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### Scientific Formal (Paper) Presentations

**CODE: SSE21-06**

**SESSION: SSE21**

**Medication Naïve Attention-deficit/Hyperactivity Disorder Subjects Have Low Brain Iron Levels as Detected by Magnetic Field Correlation Imaging**

#### Date/Times

- **DATE: Monday**
- **TIME: 3:50-4:00 PM**
- **LOCATION: S102AB**

#### PARTICIPANTS

- Vitria Adisetiyo PhD - Nothing to disclose.
- Rachael Deardorff MS - Nothing to disclose.
- Ali Tabesh PhD - Nothing to disclose.
- Els Fieremans PhD - Nothing to disclose.
- Kevin M Gray MD - Nothing to disclose.
- Adriana Di Martino undefined - Nothing to disclose.
- F. Xavier Castellanos MD - Nothing to disclose.
- Jens H Jensen PhD - Nothing to disclose.
- Joseph A Helpem PhD - License agreement, Siemens AG.

#### SUBSPECIALTY CONTENT

- Pediatric Radiology

#### PURPOSE

Stimulant medication reduces symptoms in attention-deficit/hyperactivity disorder (ADHD) through indirectly increasing dopamine (DA) levels in the striatum. Hence, it is suspected that reduced DA levels are part of ADHD pathology. However, both increased and decreased DA markers have been detected in ADHD. Interestingly, reduced DA markers have been consistently found in medication naïve patients while increased markers have been found in patients with a history of medication use, suggesting increased DA markers may reflect an adaptive response to medication. Here we assess the relationship between medication history and brain iron levels in children and adolescents with ADHD compared to typically developing controls (TDC). As brain iron is required for DA synthesis, assessing iron levels with MRI may provide non-invasive indirect measures of DA.

#### METHOD AND MATERIALS

27 TDC, 12 ADHD-naïve and 10 ADHD-medication were recruited. As indices of brain iron, magnetic field correlation (MFC) and relaxation rates ( $R_2$ ,  $R_2^*$  and  $R_2'$ ) were used. All are affected by tissue iron but differ in their sensitivities and specificities. MFC was estimated with MFC imaging,  $R_2$  with a multiple spin echo sequence and  $R_2^*$  with a multiple gradient echo sequence.  $R_2' = R_2^* - R_2$ . The globus pallidus (GP), caudate nucleus (CN), putamen (PUT) and thalamus (THL) were chosen as regions of interest because of their suspected role in ADHD in addition to having high iron content. Serum iron measures were also collected.

#### RESULTS

The ADHD-naïve subgroup had significantly lower MFC than either TDC or the ADHD-medication subgroup in 3 of the 4 brain regions studied (FDR corrected). ADHD-naïve vs. TDC: PUT ( $p = 0.005$ ,  $d = 1.0$ ), CN ( $p = 0.003$ ,  $d = 1.1$ ) and THL ( $p = 0.012$ ,  $r = 0.4$ ); ADHD-naïve vs. ADHD-medication: PUT ( $p = 0.002$ ,  $d = 1.5$ ), CN ( $p = 0.004$ ,  $d = 1.4$ ) and THL ( $p = 0.021$ ,  $r = 0.5$ ). TDC and the ADHD-medication subgroup did not significantly differ in MFC. In contrast, no significant group differences were detected using the  $R_2$ ,  $R_2^*$ ,  $R_2'$  or serum measures.

#### CONCLUSION

Similar to other DA marker measures, lower brain iron levels (indexed only by MFC) are observed in medication naïve ADHD and appear to normalize with medication.

#### CLINICAL RELEVANCE/APPLICATION

Reduced brain iron in medication naïve ADHD is a promising biomarker. MFC imaging's ability to non-invasively detect these aberrant levels may help improve ADHD diagnosis and guide optimal treatment.