ACTA NEUROBIOLOGIAE EXPERIMENTALIS

Research paper Acta Neurobiol Exp 2015, 75: 326–338

Decreased frontal, striatal and cerebellar activation in adults with ADHD during an adaptive delay discounting task

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An important characteristic of childhood attention-deficit/hyperactivity disorder (ADHD) is a bias towards small immediate versus larger delayed rewards, but it is not known if this symptom is also a feature of adult ADHD. A delay-discounting task was administered to participants with adult ADHD and a comparison group in conjunction with functional magnetic resonance imaging. Participants responded to a series of questions that required judgments between small sums of money available immediately and larger sums obtained after a temporal delay. Question parameters were adjusted by an adaptive algorithm designed to converge on each participant's discounting indifference point, an individual set point at which there is equal valuation of both choices. In all participants, robust task activation was observed in regions previously identified in functional imaging studies of delay discounting. However, adults with ADHD showed less task activation in a number of regions including the dorsolateral prefrontal cortex, superior frontal gyrus, anterior cingulate, caudate nucleus and declive of the cerebellum. Additionally, the degree to which a participant discounted delayed rewards was inversely related to task activation in the cerebellum. The results suggest that the bias towards immediate rewards in childhood ADHD may not persist behaviorally, but instead present in adulthood as alterations in frontostriatal and frontocerebellar networks.

Key words: decision making, magnetic resonance imaging, reward, impulsive behavior, psychology, neurosciences

INTRODUCTION

Attention deficit hyperactivity disorder (ADHD) is defined by developmentally inappropriate inattention, impulsivity and motor hyperactivity (American Psychiatric Association 2000). In the United States, estimates have placed the incidence of ADHD at 8.4% for children between the ages of 6–17 (Pastor and Reuben 2008). By definition, the symptoms of ADHD emerge during childhood (American Psychiatric Association 2000). However, many children diagnosed with ADHD experience a continuation of symptoms into adulthood (for review see Wender et al. 2001). A recent study found that 4.4% of adults meet APA diagnostic criteria for ADHD (Kessler et al. 2006). The persistence of syndromatic ADHD is low upon entry into adulthood; only about 15% of persons diagnosed with ADHD in childhood meet diagnostic criteria for the disorder at age 25. However, partial remission of symptoms to a subthreshold level is common in the majority of persons with the disorder (Faraone et al. 2006). Interestingly, symptoms of inattention are more likely to persist into adulthood than symptoms of hyperactivity and impulsivity (Bramham et al. 2012) although a sizeable portion of adults meet diagnostic criteria for both symptom domains. Critically, adults with ADHD and those with sub-threshold symptoms of ADHD experience significant impairment in many areas of life resulting in divergent economic, social and healthcare outcomes (Barkley 2002).

The core hyperactive/impulsive and inattentive symptoms of ADHD are hypothesized to originate from abnormalities in frontostriatal, frontoparietal, and frontocerebellar networks (Castellanos 1997, Ernst et al. 1998, Castellanos and Tannock 2002, Willcutt et al. 2005). These networks are broadly involved in

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Received 26 January 2015, accepted 24 July 2015

executive function including working memory, inhibitory control, movement and attention. Task based functional imaging studies have identified deficits in frontostriatal recruitment on response inhibition, attention, and motivation tasks in participants with ADHD (for review see Cubillo et al. 2012). Notably, there is a failure to recruit frontostriatal regions during behavioral inhibition and cognitive control tasks (Bush et al. 1999, Durston et al. 2003) and, consequently, it is hypothesized that dysfunctional recruitment of frontostriatal regions mediates the behavioral symptoms associated with ADHD (Bush et al. 2005). Structural MRI studies of ADHD have found widespread volumetric differences, including reduced grey and white matter volume in the frontal lobes, possibly reflecting delayed or abnormal neurodevelopment (Shaw et al. 2007, Frodl and Skokauskas 2012). Studies of resting state activity in children with ADHD have found differences in inter-regional correlations within frontostriatal, frontoparietal, and frontocerebellar circuits further reinforcing the notion that abnormal brain structure produces functional differences that may ultimately affect behavior (Zang et al. 2007, Castellanos et al. 2008, Uddin et al. 2008).

Persons with ADHD are frequently described as more impulsive than those without the disorder. Impulsivity is a multifaceted construct that encompasses a number of separable traits (Gerbing et al. 1987, Evenden 1999, Moeller 2001). Experimentally, a clear deficit in response inhibition has been observed in children with ADHD who make a large number of inhibitory errors coupled with a distinctive failure to activate frontostriatal regions (Oosterlaan et al. 1998, Durston et al. 2003). Additionally, a factor analysis of functional networks in a response inhibition task showed a relationship between ADHD symptomatology and recruitment of frontal and basal ganglia networks when making inhibitory errors (Whelan et al. 2012).

A growing body of literature suggests that persons with ADHD display differences in reward evaluation that are distinct from behavioral disinhibition. It has been proposed that a hypo-responsive mesolimbic dopamine system could result in a failure to attribute salience to distant future rewards, resulting in impulsive and maladaptive behavior (Tripp and Wickens 2008). Behavioral and functional imaging studies of reward evaluation also show a clear bias toward immediate rewards in children and adults with ADHD. Sonuga-Barke and colleagues (1992) discovered that persons with ADHD are more averse to delays than age-matched controls. When given a choice between a small reward followed by a short delay and a larger reward followed by a long delay those with ADHD showed a stronger preference for small immediate rewards (Sonuga-Barke et al. 1992). The number of choices in the task session was fixed, so participants with ADHD chose to accept a smaller total reward in order to avoid the long delay after large rewards (15 seconds). It is hypothesized that delay aversion stems from a conscious choice to avoid an uncomfortable delay rather than a failure of inhibition *per se* (Sonuga-Barke and Fairchild 2012). Functional neuroimaging of a delay aversion task showed adults with ADHD had increased activation in the right amygdala proportional to delay length (Wilbertz et al. 2013). Additionally, it appears that delay aversion may make an independent contribution to ADHD symptoms that is distinct from response inhibition and other executive functions (Sonuga-Barke et al. 2003). Delay Aversion Tasks evaluate decision making over short delays; comparatively few studies have investigated the evaluation of rewards in persons with ADHD over longer delays (days to years). Delay discounting tasks ask participants to make a judgment between an immediate reward and a larger reward after a delay. A well-designed study by Wilson and colleagues (2011) observed a tendency in young children with ADHD to discount future rewards more rapidly. The rewards and delays used in the study were of small size (less than $10) due to the studied age group (7–9 years). However, it is unclear if the tendency to discount delayed rewards persists into adulthood.

The present study, to our knowledge, is the first whole-brain investigation of delay discounting in adults with ADHD. We aimed to quantify differences in reward discounting over longer delays (up to 60 days) and map the corresponding cognitive processes. An adaptive delay-discounting task was used to simultaneously measure the rate in which participants discounted the value of a distal reward and the Blood Oxygen Level-Dependent (BOLD) activation. It was hypothesized that persons with ADHD would display dysregulation in frontal, striatal, parietal and cerebellar regions as measured by blunted BOLD activation. Additionally, it was predicted that participants with ADHD would make more impulsive choices by discounting the value of distal rewards.

METHOD

Participants

Twenty-one adult participants (aged 19–45 years) were recruited for this study. Ten (seven male) had received a prior diagnosis of ADHD, and reported a continuation of symptoms since their diagnosis. Participants with ADHD were recruited from an Irish national specialist Adult ADHD Service and through an ADHD support charity. Control participants were recruited from the Dublin, Ireland community through posters advertising the study and word of mouth recommendations. Ethical approval was granted by St. Patrick's University Hospital, Dublin and Trinity College Dublin Psychology Department Ethics Committee.

All participants were required to be aged between 18 and 50 years, right-handed, without neurological disorder or intellectual disability. Study inclusion criteria specific to the ADHD group included a prior diagnosis of ADHD in childhood and a continuation of ADHD symptoms affirmed by the Conners Adult ADHD Rating Scale (CAARS) (Conners et al. 1999). Study exclusion criteria specific to the control group included history of psychiatric disorder and current use of psychoactive medications. Participants in the ADHD group were exempt from these criteria because of the common use of psychoactive medication to treat ADHD symptoms and frequent co-morbidity of ADHD with other psychiatric disorders. Five participants in the ADHD group were receiving medication for treatment at the time of study. Of these, four were using a stimulant medication and one was taking a non-stimulant medication for the treatment of ADHD. Participants using stimulants were asked to discontinue their use of the medication 48 hours prior to testing. Given the pharmacokinetics of popular stimulant medications, we estimate participants were abstinent from medication for at least three half-lives. One participant using a non-stimulant, antidepressant drug was not asked to discontinue treatment prior to the study because it is not advisable to discontinue antidepressant medication for a short period. Only adults with a probable diagnosis of ADHD combined type were recruited because of evidence suggesting that reward processing is strongly correlated with symptoms of hyperactivity/impulsivity (Scheres et al. 2010). Males and females were recruited in approximate proportion to the incidence of adult ADHD in the United States (Kessler et al. 2006).

Prior to imaging, participants completed a non-standardized demographic questionnaire and a number of psychometric measures. The Wechsler Abbreviated Scale of Intelligence (WASI) 2 subtest form was used to assess overall intellectual ability (Wechsler 2006). Conners Adult ADHD Rating Scale Self-Report (CAARS) Long Form was used as a measure of current ADHD symptomatology (Conners 1999). Additionally, the Disruptive Behavior Disorders Rating Scale (DBD) (Silva et al. 2005) was used to assess the childhood symptoms of ADHD. Group demographics are summarized in Table I.

None of the participants in the study reported current use of illicit drugs (cannabis, amphetamine, cocaine, ecstasy, psilocybin mushrooms, LSD, ketamine, or heroin). There were more daily smokers in the ADHD group (n=3) than the control group (n=0). The incidence of tobacco use in the ADHD population has been shown to be reliably higher than the general population (Lambert and Hartsough 1998). Participants were not asked to refrain from smoking prior to the study.

Delay Discounting Task

The adaptive delay-discounting task employed in this study provides a measure of a participant's ability to delay the immediate gratification of a small reward for a larger future reward. Participants responded to a series of 49 questions in a single 9.5-minute run that required judgments between small sums of money available immediately and larger sums obtained after a temporal delay. The task parameters were displayed on a black background. The immediate sum appeared in a green rectangle on the left, the delay period in a red rectangle in the middle, and the later choice in a blue rectangle on the right, all in white font. Each trial lasted between 8 and 16 seconds and was terminated when the participant made a response. After a choice was selected the screen cleared and a white fixation cross appeared in the center of the screen. Stimuli presentation and response recording were managed by the Presentation® software package (Neurobehavioural Systems).

Mazur's hyperbolic discounting model was used to calculate the rate of temporal discounting for each question (Mazur 1987). The hyperbolic discounting model proposes the subjective value of a delayed choice (V) is equal to the objective value of the

Table I

Group characteristics						
	ADHD		Controls			
	M	SD	M	SD	t(19)	p
Age	28.4	8.9	25.4	5.8	0.93	0.36
Wechsler abbreviated scale of intelligence IQ	109.3	13.8	120.6	5.6	2.52	0.02
Years of education	16.8	2.0	16.2	2.1	0.69	0.50
Conners self-report ADHD scale – long form						
Inattention/memory problems	67.9	11.9	45.7	8.3	5.00	<.001
Hyperactivity/restlessness	58.2	12.4	39.2	4.3	4.78	<.001
Impulsivity/emotional lability	63.2	13.4	44.1	6.5	4.22	<.001
Problems with self-concept	60.9	10.0	42.3	5.5	5.34	<.001
DSM-IV inattentive symptoms	74.3	9.8	47.8	11.0	5.81	<.001
DSM-IV hyperactive impulsive symptoms	67.0	13.6	43.8	8.7	4.69	<.001
DSM-IV ADHD symptoms total	73.6	9.4	46.3	8.7	6.95	<.001
ADHD index	67.0	13.4	40.7	5.4	6.00	<.001
Disruptive behavior disorders rating scale (childhood)						
Number of inattentive symptoms	6.5	2.9	0.4	0.9	6.72	0.01
Number of hyperactive/impulsive symptoms	4.2	2.9	0.5	0.5	4.22	0.00
Number of oppositional defiant disorder symptoms	2.8	1.6	0.7	1.8	2.77	0.74
Number of conduct disorder symptoms	1.1	1.3	0.1	0.3	2.53	0.01

ADHD – attention deficit hyperactivity disorder; IQ – intelligence quotient; DSM-IV – diagnostic and statistical manual of mental disorders; CI – confidence interval. Equal variances assumed

delayed reward (A) divided by a term that includes the delay length (D) multiplied by a constant that describes the rate of discounting: $V=A/(1+kD)$. The parameters for a given choice in the adaptive delay-discounting task can be substituted into this equation to determine the choice's discounting constant $k_C=[(LDR/SIR)–1]/D$. The size of the small immediate reward (SIR), the size of the large delayed reward (LDR) and the length of the delay (D) were adjusted with each subsequent trial to approach the participant's indifference point, defined as the set of values at which the participant values the SIR and LDR equally. If a participant selected the immediate reward in a trial then k was decreased by 15% for the following trial. Conversely, choosing the delayed reward increased k by 15% on the subsequent trial. As the task proceeds, the value of k_c (the discounting value of an individual choice) approaches k_f (the discounting rate of the individual). When a participant is presented with a choice with a k_c equal to their individual k_f the participant is at their individual indifference point, where both choice options are considered to be equal. The immediate reward was always a random value between €20 and €30 and the

delay was always a random value between 20 and 60 days. The value of the delayed reward was calculated using the k value for the current trial. The initial k value for all participants was 0.018. To enhance involvement in the task, participants were instructed that they would receive a proportion of the reward they selected (and after the delay if they selected the delayed reward) from one of their randomly selected trials.

Functional Magnetic Resonance Imaging

Data Acquisition

Participants observed task stimuli on a head-coil-mounted mirror. All scanning was conducted on a Philips Intera Achieva 3.0 Tesla MR system (Best, The Netherlands). The MRI sequence began with a reference scan to resolve sensitivity variations. All T1-weighted image acquisitions used the parallel Sensitivity Encoding (SENSE) approach (Pruessmann et al. 1999) with a reduction factor of 2. 180 high-resolution T1-weighted anatomic MPRAGE axial images (FOV 230 mm, thickness 0.9 mm, voxel size 0.9×0.9×0.9, TR=8.4 ms, TE=3.8 ms, Flip Angle=8 degrees) were then acquired. Functional data were collected using a T2*-weighted echo-planar imaging sequence: 32 non-contiguous (10% gap) 3.5 mm axial slices covering the entire brain (TE=35 ms, TR=2000 ms, Flip Angle=90 degrees, FOV=224 mm, 64×64 mm matrix size in Fourier space).

Preprocessing

Statistical parametric mapping software (SPM8; Wellcome Trust Centre for Neuroimaging, London, UK http://www.fil.ion.ucl.ac.uk/spm) was used for image preprocessing and analysis. Data were realigned to the first functional image acquired. The structural T1 image was segmented and normalized using an iterative combination of segmentations and normalizations (Ashburner and Friston 2005). Next, the skull and soft-tissue were removed from images by only including voxels with probability values over 0.5 from the segmented grey, white and cerebrospinal fluid images. Co-registration between the functional and anatomical images was performed using the skull-stripped image. Data were then normalized to the Montreal Neurological Institute (MNI) template using the parameter file from the segmentation routine resampled into 2×2×2 mm sized voxels. Next, data were smoothed using a 6 mm full width half-maximum Gaussian smoothing kernel. Data were high-pass-filtered using a high pass cutoff of 0.008 Hz. After preprocessing participant data were manually screened for excessive head movement with the TSDiffAna toolbox.

Statistical analysis

Event-related regressors corresponding to the onset of a delay-discounting choice trial were convolved with the standard hemodynamic response. The residual effects of head motion were modeled in the analysis by including the six parameters of head motion acquired from the realignment stage of the preprocessing (Cartesian displacement and Euler angles) as covariates of no interest. The discounting constant for each participant (k_F) was estimated by averaging the discounting rates of the final two choices in the delay-discounting task (this average is the most accurate estimate of a participant's k_F as the task is designed to converge on a participant's indifference point). The difficultly of any one choice was defined as the absolute value of the difference between the discounting rate of the choice (k_C) presented and a participant's discounting constant (k_F). Choices that differ greatly from a person's discounting constant are perceived as "easy" and may result in lesser task activation. To control for the effect of choice difficulty on task activation, a parametric modulator corresponding to the relative level of difficulty for each choice was added to the within-participant general linear model. Within the time-series analysis for a given participant a parametric modulator scales the relative amplitude of the hemodynamic response for each task choice. To reduce the contribution of extreme values, the difficulty parameter was transformed by logarithm base 10. The inverse of the relative difficulty parameter was used to highlight regions of activation related to choice difficulty. The parametric modulator was defined as: $1/\log_{10}(|k_C - k_F|)$. In effect, the addition of a difficulty covariate reduced the statistical weighting of task trials that were relatively easy.

First, an activation map of all trials was constructed with a one-sample t-test (both groups combined) against a null hypothesis of zero activation. Maps of between-group activation differences were generated

by independent sample t-tests. 3dClustSim, a Monte-Carlo simulation program included in the Analysis of Functional NeuroImages software package (AFNI) (Cox 1996) was used to determine the minimum cluster size criterion for an adjusted family wise error rate of α−0.05. Significant voxels in whole-brain maps passed a voxelwise statistical threshold ($t(19)= 2.861$, $P\leq0.005$) and were part of a cluster of 75 contiguous voxels. Regions that significantly differed between participants with ADHD and controls were extracted as a region of interest (ROI). Within the ROI, a linear regression model was constructed to probe the relationship between task activation and the natural logarithm of a participant's discounting constant $\ln(k_F)$. A second 3dClustSim simulation was run for the voxels that fell within all ROIs to determine the minimum cluster size threshold for an adjusted family wise error rate of $\alpha=0.05$ (i.e., a small volume correction). Significant clusters within the ROI mask passed a voxelwise statistical threshold, $t(19)=1.729$ $P\leq0.05$, with a minimum cluster size criterion of 12 voxels. Anatomical locations of cluster centroids were identified with the Talairach Daemon (Lancaster et al. 1997, Lancaster et al. 2000) after transforming the MNI loci into Talairach coordinates (Brett et al. 2001).

Behavioral data were analyzed in the statistical package SPSS (version 20, IBM corporation). Independent samples t-tests for group differences were performed on self-reported demographic and psychometric measures. To reduce the contribution of outliers, the natural logarithm of participants' discounting constants was used (notation: $\ln(k_F)$) (Kirby et al. 1999). Additionally, correlations were tested between CAARS scores for inattention/memory problems, hyperactivity/restlessness, and impulsivity/emotional lability and $\ln(k_F)$. All statistical tests were two-tailed and the chosen threshold for significance was $P<.05$.

RESULTS

Behavioral results

Participants with ADHD had a mean $\ln(k_F)$ of −4.104 ($SD=0.556$). Controls had a mean $\ln(k_F)$ of −4.677 ($SD=0.918$) However, an independent samples t-test did not reach statistical significance $t(19)=1.622$ $P=0.104$. As expected, participants with ADHD had significantly greater ADHD symptoms in all categories of the CAARS and DBD scales, except 'oppositional defiant disorder symptoms'. Participants with ADHD and controls signficantly differed in full scale IQ, $t(19)=2.52$ $P=0.02$ (see Table I for a summary of demographic and psychometric differences). There was no relationship observed between participants' IQ and $\ln(k_F)$, $r(19)=-0.193$ $P=0.401$. However, a significant non-parametric correlation was observed between participants' $\ln(k_F)$ and CAARS t-score of impulsivity/emotional lability, $r_s(19)=0.458$ $P=0.037$.

Neuroimaging results

Fig. 1 shows task-related activation (red) and deactivation (blue) for all study participants. Regions where task activation was significantly greater in the control group than in the ADHD group (green) are detailed in Table II. These regions included the dorsolateral prefrontal cortex, superior frontal gyrus, anterior cingulate, caudate nucleus and declive of the cerebellum. There were no group differences in areas of task-associated deactivation, nor were there regions that were significantly more active in participants with ADHD. No regions of task activation were significantly correlated with IQ and its inclusion as a covariate in the between-group comparison did not alter the significance of the between-group results. Additionally, the inclusion of conduct disorder symptoms as a covariate did not change the pattern of results. Of the regions that were significantly more active within controls during the delay-discounting task, two regions within the right declive of the cerebellum were significantly correlated with participants' $\ln(k_F)$. Participants who steeply discounted delayed rewards had lesser activation in these regions. Additionally, just below the cluster threshold of 12 voxels, a region within the middle frontal gyus (11 voxels in size) was significantly correlated with participants' $\ln(k_F)$. Descriptive statistics and scatterplots for all three regions are provided in Fig. 2.

DISCUSSION

We report what is, to our knowledge, the first fMRI whole-brain analysis of delay discounting behavior in adults with ADHD. In the absence of significant group differences in discounting rate, persons with ADHD showed significantly less activation in several regions associated with choosing between immediately available and delayed rewards (Fig. 1). Moreover, three

regions (one just below the cluster size criterion) within those that differed by group showed a significant correlation with participants' rate of delay discounting; these were in left dorsolateral prefrontal cortex and right cerebellum (Fig. 2). These findings provide evidence for neurobiological differences in adult ADHD in regions involved in delay discounting behavior.

One previous fMRI study of delay discounting and ADHD focused on adolescents, it reported widespread decreases in frontal and parietal cortices as well as the cerebellum (Rubia et al. 2009). Additionally, there have been a number of neuroimaging studies on adults with ADHD that identify the continuation of dysregulated reward processes. A study of immediate and delayed reward processing in adults observed hyporesponsiveness in the ventral striatum and hyper-responsiveness in the amygdala and the caudate (Plichta et al. 2009). Two studies of the monetary incentive delay (MID) task in adolescents showed altered frontostriatal activation in proportion to hyperactive impul-

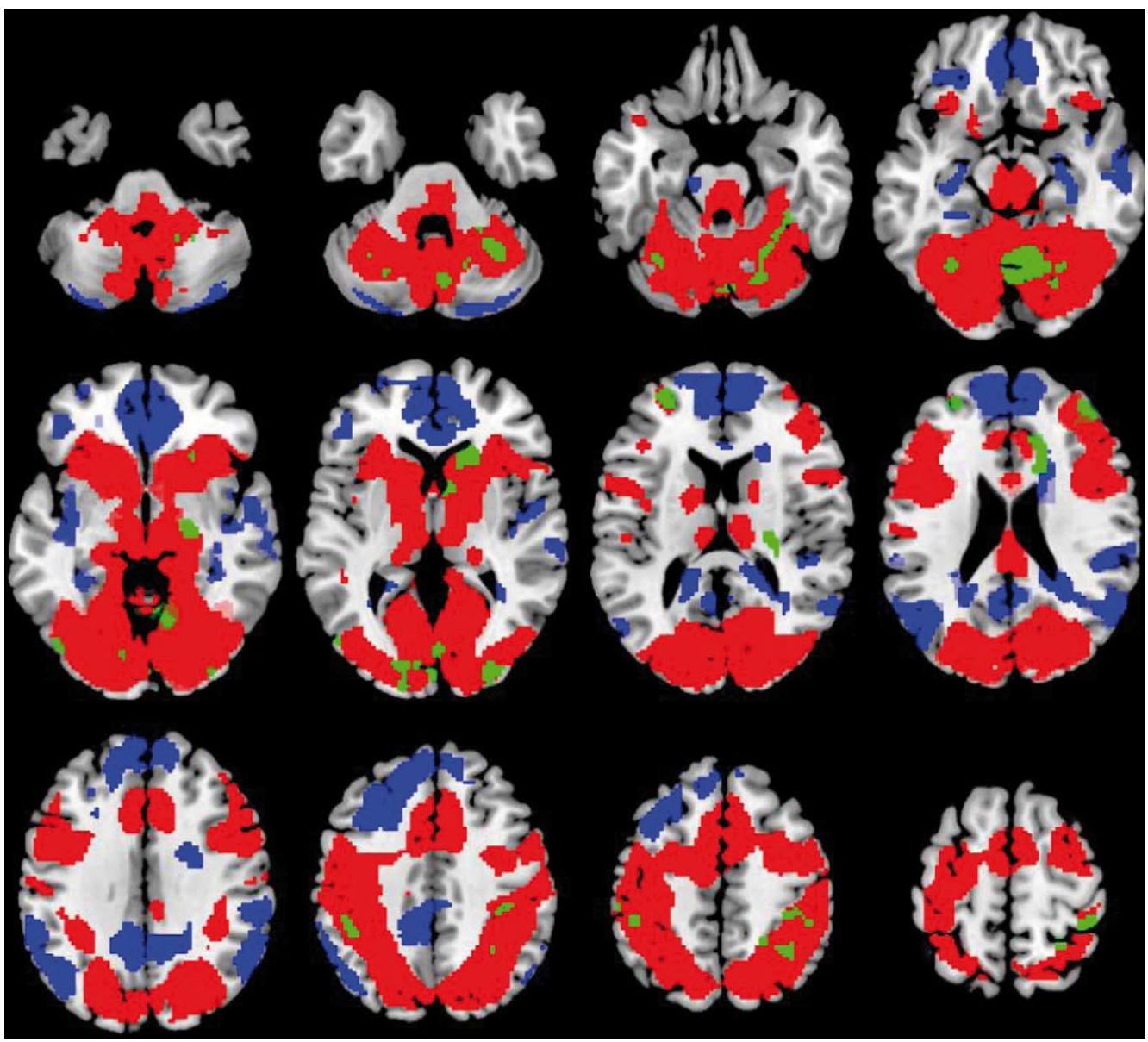

Fig. 1. Task activations and group differences. Axial sections: regions of task activation (red) and deactivation (blue) in all participants during the adaptive delay discounting task. Regions where controls had significantly more task activation than participants with ADHD are identified in green.

Table II

Cluster centroids – control group greater than ADHD group					
Cluster	Structure	Volume(μl)	HS	MNI coordinates [x, y, z]	B.A.
Frontal Lobe					
1	Superior Frontal Gyrus	968	L	[−30, 51, 17]	10
2	Anterior Cingulate	1152	R	[15, 21, 21]	32
3	Middle Frontal Gyrus	704	R	[39, 44, 25]	10
Parietal Lobe					
4	Inferior Parietal Lobule	1048	L	[−50, −35, 46]	40
5	Precuneus	648	R	[33, −51, 48]	7
6	Postcentral Gyrus	1728	R	[39, −35, 53]	3
7	Sub-Gyral	320	R	[24, −48, 56]	40
Temporal Lobe					
8	Inferior Temporal Gyrus	304	L	[−47, −77, −2]	19
Occipital Lobe					
9	Cuneus	1912	L	[−7, −86, 2]	17
10	Middle Occipital Gyrus	904	R	[32, −88, 1]	18
Subcortical					
11	Caudate Head	1184	R	[17, 21, 3]	
12	Lateral Globus Pallidus	608	R	[22, −17, −4]	
13	Caudate	312	R	[6, 5, 6]	
Cerebellum					
14	Declive	416	L	[−25, −67, −29]	
15	Declive	760	L	[−33, −61, −21]	
16	Declive	9600	R	[14, −62, −21]	
17	Declive	320	R	[42, −62, −22]	

MNI – Montreal Neurological Institute; HS – Hemisphere; B.A. – Brodmann Area

sive symptoms (Scheres et al. 2007, Ströhle et al. 2008). A combination of increased and reduced activation was observed, with hypo-activity in the striatum for reward anticipation and increased activity in the DLPFC and orbitofrontal cortex for reward receipt. Although there are some inconsistencies between each of these studies, evidence suggests for reward processes frontal, striatal and cerebellar dysfunction persists in adults with ADHD across a variety of behavioral tasks, including the delay-discounting.

More broadly, there is a significant literature documenting deficits in executive function in ADHD. Weaker task activation in children with ADHD has been observed in regions related to executive function for a wide variety of experimental tasks (for review see Cubillo et al. 2012). Fewer fMRI studies of executive function have been conducted on adults with ADHD. Of the studies that have been conducted, several have shown decreased activation as well as functional connectivity in frontostriatal, frontocerebellar and frontoparietal networks (Bush et al. 1999, Valera et al. 2005, Wolf et al. 2009). Conversely, there are other studies in adults that show increased activation throughout the frontal, parietal and occipital lobes during tasks of executive function (Hale et al. 2007, Banich et al. 2009, Dibbets et al. 2010). It has been hypothesized that inconsistencies across studies of adult ADHD, as compared to child/adolescent ADHD, may be due to confounding factors such as the need for retrospective diagnoses, medication effects, symptom remission and comorbid disorders (Cubillo and Rubia 2010). The present study adds support to the hypothesis that frontostriatal, frontocerebellar and frontoparietal hypo-activation persists into adulthood.

Of regions that differed between groups in this study, the right declive of the cerebellum and left DLPFC (albeit just below the cluster size criterion) were inversely correlated to participants' $\ln(k_F)$. Decreased activation of the DLPFC has previously been associated with greater discounting of future rewards (Hoffman et al. 2008, Bickel et al. 2009). A structural imaging study found that dorsolateral and inferolateral prefrontal cortex grey matter volumes were inversely correlated with participants discounting constant (Bjork et al. 2009). Additionally, disruption of the left lateral prefrontal cortex with transcranial magnetic stimulation increased the frequency with which participants chose an immediate reward in a delay discounting task, suggesting that the left PFC is critical for self-control processes that defer immediate reward (Figner et al. 2010). The finding that task activation in the declive was correlated with partici-

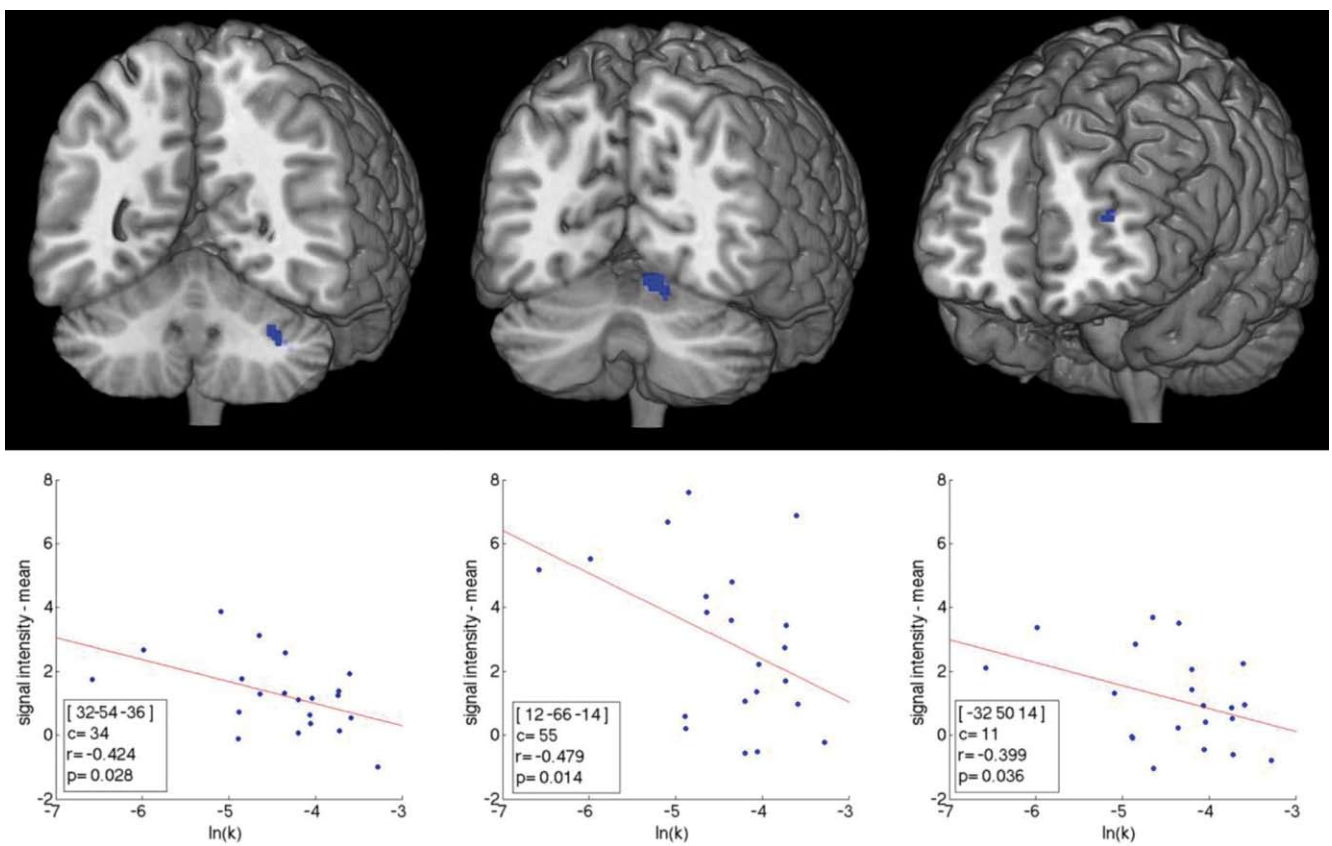

Fig. 2. Correlations between activation and discounting rates. Regions within the group differences map where task activation is inversely correlated with the natural logarithm of participant discounting constants. Region loci, correlation confidents, p-values, and least squares regression lines are detailed within scatterplots.

pants' $\ln(k_F)$ is, to our knowledge, a novel finding and it suggests a role for frontocerebellar circuitry in intertemporal choice. Previous studies have shown that persons with ADHD have deficits in motor and perceptual timing functions that are dependent on cerebellar activation (Noreika et al. 2013). It has been proposed that the cerebellum is involved in the time dependent perception of a delayed reward (Rubia et al. 2009). Additionally, a meta-analysis of structural MRI studies in ADHD has shown abnormal cerebellar structure with the largest differences observed in the right lobe (Valera et al. 2007). An altered perception of time in the context of a delayed reward is a potential mechanism for more impulsive discounting.

Behaviorally, participants with ADHD trended toward discounting future rewards more than controls but statistical significance was not achieved. Past studies of delay aversion (for very short delays) have shown robust differences between persons with ADHD and controls (Sonuga-Barke et al. 1992, Tripp and Alsop 2001, Scheres et al. 2010). However, reports of delay discounting over long periods of time are inconsistent. There have been accounts of more impulsive delay discounting in both children and adults (Conners et al. 1999, Scheres et al. 2010, Hurst et al. 2011) but other studies have reported a null result (Scheres et al. 2006, Scheres et al. 2008). Interestingly, a well powered study of delay discounting in children showed a significant result, so long as IQ was not a covariate in the study design (Wilson et al. 2011). Past work has shown that discounting of future rewards is strongly influenced by participant age and IQ (Olson et al. 2007). It is typical for a sample of subjects with ADHD to have a slightly lower average IQ than the general population (Kuntsi et al. 2004, Mayes et al. 2000). The difference in IQ is a frequently observed finding and is typically not controlled for in experimental designs. In the present study, control and ADHD groups did differ in IQ but there were no regions of task activation that were significantly correlated with IQ, and its inclusion as a covariate did not significantly alter the between-group results. There was no correlation between participant age and their discounting constants. However, there was a significant correlation between participants' $\ln(k_F)$ and CAARS t-score of impulsivity/emotional lability suggesting that individual differences in delay discounting are linked to participants impulsive symptoms.

It is important to note some of the limitations of this study. The sample size was small and did not capture group differences in delay discounting. However, functional imaging was able to detect substantial ADHD-related differences and neural correlates of discounting rate. By design, participants recruited for this study had both hyperactive/impulsive and inattentive symptoms. However, most adults with ADHD have primarily inattentive symptoms (Mick et al. 2004). A previous investigation of ADHD subtypes and delay aversion found only the combined type ADHD was related to temporal discounting (Scheres et al. 2010). The present study found impulsive discounting was most strongly correlated to symptoms of hyperactivity/impulsivity. However, the relationship between delay discounting and ADHD subtype remains unexplored.

CONCLUSION

Most of what is known about the neurobiological mechanisms of ADHD comes from studies of children and adolescents. The findings presented here are consistent with the continuation of frontostriatal, frontocerebellar and frontoparietal network dysfunction into adulthood for those with combined type symptomology. Additionally, we present new evidence that the cerebellum may mediate impulsive discounting in adults with ADHD. Given the relevance of intertemporal choice to health, social and economic outcomes, emerging knowledge of differences in delay discounting are of substantial clinical and conceptual importance.

ACKNOWLEDGEMENTS

A University College Dublin Seed Funding Award supported this research.

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