Magnetic Field Correlation Imaging of Brain Iron in Attention-Deficit/Hyperactivity Disorder


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Introduction

Several groups have found significantly lower serum iron (ferritin) in attention-deficit/hyperactivity disorder (ADHD) that correlated with higher symptom severity [1-3]. Since the extent to which serum ferritin correlates with brain iron remains unclear, we are interested in examining brain iron in ADHD due to its role in myelin development and dopamine metabolism in the fronto-striatal pathway, both of which are implicated in this disorder [4, 5]. The purpose of this study is to quantify brain iron in ADHD compared to typically developing controls (TDC) using a recently developed imaging method called magnetic field correlation (MFC) imaging together with the more conventional iron measures of R2 and R2*. Brain iron is detected in MRI mainly via the effect of magnetic field inhomogeneities (MFIs) on MR signal dephasing. MFC has a more direct relationship to MFIs than either R2 or R2*, in part because it is independent of dipolar relaxation mechanisms [6, 7]. The globus pallidus (GP), caudate nucleus (CN), putamen (PUT), nucleus accumbens (ACC) and thalamus (THL) were chosen as bi-hemispheric regions of interest (ROIs) because of their suspected role in ADHD in addition to having high iron content [8]. Serum measures of iron were also collected in the same study visit.

Materials & Methods

This study involved a total of 49 participants: 22 individuals with ADHD (15 males) with a mean age of 12.6 ± 2.8 years (range: 8.3-18.2 years) and 27 typically developing children (TDC; 12 males) with a mean age of 13.3 ± 2.6 years (range: 8.6-18.1 years). ADHD subjects were recruited from the NYU Child Study Center, while children were recruited from the NYU School of Medicine, New York, NY. ADHD subjects were selected based on DSM-IV criteria for ADHD, either medication naïve (n=12) or off medication for at least 4 hours prior to the scan day. TDC subjects were either drug naïve (n=12) or off medication for at least 4 hours prior to the scan day. Neither of these groups met current DSM-IV criteria for ADHD. These regions are likely involved in ADHD in addition to having high iron content [8]. Serum measures of iron were also collected in the same study visit.

Results

ADHD and TDC groups did not significantly differ in age (p = 0.40) or in any of the serum iron measures. However, MFC means were significantly lower in the ADHD group for the CN (TDC mean ± SEM: 248.4 ± 14.7, ADHD: 208.4 ± 10.7, p = 0.033) and for the GP (TDC: 470.2 ± 31.1, ADHD: 390.7 ± 19.7, p = 0.036) while no significant group differences were detected in either R2 or R2* (Figure 1). Trends of lower MFC in ADHD were found in the PUT (TDC: 204.9 ± 13.2, ADHD: 176.0 ± 9.8, p = 0.085) and ACC (TDC: 806.6 ± 83.1, ADHD: 610.9 ± 58.1, p = 0.060) and with R2* in the ACC (TDC: 23.9 ± 0.9, ADHD: 21.9 ± 0.6, p = 0.075).

Discussion

Consistent with another study of brain iron in ADHD, these results suggest that brain iron in basal ganglia regions is reduced in ADHD [12]. In particular, we found significantly lower levels in the CN and GP compared to age-matched TDC. These regions are likely targets of ADHD stimulant medications that function, in part, by indirectly increasing dopamine concentrations [13]. As iron plays a role in dopamine metabolism, we speculate that mechanisms for iron absorption into the brain maybe aberrant in ADHD even when serum iron levels are normal.

References