Etiology of ADHD: Genetic, Environmental, and Neurobiological Factors in ADHD

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Nature vs nurture a debate as old as time. Is each individual's DNA contain the information that makes them unique and predisposition to certain ailments, behaviors, or physical attributes or does the environment we exist in play a more significant role. The past for decades we have seen this debate play itself out through a focus on ADHD in children. Erik Willcutt from the University of Colorado at Boulder argues that the primary cause for ADHD are genetic. He demonstrates and supports his claim through comparing behavioral and genetic approaches to ADHD. Willcutt does not completely dismiss environmental factors and ultimately agrees that it is both nature and nurture, with the clear distinction that genetic disposition is the primary cause.

Willcutt's work is progressive because he takes the nature vs nurture debate to the next level. Behavioral genetic and environmental studies have concluded that both play a role in the etiology of ADHD. The next question to ask is what specific genes and environmental factors are responsible. The author uses the Diagnostic and Statistical Manual of Mental Disorders Vol. 4 (DSM-4) to define ADHD as the presence of excessive symptoms of inattention and/or hyperactivity-impulsivity. When sufficient data exists Willcutt uses studies from the DSM-4 but also reviews relevant studies that use other measures to provide a complete picture of the current state of knowledge surround ADHD.

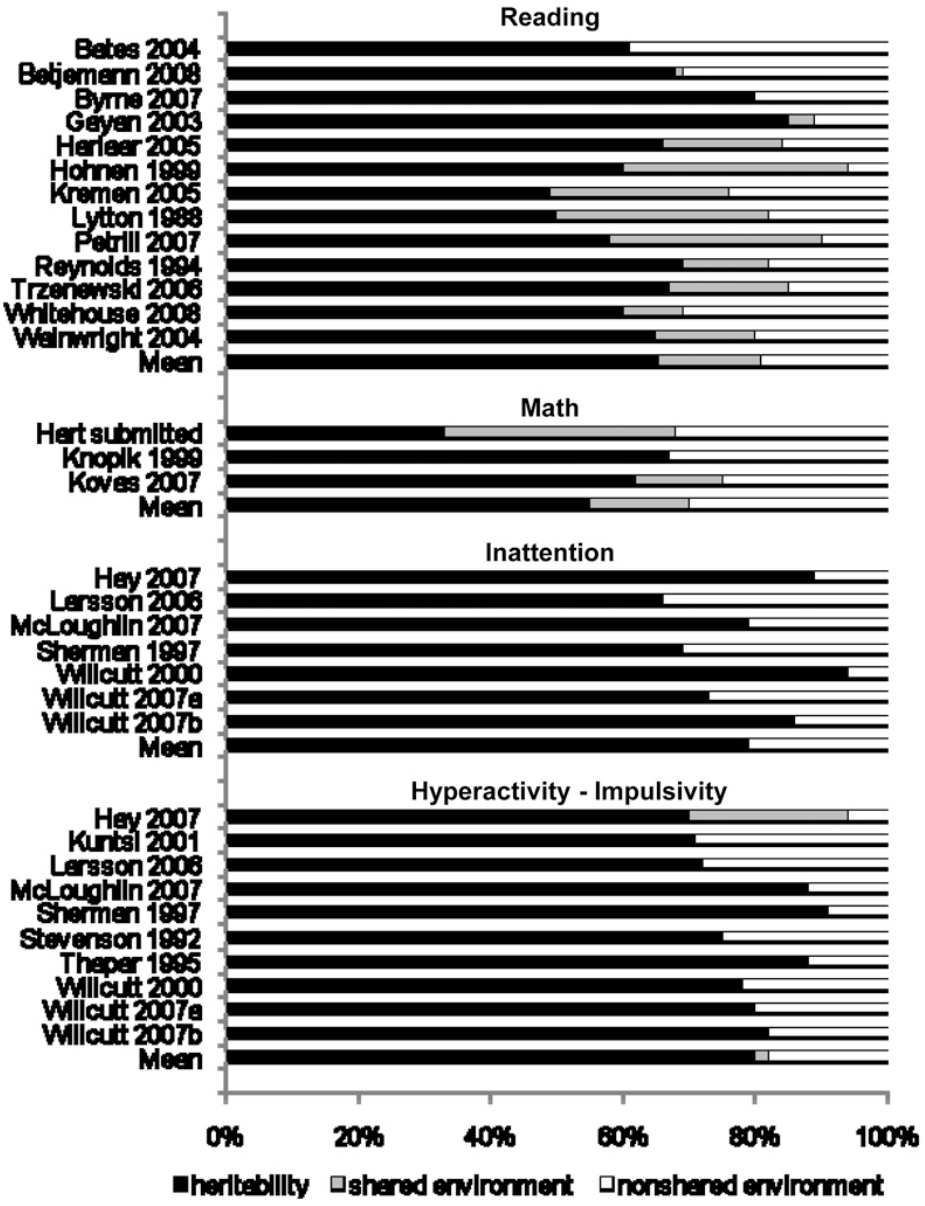
The author begins with a look at the behavioral genetic studies. The cause of ADHD is primarily genetic with some environmental influence. Willcutt divides the environmental into shared and nonshared environmental influences to makes sense of the familial studies. Previous studies confirm that ADHD is 6-8 times higher in first degree siblings than the base

rate of ADHD among the general population. The “risk” of ADHD was consistent among both boys and girls and across Caucasian and African American probands. The familial evidence studies support the hypothesis that ADHD is genetic but fall short of the complete picture. Members from the same immediate family share both genes and environments what about those outside those parameters.

Willcutt goes one step further and looks at adoption studies to begin to address this issue. Biological relatives of individuals who are adopted at birth share the same genes but different environments. Inversely adoptive relatives share the same environment but not genetic makeup. This type of research introduces specific environmental factors alongside genes. However, there are to main constraints Willcutt points out. First, adoptive parents are not representative of the population. This is because adoption agencies look for high functioning parents with optimal environments. Second limitation is the availability of attaining adoption records as they are often sealed.

One of the final areas that Willcutt looks toward in the behavioral genetic space are twin studies. Specifically he focused on research that compares monozygotic (identical) twins and dizygotic. As you may expect the twin studies support the genetic etiology of ADHD. There are higher rates of ADHD among monozygotic twins compared to the same sex dizygotic twins. Roughly a 50% higher rate of ADHD. Keep in mind this research also corroborates the presence of environmental factors. The presence of ADHD in twin studies is not 100% as would be expected if only nature was a factor.

Figure 1 Twin studies of reading, math, and DSM-IV ADHD symptom dimension



The author summarizes the research on behavioral genetic studies by demonstrating that ADHD is primarily familial due to familial genetic influences. Nonshared environmental factors contributed to a variance in ADHD but shared factors did not have a significant influence as demonstrated in twin and adoption research. Based on the research presented there is a

greater effort to identify the specific environmental and genetic factors that increase the likelihood of ADHD.

Environmental specific research suggests that prenatal or perinatal complications have a slight but significant influence on ADHD. Such factors include cigarette smoking or alcohol consumption during pregnancy, low birth weight, fetal distress, and family problems during the pregnancy. The research suggests that these factors made act as additives to genetic influences to increase a risk of ADHD. The studies the Willcutt references are unique in that they control for parental ADHD. This is significant because the evidence is not confounded with the familial aspects of ADHD. Most other studies according to Willcutt do not control for these factors.

Lastly, the author takes a look at Molecular Genetic studies. 99.9% of the genetic code among all people is identical the 0.1% is where these studies focus. He begins with research on linkage studies. He explains how the majority of human cells have two full sets of 23 chromosomes. 23 from the father and 23 from the mother. Sometimes however a child will not inherit one of the chromosomes and instead a partial will attach and complete the 23 pairs. Linkage analysis works because there is a known genetic marker is identified. This marker is the known factor and can be used to compare the 23 chromosomes of individuals with ADHD and those without. By identifying the position of the partial chromosomes in relation to the known Marker.

The molecular genetic studies of ADHD have primarily employed two methods to identify genes associated with the disorder: candidate gene studies and linkage analysis.

Candidate gene studies focus on specific genes related to biological systems implicated in ADHD, such as those affecting dopamine pathways. One extensively studied gene is DAT1, involved in dopamine reuptake, with mixed results on its association with ADHD. Similarly, the DRD4 dopamine receptor gene has shown inconsistent associations. Despite identifying candidate genes, the small effect sizes and inconsistent replications suggest that individual genes may not be sufficient to explain ADHD's genetic basis. Linkage analysis, aiming to identify regions in the genome linked to ADHD, has been conducted on a broader scale. While genome-wide screens did not reveal genes with large effects, they identified potential regions on chromosomes 5, 10, 12, and 16. Another study focused on chromosome 6, a region associated with reading disability and found significant linkage to ADHD, suggesting a shared susceptibility locus. Overall, these studies highlight the complexity of ADHD genetics, indicating that multiple genes and environmental factors likely contribute to its etiology.

Being diagnosed with ADHD about 2 years ago was a pivotal moment in my life, providing clarity to the challenges I had faced but couldn't quite understand. The realization that my struggles with focus, organization, and impulsivity had a neurological basis was both validating and overwhelming. Navigating daily tasks often felt like trying to solve an intricate puzzle without all the pieces. The diagnosis brought a mix of emotions relief that there was an explanation for my difficulties and apprehension about the journey ahead.

Learning more about ADHD opened a door to self-discovery. It was not just a label; it was an understanding of the unique way my brain functions. While medication became part of my management plan, the diagnosis prompted a broader exploration of coping mechanisms and strategies. Time management, organization, and breaking tasks into smaller steps became crucial

tools in my daily life.The journey with ADHD is dynamic and comes with its share of triumphs and setbacks. Finding a supportive network, whether through friends, family, or ADHD communities, has been invaluable. It's about embracing the strengths that come with ADHD — creativity, hyperfocus, and resilience — while acknowledging and working through the challenges.

Every day is a new opportunity to learn more about myself and refine the coping mechanisms that make life more manageable. The diagnosis has become a starting point for growth, self-acceptance, and a continual journey toward understanding and thriving with ADHD.

In summary, the data provided suggest that ADHD, like many other psychological traits and disorders, is likely influenced by a combination of numerous genetic and environmental risk factors, none of which alone is necessary or sufficient for the development of ADHD. Interactions among these factors and potential moderating variables further contribute to the complexity of ADHD's etiology. To comprehensively understand the disorder, future studies must employ well-characterized samples, typing each relevant gene and measuring environmental risk factors. Multivariate analyses could then assess the relative contributions of each factor and explore potential interactions. The evolving automation and efficiency of DNA collection and genetic analysis present promising opportunities for researchers with modest budgets to incorporate genetically informative methods into their studies. Collaboration between behavior genetic researchers and those investigating the neurocognitive aspects of ADHD is becoming more accessible, promising a synergistic approach that strengthens research efforts in both domains.

References

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