerking zoals geobserveerd bij kinderen met ADHD niet geheel verklaard kan worden door een motivatieprobleem. Meerdere neurocognitieve disfuncties waaronder een afwijkende gevoeligheid voor contingenties lijken bij te dragen aan de ontwikkeling van ADHD.

Naast de bevinding dat kinderen met ADHD vergeleken met controle kinderen gevoeliger zijn voor de aanwezigheid van externe contingenties (onafhankelijk of dit beloning of straf betreft), blijken kinderen met ADHD anders te reageren op de frequentie van aanbieding van deze contingenties. Kinderen met ADHD bleken verminderd gevoelig te zijn voor straf als deze infrequent vergeleken met frequent werd aangeboden; meer studies zijn echter nodig om dit te bevestigen.

Psychofysiologisch gezien is er enige evidentie voor een afwijkende autonome respons op contingenties bij kinderen met ADHD vergeleken met gezonde kinderen, hoewel de bevindingen niet eenduidig zijn. Kinderen met ADHD vergeleken met gezonde kinderen lieten een afwijkende psychofysiologische respons zien op feedback, wat verdween wanneer de feedback verbonden werd aan contingenties zoals het winnen of verliezen van geld. De afwijkende fysiologische respons bij ADHD kinderen ging gepaard met een verminderde taakprestatie vergeleken met de gezonde controlegroep, hoewel het niet duidelijk was of dit een causale relatie betrof.

Implicaties

De bevinding dat kinderen met ADHD profiteren van contingenties, benadrukt de rol van gedragsmatige interventies die gebruik maken van straf (time out) en beloning om gedrag te sturen (mediatietherapie). Contingentieprogramma's die gebruik maken van deze positieve en negatieve bekrachtiging, blijken effectief in het verhogen van taakrelevant gedrag bij kinderen met ADHD. Het is daarom van belang te onderzoeken onder welke condities (beloning, straf, duur of frequentie van de contingentie) kinderen met ADHD optimaal presteren.

Mogelijk is een afwijkende gevoeligheid voor contingenties bij kinderen met ADHD het gevolg van een leergeschiedenis. Tijdens de ontwikkeling worden kinderen met ADHD geconfronteerd met cognitieve en motorische problemen die kunnen leiden tot sociale afwijzing. Deze ervaringen kunnen ertoe bijgedragen hebben dat de perceptie van straf en beloning verstoord is. Toekomstige studies zullen zich moeten richten op de factoren tijdens de ontwikkeling van kinderen met ADHD die kunnen bijdragen aan de afwijkende gevoeligheid voor straf en beloning.

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