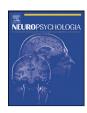
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Delay Aversion in Attention Deficit/Hyperactivity Disorder: An empirical investigation of the broader phenotype

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ABSTRACT

Background: Delay-related motivational processes are impaired in children with Attention Deficit/ Hyperactivity Disorder (ADHD). Here we explore the impact of ADHD on the performance of three putative indices of Delay Aversion (DAV): (i) the choice for immediate over delayed reward; (ii) slower reaction times following delay; and (iii) increased delay-related frustration—to see whether these tap into a common DAv construct that differentiates ADHD cases from controls and shows evidence of familiality. Method: Seventy seven male and female individuals (age range 6–17) with a research diagnosis combined type ADHD, 65 of their siblings unaffected by ADHD and 50 non-ADHD controls completed three delay tasks

Results: As predicted the size of the correlation between tasks was small but a common latent component was apparent. Children with ADHD differed from controls on all tasks (d=.4-.7) and on an overall DAv index (d=.9): The battery as a whole demonstrated moderate sensitivity and specificity. In general, deficits were equally marked in childhood and adolescence and were independent of comorbid ODD. IQ moderated the effect on the MIDA. Scores on the DAv factor co-segregated within ADHD families.

Discussion: There is value in exploring the broader DAv phenotype in ADHD. The results illustrate the power of multivariate approaches to endophenotypes. By highlighting the significant, but limited, role of DAv in ADHD these results are consistent with recent accounts that emphasize neuropsychological heterogeneity.

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1. Introduction

In recent years the phenotype of childhood disorders, such as Attention Deficit/Hyperactivity Disorder (ADHD), has been extended from observable clinical symptoms (i.e. the exophenotype) to neuro-psycho-biological characteristics thought to mark putative causal pathways to the disorder (i.e. endophenotypes; Castellanos & Tannock, 2002). A range of ADHD endophenotypic markers have been proposed. These have typically focused on cognitive processes encompassed by the concept of executive function (Doyle et al., 2005). Researchers are extending this to candidate endophenotypes in the motivational and

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cognitive-energetic domains (Andreou et al., 2007; Bidwell, Willcutt, DeFries, & Pennington, 2007; Marco et al., in press).

An altered response to delayed outcomes, first identified as a relevant factor in ADHD by Douglas and Parry (1983), is one such candidate (Sagvolden, Johansen, Aase, & Russell, 2005; Sonuga-Barke, 2002, 2003, 2005). The fact that children with ADHD exhibit a preferential response to immediate as compared to delayed outcomes is one of the most consistent findings in the motivational literature (Luman, Oosterlaan, & Sergeant, 2005; Sonuga-Barke, Sergeant, Nigg, & Willcutt, 2008). For instance, when given the choice, children with ADHD have a stronger preference for smaller sooner (SS) over large later (LL) rewards than controls, even when this leads to less rewards over a testing sessions (Antrop et al., 2006; Dalen, Sonuga-Barke, Hall, & Remington, 2004; Kuntsi, Oosterlaan, & Stevenson, 2001; Luman et al., 2005; Marco et al., in press; Schweitzer & Sulzer-Azaroff, 1995; Solanto et al., 2001; Sonuga-Barke, Taylor, Sembi, & Smith, 1992). A recent review (Sonuga-Barke et al., 2008) of two tasks commonly used to index this tendency

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(Maudsley Index of Delay Aversion, MIDA; Kuntsi et al., 2001; and the Choice Delay Task, CDT; Sonuga-Barke et al., 1992) reported pooled effects sizes for case-control differences which compare favourably with those reported for executive function deficit (Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005). Data from other paradigms also support altered response to delay as a putative endophenotypic marker for ADHD. Children with ADHD display a bias towards task responses tied to immediate rewards (Tripp & Alsop, 2001); they prefer reward immediacy to high reward rate or task ease (Neef et al., 2005), and they discount future rewards (Barkley, Edwards, Laneri, Fletcher, & Metevia, 2001; but see Scheres et al., 2006 for a counter case). According to a number of theories these effects are thought to be grounded in the neurobiology of the frontostriatal reward circuits of the brain (with especially prominent roles for the orbito-frontal cortex and ventral striatum; Cardinal. Pennicott, Sugathapala, Robbins, & Everitt, 2001; Sagvolden et al., 2005: Scheres, Milham, Knutson, & Castellanos, 2007), and are modulated by alterations in catecholamine functioning (especially dopamine; Tripp & Wickens, 2007; Winstanley, Theobald, Dalley, Cardinal, & Robbins, 2006).

The *Delay Aversion* (DAv) model of ADHD makes a number of specific predictions about the effects of delay in different contexts. These differentiate it from other motivational models (Sagvolden et al., 2005; Sonuga-Barke et al., 2008; Tripp & Wickens, 2007). These predictions are derived from the theory that the constitutionally based delay-related effects associated with fundamental alterations in the signaling of delayed rewards, discussed above, are compounded by an acquired secondary motivation to escape or avoid delay. This is hypothesized to be conditioned over time in response to repeated exposure to social censure and failure in delay-rich settings experienced by children with altered delay-reward signaling (Sonuga-Barke, 2003), predictions that are yet to be tested empirically.

Furthermore, in the model, this acquired motivational attitude is expressed in different ways as a function of whether or not environmental delay levels can actually be reduced (i.e. whether there is a choice or not). So for instance, in the choice settings described above the constitutionally based and acquired elements combine to create a marked preference for immediate over delayed outcomes (Sonuga-Barke et al., 2008). This model of choice behaviour is supported by a recent study demonstrating that ADHD children and adolescents chose SS over LL more than controls and this tendency was exacerbated in a condition when this response style reduced total delay across a session (Marco et al., in press).

While the preference for SS over LL expressed in choice situations is regarded by many as the hallmark of DAv, the DAv theory implicates a broader phenotype marked by a characteristic response to the imposition of delay in situation where escape and avoidance of it is not possible (Sonuga-Barke, 1994, 2005). Although much less frequently investigated than choice behaviour, these putative markers of the DAv endophenotype were described in the earliest theoretical formulation (Sonuga-Barke, 1994). According to the model, the imposition of fixed delay creates frustration and emotional arousal and leads to attempts to modify the experience of waiting and so reduce the aversiveness of delay. In terms of behaviour it is hypothesized that this will be achieved by engaging in patterns of stimulus-seeking behaviour that speed up the passage of time (i.e. increased activity and attention) but may reduce the quality of performance especially on long and boring tasks or under slow event rate conditions.

These predictions are supported by data from a number of studies using tasks with a fixed delay component. For instance, children with ADHD are unusually vigilant to environmental delay-related cues (Sonuga-Barke, De Houwer, De Ruiter, Ajzenstzen, & Holland, 2003) suggesting an increased emotional salience for delay. They

find the imposition of unexpected delay more frustrating than controls as indexed by an increased rate of responding during the delay period on the Delay Frustration Task (DeFT; Bitsakou, Antrop, Wiersema, & Sonuga-Barke, 2006). They show more activity and increased responding during fixed periods of delay or the extinction of reinforcers (Sagvolden, Aase, Zeiner, & Berger, 1998). Finally, in terms of time on task and event rate effects children with ADHD tend to disengage from long and boring tasks with the passage of time and there is a consistent effect of slow event rate and/or long inter-stimulus interval on ADHD children's performance, reaction times and reaction time variability (Aase & Sagvolden, 2006; Andreou et al., 2007; Wiersema, van der Meere, Roeyers, Van Coster, & Baevens, 2006).

According to the DAv model these different expressions of delay-related behaviour in different choice and non-choice settings and on different tasks by children with ADHD are manifestations at least in part of an underlying core latent construct or trait—DAv. This particular prediction of the DAv theory has not been tested to date. The current study therefore set out to explore the relationship between three putative elements of the broader DAv construct by examining the relationship between performance on three different delay tasks (choice between LL and SS; delay-related frustration in non-choice tasks and increased RTs under conditions of low event rate or long inter-stimulus intervals) and their power to discriminate ADHD cases from controls. The prediction, based on the DAv hypothesis is that these delay-related expressions will covary one with another to some degree, with each tapping into a single common latent-factor.

The extent to which this covariation between domains will be observed in the laboratory will depend on the features of the specific tasks employed. This is because, for any particular delay task performance will be determined by a myriad of factors in addition to any common effects of delay that may be present. This means that if different expressions of DAv are measured by similar tasks tapping related psychological processes, in addition to response to delay, then correlation between tasks are likely to be high-however, the extent to which this high correlation is due to delay-related elements or other elements shared between the tasks would be difficult to determine. Under such circumstances high correlations between delay tasks may, therefore, be in part spurious. If the tasks are very different and tap different psychological processes, in addition to the delay-related response, then the correlations will be much lower. Adopting this second strategy to testing delay-related domain covariation is more conservative and may underestimate the actual correlation between domains but it allows us to be more confident that manifest correlation between tasks is the product of the common focus on delay across tasks and not a spurious effect of other similarities between the tasks. This latter strategy was adopted in the current paper with the three tasks differing very greatly in their form and their response. One task was a choice task requiring a single choice response, one was a reaction time task and one was button pressing task for which the relevant output was responses per unit of time. For this reason we predicted that in the current study the correlations between tasks would be low, but a common latent factor that captures the variance shared by the tasks would be especially good at differentiating ADHD from control children.

The study also explored the co-segregation of ADHD and DAV within families by comparing DAV as a latent trait in ADHD probands and their unaffected siblings. Such an analysis will start to address the question of whether some pathways between initial causes with a familial component (i.e. genes and shared environments) and ADHD are mediated by DAV (i.e. whether DAV is an endophenotype of ADHD). According to the DAV theory, the implication of biological (i.e. dopamine function in determining

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