# Financial Disclosures (Past 2 Years)

<table>
<thead>
<tr>
<th>Source</th>
<th>Research or CME Funding</th>
<th>Consult Fees</th>
<th>Speakers Bureau</th>
<th>Royalties or IP</th>
<th>In Kind Services</th>
<th>Stock / Equity</th>
<th>Honorarium or expenses for this meeting</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHE Inhibitor Patent</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shire/Takeda</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Guilford Press</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Akili</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VAYA</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vallon</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tris</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Otsuka</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IronShore</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Supernus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sunovion</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genomind</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arbor</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Oxford Univ. Press</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>
Structural and Functional Brain Anomalies in ADHD
Meta-analysis of fMRI Inhibition Tasks
(Hart et al., JAMA Psychiatry, 2013)

Regions of decreased (red and orange) and increased (blue) activation in ADHD patients compared with controls.
Regions of decreased (red and orange) and increased (blue) activation in ADHD patients compared with controls.
Meta-Analysis of subcortical and cortical brain regions across the lifespan (ENIGMA-ADHD, n>4000)
(Hoogman et al., Lancet Psych, 2018; Hoogman et al., submitted)

Note: In children all case-control findings are significant, in adolescents only the hippocampus result is. No differences are significant in adults.
Questions Raised by the ENIGMA-ADHD Study

• Do the data support any evidence for structural brain abnormalities in ADHD adults?
• In some cases, can the brain recover from ADHD?
• **Training Phase:** Derive complex predictive model using 70% of the data using Random Forests

• **Validation Phase:** Assess accuracy of model with 15% of the data

• Iterate between test and validation phase to find the best model

• **Test Phase:** Use the last 15% of the data to assess the accuracy of the model in an independent data set
ROC Curves
(Zhang-James et al., submitted)
Feature Importance
(Zhang-James et al., submitted)
Recovery of Brain Imaging Anomalies in Adulthood
The Age Dependent Decline of ADHD
(Faraone et al., Nature Reviews Disease Primers, 2015)
Developmental Trajectories: the ADHD Caudate Normalizes with Age

(Castellanos et al., JAMA, 2002)
Hypothesis: ADHD is characterized by delay rather than deviance in cortical maturation
Rate of Prefrontal Cortical Thinning
(Shaw et al., Am J Psychiatry, 2011)
ADHD Symptoms and Total Brain Volume in Healthy Adults
(Hoogman et al., PLOS One, 2012)
Effects of Stimulants on Brain Structure and Function
Percent of patients on long-term stimulant treatment predicts more normal right dorsolateral PFC activation (p<0.0005)
Meta-regression analysis for attention shows that the percentage of patients receiving long-term psychostimulant treatment is associated with more normal right caudate activation relative to healthy controls.
Meta-Analysis of sMRI Studies,
(Nakao et al., Am J. Psychiat, 2011)

Percentage of patients on stimulant medication was correlated with gray matter volume in the right caudate, controlling for age.
Longitudinal Study of Stimulant Treatment and Cortical Thickness
(Shaw et al., AJP, 2009)

Left Middle/Inferior Frontal Gyrus
Right Medial PFC

No evidence that psychostimulants were associated with ‘slowing’ of overall growth of the cortical mantle
Summary: Functional Effects of Brain Networks in ADHD
• Under-activation of fronto-striatal and fronto-parietal networks consistent with impaired goal-directed executive processes
• Under-activation of frontal control over the limbic system consistent with the emotional dysregulation seen in ADHD

• Lower activation of the ventral striatum in ADHD in anticipation of reward leads to poor executive control over reward regulation.
• Under-activation of ventral attention networks leads to poor executive control of attention to behaviourally relevant external stimuli.

ADHD patients show small or absent anti-correlations between the default mode network (DMN) and the cognitive control network, lower connectivity within the DMN itself, and lower connectivity within the cognitive and motivational loops of the fronto-striatal circuits.

The medicines that treat ADHD work in the pathways implicated by neuroimaging studies.

Thanks for Listening!

Free CME: www.adhdinadults.com

MyADHD Blogs: www.linkedin.com/in/stephenfaraone

Tweets: @StephenFaraone

7th World Congress on ADHD
From Child to Adult Disorder
25 – 28 April 2019
Lisbon, Portugal