

# Learnings from the Genetics of ADHD



## ADHD is a Disorder of the Brain

### Genetic Risk for ADHD is Expressed in the Brain

The genetic data support neuroimaging data in establishing ADHD as a brain disorder rooted, in part, in one's own biology<sup>1</sup>

### History of Stigma Regarding (ADHD)<sup>2-4</sup>

1

Due to misinformation, some people still view ADHD as a disorder due to poor motivation or poor parenting.

2

This "blame the person/parent" approach creates stigma and worsens access and adherence to treatment.

3

To reduce stigma, it's important to educate individuals and their families that ADHD is a brain disorder.



## ADHD has Existed for Tens of Thousands of Years<sup>5</sup>

### ! ADHD is not a new disorder, in fact the genetics of ADHD date back to Paleolithic times

- Individuals with ADHD and their caregivers need to know that data support the conclusion that **ADHD is a biological disorder which may require management** for its underlying biological differences and not just its symptoms



## ADHD Runs in Families

- The **parents, siblings and children** of individuals of all ages with ADHD **are at high risk** for the disorder: they should be screened and may require management for ADHD themselves<sup>6</sup>
- ! **Symptoms of ADHD in parents may interfere with their ability to implement a medical and psychosocial treatment plan provided by their child's healthcare provider<sup>7,8</sup>**



## Genetics of ADHD are Similar in Males and Females<sup>9</sup>

- Genetic data suggests the biology of the disorder is similar in males and females so differential diagnosis and treatment is not warranted
- However, ADHD in girls frequently manifests differently with a predominance of inattention over hyperactivity/impulsivity
- Thus, girls with ADHD are sometimes not diagnosed or treated



## Subthreshold Symptoms of ADHD are Meaningful

- Genetic studies support the idea that **ADHD diagnosis and symptoms** are correlated and **exist along a continuum** of expression<sup>10</sup>
- Substantial data indicate that **subthreshold ADHD** can be an **impairing disorder** which may require treatment, however there are several diagnostic challenges, as individuals may have:
  - Difficulty with retrospective recall<sup>11</sup>
  - Less severe ADHD<sup>10</sup>
  - A history of supportive, well-structured home and school environments (e.g. psychological scaffolding)<sup>10</sup>
  - Been self-medicating<sup>12</sup>
  - A subthreshold case with many symptoms (e.g. 5 inattentive & 5 hyperactive-impulsive)<sup>10</sup>
- Additionally, DSM 5 may have **low sensitivity** for some cases of **adult ADHD** due to lack of criteria for **emotional dysregulation and executive dysfunction**<sup>13-14</sup>



## Relationship of Genetics, Subthreshold Symptoms & Onset of ADHD

### Early Onset

- Genetics support ADHD symptom severity as existing along a continuum, thus diagnosing “young for grade” youth may be appropriate<sup>15</sup>

### Late Onset

- Genetic correlation between childhood and adults with persistent ADHD is 0.81, which is high but less than perfect, suggesting that different genes regulate onset and persistence of the disorder<sup>16</sup>
- When onset occurs later than the DSM 5 requirement of age 12, onset may have been delayed because the individual may have:<sup>17</sup>
  - A milder condition
  - Social and emotional scaffolding that protected them from ADHD
  - Childhood onset but cannot recall the symptoms
- Clinicians should be cautious in diagnosing late onset ADHD but also should not rule out the diagnosis due to onset after age 12<sup>17</sup>



## Polygenic Risk for ADHD is Correlated with Adversity & Parental Education

! Polygenic risk is the estimated effect of many genetic variants on an individual's phenotype<sup>18</sup>

- ADHD polygenic risk correlates with adversity<sup>18</sup>
  - For children living in adverse environments, don't assume that their ADHD is “situational” unless it only occurs in one environment<sup>18</sup>
- Parental education correlates with, but does not moderate, ADHD polygenic risk<sup>19</sup>
  - Lower IQ is correlated with polygenic risk for ADHD<sup>19</sup>
  - Thus, it's important to be aware that some parents of youth with ADHD may not have sufficient intellectual resources to understand, implement and adhere to treatment regimens<sup>7</sup>



## Somatic & Psychiatric Comorbidities are Common in ADHD

- Somatic comorbidity in ADHD is real and genetically driven<sup>20</sup>
  - Individuals with ADHD should be screened for somatic comorbidities
  - Since ADHD worsens somatic outcomes, some individuals may need cognitive behavior therapy modules focused on helping them manage disease such as diabetes, asthma, and obesity
- Psychiatric comorbidity is common in ADHD<sup>21</sup>
  - Psychiatric disorders are correlated with one another at the level of DNA<sup>21</sup>
  - Many patients with mood and anxiety disorders likely have ADHD too<sup>22</sup>
  - Multiple comorbidities are to be expected in some patients<sup>22</sup>



## ADHD Genetic Screening & Pharmacogenomics are NOT Ready for the Clinic

- DNA cannot be used to diagnose ADHD<sup>23</sup>
  - Current polygenic risk scores are not sufficiently accurate for use in the clinic
- DNA variants are associated with drug responses but utility in the clinic has not been properly demonstrated<sup>24</sup>
  - Randomized, controlled clinical trials demonstrating pharmacogenetically guided treatment as better than treatment as usual are still needed

## References & Acronym List

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ADHD – Attention Deficit/Hyperactivity Disorder    DNA – Deoxyribonucleic acid    DSM – Diagnostic & Statistical Manual of Mental Disorders    IQ – Intelligence quotient