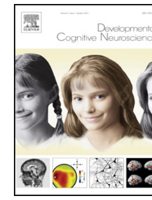
Developmental Cognitive Neuroscience 14 (2015) 38–49

Contents lists available at ScienceDirect

Developmental Cognitive Neuroscience

journal homepage: http://www.elsevier.com/locate/dcn



Feedback associated with expectation for larger-reward improves visuospatial working memory performances in children with ADHD

Rubi Hammer[a,b,*], Michael Tennekoon[a,b], Gillian E. Cooke[a,c], Jessica Gayda[a], Mark A. Stein[d], James R. Booth[a,b,e]

[a] *Department of Communication Sciences and Disorders, Northwestern University, Evanston, IL, United States*
[b] *Interdepartmental Neuroscience Program, Northwestern University, Evanston, IL, United States*
[c] *Beckman Institute for Advanced Science, University of Illinois, Urbana-Champaign, IL, United States*
[d] *Department of Psychiatry and Behavioral Sciences, University of Washington School of Medicine, Seattle, WA, United States*
[e] *Department of Communication Sciences and Disorders, The University of Texas at Austin, Austin, TX, United States*

A R T I C L E I N F O

Article history:
Received 15 September 2014
Received in revised form 8 June 2015
Accepted 16 June 2015
Available online 23 June 2015

Keywords:
ADHD
Executive functions
Feedback processing
Reward processing
Working memory

A B S T R A C T

We tested the interactive effect of feedback and reward on visuospatial working memory in children with ADHD. Seventeen boys with ADHD and 17 Normal Control (NC) boys underwent functional magnetic resonance imaging (fMRI) while performing four visuospatial 2-back tasks that required monitoring the spatial location of letters presented on a display. Tasks varied in reward size (large; small) and feedback availability (no-feedback; feedback). While the performance of NC boys was high in all conditions, boys with ADHD exhibited higher performance (similar to those of NC boys) only when they received feedback associated with large-reward. Performance pattern in both groups was mirrored by neural activity in an executive function neural network comprised of few distinct frontal brain regions. Specifically, neural activity in the left and right middle frontal gyri of boys with ADHD became normal-like only when feedback was available, mainly when feedback was associated with large-reward. When feedback was associated with small-reward, or when large-reward was expected but feedback was not available, boys with ADHD exhibited altered neural activity in the medial orbitofrontal cortex and anterior insula. This suggests that contextual support normalizes activity in executive brain regions in children with ADHD, which results in improved working memory.

1. Introduction

Attention deficit and hyperactivity disorder (ADHD) is a common neurodevelopmental disorder that affects 5–8% of the worldwide childhood population, is more prevalent in males, has high heritability (70–80%), and frequent comorbidity with other psychiatric disorders (Boyle et al., 2011; Larson et al., 2011; Thapar et al., 2013; Willcutt et al., 2010). Numerous studies show that abnormal reward processing and difficulty in delaying gratification characterize ADHD youth (Scheres et al., 2010; Ströhle et al., 2008; van Meel et al., 2011). A second, possibly related, characteristic of ADHD is greater reliance on external feedback, which is primarily evident in poor autonomous capacity in monitoring decision errors (Groom et al., 2010; Shiels and Hawk, 2010; van de Voorde et al., 2010). Feedback and reward may have an interactive effect, as in many scenarios feedback provides an external sensory indication for an expected reward that follows a desired action. Altered feedback and reward processing may also be related to the apparent deficits in response inhibition, altered working memory, and poor capacity in long term planning characterizing ADHD (Booth et al., 2005; Rubia et al., 2005; Wong and Stevens, 2012), though the causal nature of such relationships is unclear (Raiker et al., 2012; Schecklmann et al., 2012; Skogan et al., 2014).

Earlier findings suggest that behavioral intervention, which involves feedback and/or reward, may help children with ADHD to gain normal-like cognitive skills (Hoekzema et al., 2010; Kray et al., 2011; Lévesque et al., 2006; Strand et al., 2012; but see also Sonuga-Barke et al., 2013). Nonetheless, these studies differed from one another in the administration of feedback and reward, which likely contributed to the inconsistency in the reported findings. This limits the ability to infer which contextual factors

* Corresponding author at: Department of Communication Sciences and Disorders, 2240 Campus Drive, Northwestern University, Evanston, IL 60208-2952, United States. Tel.: +1 847 497 1726.
E-mail addresses: rubi.hammer@northwestern.edu, rubihammer@gmail.com (R. Hammer).

http://dx.doi.org/10.1016/j.dcn.2015.06.002

benefit behavioral intervention in ADHD. Here we studied the interactive effect of feedback and reward on the performance of boys with ADHD combined-type in visuospatial working memory (VSWM) tasks. We disassociated the manipulation of the amount of expected monetary reward (large-reward versus small-reward) from the availability of trial-by-trial feedback (no-feedback versus feedback), and tested if either one of these two factors is necessary or sufficient for improving VSWM performance of boys with ADHD. The functional magnetic resonance imaging (fMRI) data collected from the ensemble of VSWM tasks enabled determining if the reliance of children with ADHD on feedback and reward is associated with altered neural activity in a single brain region, or if it is associated with altered neural activity in several brain regions. Moreover, the fMRI data enabled determining if any context dependent behavioral improvement in VSWM tasks in ADHD is associated with the normalization of patterns of brain activity in the same neural network used by normal controls (NC), or if it is associated with a compensatory neural mechanism not being used by NC.

The VSWM network primarily includes the superior to inferior parietal cortices and the dorsolateral prefrontal cortices, and it overlaps with the dorsal attention network (Awh and Jonides, 2001; Barbey et al., 2013; Gazzaley and Nobre, 2012; LaBar et al., 1999). This network enables short-term storage of events that are in the focus of attention and the volitional direction of attention to chosen stimuli. Individuals with ADHD exhibit lower levels of activity during working memory tasks, as compared with NC, in several regions within the VSWM network, including the inferior-parietal cortex (Vance et al., 2007) and middle frontal gyrus (Ehlis et al., 2008; Fassbender et al., 2011). Moreover, it has been suggested that poor working memory, poor response inhibition and poor action selection in ADHD all stem from right dorsolateral prefrontal cortex abnormalities (Clark et al., 2007; McNab et al., 2008).

The VSWM network has an extensive interaction with the ventral attention network, which includes the inferior frontal gyrus, the ventral medial prefrontal and orbitofrontal cortex (OFC), and the temporoparietal junction and superior temporal cortex (Prado and Weissman, 2011; Weissman and Prado, 2012). The ventral attention network acts as a salience detection system, enabling the involuntarily reorientation of attention to unexpected external events (Corbetta et al., 2008; Vossel et al., 2014). This may be related to the role of the ventral attention network in reward processing, which also involves the ventral striatum, anterior cingulate and the limbic system (Kable and Glimcher, 2007; Kennerley and Wallis, 2009; Klingberg, 2010; Rushworth et al., 2011). It has been suggested that the OFC, together with other ventral frontal cortices, is specifically involved in processing the properties (quantity and quality) of reward-related stimuli (Howard et al., 2015; Pauli et al., 2012; Roesch and Olson, 2004). This enables the OFC to serve as a specialized short term memory buffer, monitoring which recent actions were rewarded and predicting which future actions are most likely to be rewarded (Kahnt et al., 2010). Individuals with ADHD show relatively low sensitivity to reward related information as compared with NC, evident in lower neural activity levels in the ventral striatum (Ströhle et al., 2008), and poor OFC responsiveness to reward (Cubillo et al., 2012; Wilbertz et al., 2012).

The anterior insula plays a critical role in mediating between the ventral and dorsal executive networks (primarily in the right hemisphere), and it exhibits significant functional connectivity to dorsal prefrontal brain regions involved in goal-directed behavior (Eckert et al., 2009). A second key brain region playing a related role is the anterior cingulate, which interacts with primary sensory cortices in tasks that require action selection and attention control (Crottaz-Herbette and Menon, 2006; Silvetti et al., 2013). Despite primarily being associated with the limbic system, the anterior insula and the anterior cingulate are more recently considered as part of a salience detection network, and it is suggested that they complement the central executive network in risk/gain prediction (Menon and Uddin, 2010; Preuschoff et al., 2008; Späti et al., 2014; Taylor et al., 2009). Whenever decision switching or response inhibition is required, children with ADHD are likely to exhibit poor cognitive control associated with lower levels of neural activity in the anterior insula, as compared with NC subjects (Cubillo et al., 2010; Morein-Zamir et al., 2014).

Since children with ADHD display increased reliance on external feedback and reward, we hypothesized that either the lack of trial-by-trial feedback (Wiersema et al., 2009), or an expectation for insignificant reward (Bitsakou et al., 2009), would result in an impaired VSWM performance in ADHD. Since the VSWM network and the processing of reward and feedback involve several brain regions, we expected impaired performances in ADHD to be associated with abnormal pattern of neural activity distributed across several brain regions, where the specific nature of this distributed pattern would depend on the characteristics of the performed task (i.e., conditioned by the expected reward size and feedback availability). In contrast, trial-by-trial feedback associated with large-reward simulate a scenario where there is an immediate association between a desired action and a rewarding outcome, and thus this may result with better VSWM performances in ADHD. Here we had two alternative hypotheses: (i) performance improvement in ADHD would be associated with brain activity becoming more normal-like. (ii) Performance improvement in ADHD would be associated with an engagement of a compensatory neural mechanism, which is not engaged in NC children.

Nevertheless, it is also possible that the reward and feedback manipulation would have no evident impact on VSWM in ADHD, that each of the two factors would have a similar impact on VSWM as the other, or that only one of the two factors would impact VSWM. The current study is the first to test children with ADHD by using an independent manipulation of feedback and reward. This enabled testing if either one of these two factors is necessary or sufficient for normalizing VSWM performance in ADHD. It also enabled better characterizing neurocognitive abnormalities in ADHD, by providing key insights for how reward and feedback information are integrated in normally developing brains.

2. Experimental procedures

2.1. Participants

Seventeen boys with a prior diagnosis of ADHD combined type and 17 age-matched Normal Control (NC) boys participated in the experiment. At the time of the fMRI scanning session, the boys with ADHD were off-medication for at least 24 h. Participants gave their informed consent (and parental consent) in accordance with the policies of the Institutional Review Board (IRB) at Northwestern University. Diagnoses were confirmed both by the parental report on the home version of the ADHD rating scale (DuPaul et al., 1998) and by an evaluation conducted in an interview session using the Kiddie Schedule for Affective Disorders and Schizophrenia for School Aged Children: Present and Lifetime (K-SADS-PL) version (Kaufman et al., 1997). All participants received the K-SADS-PL Disruptive Screening and Disruptive Behavior modules (used for assessing ADHD), as well as the Oppositional Defiant Disorder and Conduct Disorder modules (used for detecting comorbid disorders with shared symptoms). If the screening was positive for another disorder (which happened rarely), the participant was administered with additional modules as warranted. Individuals that were diagnosed as having another significant ongoing condition were excluded from the sample reported here.

Mean total ADHD score based on parent report was higher in the ADHD group than in the NC group (Table 1). Boys in the ADHD combined type group had both an inattentive and