Boys with Comorbid ADHD and RD Show Increasing Disengagement with Age During a Sustained Attention Task

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Background: Attention-Deficit Hyperactivity Disorder (ADHD) is a common neurodevelopmental disorder. Structural imaging consistently identifies the dorsal prefrontal cortex (dPFC), basal ganglia (BG), dorsal anterior cingulate cortex (dACC), and parietal lobe (PL) as having delayed, or ultimately underachieved, development in ADHD[1]. Likewise, fMRI studies employing inhibition- or attention-related tasks implicate altered activation in these regions as contributing to ADHD[2], but only with group effects. We have, however, recently shown an age effect with increasing disengagement in ADHD children[3]. Additionally, worse inattentive symptoms have been linked with poorer reading performance and may play a role in explaining the high comorbidity, as high as 45%, between ADHD and a reading disability (RD) [4,5]. However, it is unclear to what extent neural dysfunction and disengagement with age is present in ADHD+RD compared to typically developing children (TDC), which is the main objective of this study. We hypothesize that during a sustained attention task, ADHD+RD boys would show more pervasive patterns of disengagement with age than ADHD-RD boys.

Methods: 21 typically developing (TDC, age_{mean} = 11.2), 18 DSM-IV ADHD-RD (age_{mean} = 11.6), and 14 DSM-IV ADHD+RD (age_{mean} = 10.6) boys from the Detroit, MI and Windsor, ON metropolitan areas completed an fMRI sustained attention task. An aptitude-achievement discrepancy on multiple reading domains constituted an RD diagnosis. All ADHD participants were off medication for 24 hours prior to the exam.

The fMRI paradigm contained 90sec epochs of sustained attention to single ("0") or double digit ("00") targets interspersed with 30sec fixation epochs. Approximately half of the subjects in each group completed a 5min. version (two task epochs) and the others completed a 6min.15s version (three task epochs). Visual stimuli were projected as white digits on a gray background using Presentation® software (15.0, www.neurobs.com). Participants responded to the infrequent targets (1 target:4 stimuli) using an fMRI-compatible button box.

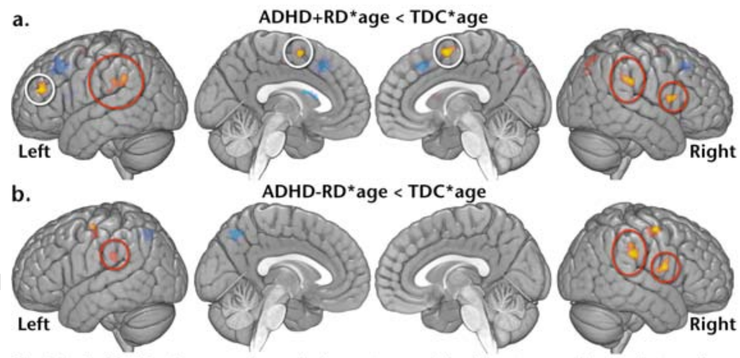

Fig. 1 Both ADHD subgroups show similar patterns of significant group-by-age interactions.

Functional volumes were collected using a gradient echo EPI sequence [TR: 2.6s, TE: 29ms, FOV: 256mm^2, acquisition matrix: 128x128, 36 axial slices, pixel dimension: 2x2x3mm^3] on a Siemens 3T Verio with a 12-channel volume head coil. Structural, T_1-weighted 3D MPRAGE [TR= 2.2s, TE= 3ms, TI= 799ms, flip-angle= 13^0, FOV= 256x256, 256 axial slices of thickness= 1mm, matrix= 176x256, and scan-time= 6min:27s] scans were the basis for anatomical coregistration of functional data.

After visual inspection for artifacts, subject images were realigned, unwarped, coregistered, normalized to the MNI-152 template, and smoothed (FWHM 6mm^3). Individual activation patterns were modeled using the canonical hemodynamic response function after modeling autocorrelations, using AR(1), and high pass filtering, 256 Hz. Covariates of no interest included outlier volumes and a geometric, motion summary, both calculated with ART (http://www.nitrc.org/projects/artifact_detect/). A group-by-age interaction and main effects were assessed based on the attention greater than fixation contrast for either ADHD+RD or ADHD-RD versus TDC. In line with previous ADHD studies, comparisons were limited to the PFC, dACC, BG, and PL. Reported clusters exceeded the minimum voxels required by Monte Carlo simulation (3dClustSim[6]) at peak p < .025 for cluster-level significance < .05.

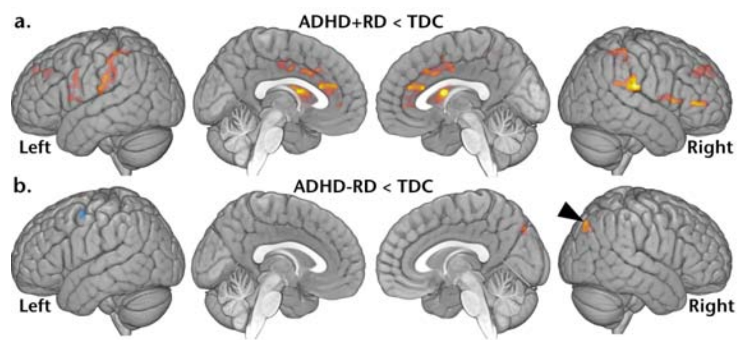

Fig. 2 ADHD+RD (n = 14), but not ADHD-RD (n = 18), shows multiple areas of hypoactivation compared with TDC (n = 21) during a sustained attention task.

Results: The three groups did not differ in age, FSIQ or performance on the sustained attention task (e.g., d' main effect: F = 1.3). Group-by-age interactions showed decreasing engagement in both ADHD subgroups along the right PFC [BA 6/44] and bilateral, inferior PL [iPL, BA40] compared with TDC (Figure 1). ADHD+RD showed additional areas of decreasing activation in the mPFC [BA 10] and sPFC [BA 6]. ADHD+RD also showed increasing engagement of bilateral sPFC and right caudate with age relative to controls. For main effects, ADHD+RD showed hypoactivation of multiple PFC, dACC, BG, and PL areas, but only the right PL [BA 7] was decreased in ADHD-RD (Figure 2).

Conclusions: Similar to previous results for ADHD-RD (Mohl et al.), ADHD+RD showed decreasing engagement of multiple areas with age compared with controls during a sustained attention fMRI task (**Figure 1**). However, the main effects showed that hypoactivations commonly reported in ADHD literature were observed predominately in the ADHD+RD subgroup alone (**Figure 2**). The results partially support our hypothesis of more pervasive disengagement in ADHD+RD and suggest a neural basis for the strong association between inattention and reading problems.

References: 1. Stanley JA, Kipp H, Greisenegger E, et al. Evidence of Developmental Alterations in Cortical and Subcortical Regions of Children With Attention-Deficit/Hyperactivity Disorder: A Multivoxel In Vivo Phosphorus 31 Spectroscopy Study. Arch Gen Psychiatry 2008;65:1419. 2. Cortese S, Kelly C, Chabernaud C, et al. Toward Systems Neuroscience of ADHD: A Meta-Analysis of 55 fMRI Studies. American Journal of Psychiatry 2012;169:1038–55. 3. Mohl B, Goradia D, Khatib D, et al. fMRI Evidence of Increasing Disengagement of Sustained Attention-Related Activation with Increasing Age in ADHD Children. 2013. ISMRM Abstract. 4. Purvis KL, Tannock R. Phonological processing, not inhibitory control, differentiates ADHD and reading disability. Journal of the American Academy of Child & Adolescent Psychiatry 2000;39:485–94. 5. Willcutt EG, Pennington BF, Boada R, et al. A comparison of the cognitive deficits in reading disability and attention-deficit/hyperactivity disorder. J Abnorm Psychol 2001;110:157–72. 6. Ward BD. Simultaneous inference for fMRI data. AFNI 3dDeconvolve Documentation, Medical College of Wisconsin 2000.