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Section 1. ADHD and Genetics

Whether human behaviors and personalities are due to nature or nurture has long been settled—it's always both. Our brains manufacture our thoughts, feelings, and actions, but our brains are always performing in, and the product of, the world with which they interact.

Although “both nature and nurture” is a more nuanced answer than attributing who we are entirely to genes or entirely to the environment, it lacks precision. The relative importance of genes and environment matter, and not merely as the object of intellectual curiosity. If we want to change behaviors or traits, it's useful to know what role genetics plays, and how it interacts with environmental forces. A more detailed understanding gives us more leverage for intervention.

In the three decades since I earned my doctorate in neuroscience, brain research has grown exponentially. Researchers have sliced, diced, and stained brain samples and whole brains; wired them for recordings; and spritzed them with chemicals to discover how we process information and build our individual personalities and predilections. Yet we still have much more to learn.

Studies on how the environment influences the brain have lagged even further behind, in part because the large number of potentially relevant variables makes it challenging to reliably reproduce real-world conditions in a research project. It is also difficult to examine just one environmental variable while holding everything else constant.

As one example, an exploration of the genetic contributions to ADHD provides insight regarding how biology can influence not just mental health conditions but our everyday behaviors as well. Studies on the origins of ADHD reveal that genetic factors go far beyond just having a good or bad variant of a particular gene. A recent study even shows that a mother's genes influence the environment she creates for rearing her children (Mahjani et al. 2025). A greater understanding of, and appreciation for, genetic complexity is currently needed in our society.

All in the Family

When I started working as a psychiatrist in the 1990s, ADHD was considered to exist only in children. The dogma was that all children outgrew it before they became adults. We now know that to be false, even though the misconception lasted for decades.

Not appreciating the lifelong persistence of ADHD in a majority of children who have it was due to two factors: the siloing of clinical medicine and confirmation bias. Siloing refers to the impact that specialization has on determining which doctors see which patients. Children with ADHD were seen by child psychiatrists or pediatricians. When the children became adults, they left these doctors behind. The new physicians they saw as grown-ups weren't trained to recognize ADHD in adults, so they didn't recognize the symptoms of ADHD even when they were robustly displayed. Confirmation bias describes the human tendency to seek out, be aware of, and register information that supports the ideas we already hold, which serves to confirm our beliefs, while simultaneously ignoring, or even suppressing, information that might lead us to different conclusions. If you don't believe ADHD exists in adults, you limit your ability to see it.

Awareness that adults could have ADHD arose in part from clinics treating childhood ADHD. Practitioners noticed that the parents of these children exhibited a broad array of ADHD symptoms themselves: They were late in dropping off and picking up their kid for appointments, forgot to refill medications on time, and misheard or didn't follow through with treatment recommendations. Clinicians eventually realized that not only did ADHD persist into adulthood, but that it also tended to run in families.

Twins and Adoption

Many traits occur in families. These include aspects of our physical bodies, like height, as well as mental health traits, such as the predisposition to be melancholy or to seek out novelty. But just because some traits run in families doesn't mean they're genetically driven. All your siblings may be fans of mariachi music, but this has likely more to do with cultural and family influences than with your genes. Researchers have used studies of twins and of adoption to try to tease apart genetic and environmental influences.

Identical twins have identical genes, whereas fraternal twins are no more closely related than non-twin siblings—with whom they share, on average, half of their genes. But both kinds of twins are assumed to share the same non-genetic family environment. Adoption studies look at adopted children and whether they more closely resemble their biological parents (with whom they share half their genes, but a different environment) or their adoptive parents (with whom they share no genes, but do live in a common environment). In these studies, the researchers look at concordance, which isn't whether both individuals like purple grapes or whether they flew on supersonic jets, but whether they share the same observable trait or both lack that specific trait.

Geneticists can determine heritability, or the extent to which the variation of a trait within a population is attributable to genetic rather than environmental factors. Heritability of 100 percent means that genes are the only determinative factor for a trait, and 0 percent indicates it is all due to the environment. For reference, most studies on height have found a heritability of around 80 percent—strongly shaped by genetics, but subject to nutrition, disease, and other environmental factors as well.

The heritability for several mental health conditions is as large as the heritability for height. ADHD is among the mental health conditions with the greatest heritability—75 to 80 percent in most studies, indicating that at a population level, genetics plays a considerably larger role than does the environment (Grimm, Kranz, and Reif 2020).

Critics have pointed out several potential flaws with twin studies:

- New mutations can mean that even identical twins can carry different gene variants.
- Identical twins may be treated more similarly than are fraternal twins.
- Twinship itself may render these individuals different from the general population.
- The twins chosen for studies may not be representative of twins in general.

Even after accounting for these potential weaknesses, geneticists have used twin and adoption studies to corroborate heritability for a number of mental health conditions (Besterman et al. 2024):

- 75 to 80 percent for schizophrenia, autism, ADHD, and bipolar disorder
- 55 to 65 percent for nicotine and alcohol abuse disorders
- 35 percent for major depression

So ADHD, and several other mental health conditions, have a very strong genetic component, but that leaves plenty of room for the environment to influence any individual's life trajectory.

Good Genes

A clothing manufacturer recently promoted controversy about whether beautiful white actresses have good genes/jeans (Chakravarty 2025). The idea underlying this claim requires an understanding that genes, composed of DNA, code for the proteins in our bodies; that we inherit two copies of each gene, one from each parent; and that different variants of

each gene can either slightly or profoundly affect the capabilities of the protein being coded for and help determine the appearance and other characteristics of an individual.

In the 1990s, there was excitement regarding early studies associating ADHD with genetic variants coding for dopamine receptors (Benjamin et al. 1996) or dopamine transporter molecules (Waldman et al. 1998). Given that all of the medications at that time that were used to treat ADHD increased activation of dopamine circuits in the brain, it was a reasonable assumption that genetic problems with dopamine systems could result in ADHD.

Some subsequent studies replicated these findings, but others failed to find a connection with ADHD and specific gene variants. It turns out that only in some families are genes for dopamine receptors or transporters implicated in causing ADHD. None of these individual gene variants is the prevailing cause of ADHD in the population, which is why simple genetic tests aren't currently useful in predicting who will develop ADHD. Hopes of tying serotonin system genes to depression or other simple brain genetic variants to other mental health conditions have largely led to finding a similar lack of strong associations. But given the strong evidence of a genetic role in these conditions, researchers continued looking for how genes contribute.

A Whole Lot of Genes

As it became easier to scan genetic sequences in the last twenty years, researchers could move beyond looking at specific “candidate” genes, as described above, to exploring much bigger samples of the human genome. Relatively quickly, what became apparent, for ADHD and many other conditions, was that much of the genetic contribution is polygenic. This means that hundreds or even a few thousand genes each contribute a tiny bit to the increased likelihood of developing a condition. With modern gene-sequencing approaches, this allows researchers to develop polygenic risk scores—having a large number of the at-risk variants of relevant genes means that individual is relatively more likely than someone with a bunch of the low-risk variants to develop a condition.

But again, this only provides a measure of relative risk; even many of the individuals with dozens and dozens of the high-risk variants fail to develop any particular condition. Furthermore, it became clear that many of these tiny-risk genes were general to developing *any* mental health condition; some of these tiny-risk genes predispose people to a subset of mental health conditions (ADHD and autism) while another subset predispose people to a *specific* mental health condition.

Polygenic scores are derived from looking at very large populations, but so far, the groups in the databases are largely skewed toward Caucasian people of European ancestry, making polygenic scores less reliable for individuals of different heritages. Furthermore, even within these overly studied populations, the polygenic risk scores only capture a limited portion of the genetic heritability suggested by twin and adoption studies.

Genetics Isn't Simple

Multiple factors complicate the genetics end of the nature-versus-nurture interaction. I'll highlight four of these, and explain the terms further below:

- Penetrance (whether a gene gets expressed)
- Epigenetics (whether a gene gets turned on or off)
- Copy number variants (omissions or duplications of large blocks of DNA)
- Mitochondria (all of our DNA isn't in the cell nucleus)

Penetrance. Penetrance refers to the extent to which someone who has the genes that typically code for a particular condition actually expresses that trait. In the real world, penetrance is never 100 percent, even in situations where textbooks sometimes claim perfect penetrance. One example is Huntington's disease, a progressive neurologic and psychiatric condition that causes writhing movements, flailing limbs, and often depression, psychosis, and dementia. Despite its genetic origins, Huntington's disease doesn't usually start causing symptoms until someone is in their thirties, forties, or fifties. Purportedly everyone who has the gene will sooner or later develop Huntington's disease (Franklin et al. 2024), so penetrance is often claimed to be 100 percent.

One of the very first patients I worked with in medical school was a nineteen-year-old woman who was already experiencing cognitive and psychiatric aspects of Huntington's. In some families, Huntington's disease shows up earlier with each succeeding generation. My patient was put up for adoption shortly after birth, when her biological mother, in her early thirties, began displaying signs of Huntington's. It turned out that my patient had a brother, a year older, who had been adopted by a different family. This brother died in a bicycle/car accident at the age of twelve. Years later, a stored sample of his blood was tested, revealing that he too had inherited the Huntington's gene. He had the gene, but he never developed symptoms of Huntington's because he died too young. Although his case was unusual, it demonstrates that even for Huntington's, even though the penetrance is very high, it's not a perfect 100 percent. In most cases, for most conditions, factors other than early death are what reduce penetrance.

Epigenetics. Epigenetics refers to factors that heighten or diminish the expression of genes, without structurally altering the gene itself. Genes are the blueprints for making proteins, but throughout one's life, small molecules can be affixed to sections of the DNA near the genes, and these can either suppress the body's ability to make proteins from that message or, in other cases, boost the production of those proteins.

Early life trauma is a particularly effective way of epigenetically turning on or off certain genes, with a clear impact on the propensity to develop certain mental health conditions later in life. Epigenetics represents one common reason that penetrance is less than 100 percent. Epigenetics is also one reason why many of the commercially available genetic tests that purport to tell you whether you are at high risk for a condition, or whether you should avoid or make use of a particular medication, are, for the most part, not terribly useful. Which genes you have inherited is important, but at least as vital is whether those genes are ever activated or expressed in particular cells. Epigenetics likely represents a common pathway by which many environmental and behavioral factors are increasing the presence of ADHD symptoms in modern populations.

Copy number variants. The discussions above regarding different variants of genes are generally addressing single-point mutations, where one small unit of DNA is varied, resulting in a different amino acid being inserted into a protein. In some cases, these substitutions are innocuous; other times, they have a minor effect on the protein; and sometimes, they dramatically decrease or increase the functioning of that protein.

But our incredibly long and twisted strands of DNA can suffer other changes as well. Copy number variants refers to thousands of units of DNA being either deleted or duplicated. Recent research indicates that copy number variants make up a significant portion of the genetic heritability for mental health conditions that isn't captured by single-point mutations or summed up in the polygenic risk scores (Sha et al. 2025). The ability to direct and maintain attention, whether in ADHD or in the general population, is one of those traits influenced by copy number variants.

Mitochondria. Every individual inherits half their nuclear DNA from each parent. But the powerhouses of the cells, the mitochondria that generate chemical energy, suppress oxidative stress, and help regulate a number of other cellular functions, also contain DNA. Almost all the time, an individual's mitochondria are all inherited through one's mother; hence, mitochondrial DNA is derived from the mother's egg, not the father's sperm.

This mitochondrial DNA is potentially quite important; some psychiatrists believe that impairment of normal mitochondrial function helps cause all mental health conditions (Palmer 2022). While a correlation between dysfunctional

mitochondria and a number of conditions has been established, it is not at all clear whether this is just an association or whether mitochondrial dysfunction is actually causing these conditions. Researchers have found an association between variants of mitochondrial genes and higher rates of developing ADHD (Chang et al. 2020).

How Genes Can Shape Environments

Scientists studying nature-versus-nurture influences have long been aware of an additional layer of complexity. A parent's genes aren't just directly passed down to their children but also might shape the environment in which they rear their children. Features of one's physical environment early in life are linked to the likelihood of developing ADHD later in childhood. Factors associated with higher rates of developing ADHD include exposure to:

- lead
- cigarette smoke
- acetaminophen (Tylenol)
- major trauma
- poverty
- overly harsh and inconsistent parenting

Given the strong genetic component to ADHD, many children with ADHD grow up with parents who have ADHD. ADHD in a parent increases the likelihood that a child is exposed to many of the risk factors above. This can make it very hard to sort out whether these factors themselves have a causal role in contributing to ADHD or whether their presence just echoes the fact that the parent has ADHD. There are still scientific arguments about whether cigarette smoking (Jansone et al. 2023) or Tylenol use (Ahlqvist et al. 2024) by a mother when she is pregnant directly increases the likelihood of having a child with ADHD or whether mothers with ADHD are just more prone to these behaviors.

A recent study, led by Mount Sinai School of Medicine geneticist Behrang Mahjani showed that a mother's genes increase the likelihood that her offspring will develop ADHD in two different ways (Mahjani et al. 2025). Sixty-six percent of the overall risk of developing ADHD was caused by the genes that the mother directly passed on to her child, but an additional 14 percent was attributable to the "genetic nurture effect," or how the mother's genes shaped the child's environment. The study didn't examine which specific features of the child's environment are shaped by the mother's genetics, but Mahjani suggested that "the mother's genes may affect her stress levels, health, or behaviors, and these influences can shape the child's development independently of the genes the child inherits" (Bender 2025).

The study examined all children born in Sweden during a ten-year period, totaling a million individuals, and essentially used an extension of the twin study concept. They looked at siblings, half-siblings, and cousins, including whether the cousins were maternal parallel (cousins whose mothers were sisters) rather than paternal parallel (cousins whose fathers were brothers) or cross-cousins (all other first cousin possibilities). This meant that they could compare ADHD concordance rates among groups of children with varying degrees of direct genetic connection as well as varying degrees of similar maternal environments. Mahjani's team had previously found a role for maternal genetic nurturance for OCD and Tourette's syndrome, but maternal genetic nurturance is smaller for those conditions than for ADHD. Any possible paternal nurturance contribution to ADHD risk is substantially smaller than the maternal nurturance effect. Mahjani's study needs to be replicated in other populations, but it already signals that a fruitful direction for further research will be sorting out which aspects of genetically determined maternal nurturance are the ones that propel kids onto the path of developing ADHD.

Genetics contribute to the development of ADHD through several different paths:

- Uncommon variants of dopamine receptor and transporter genes
- Mitochondrial genes
- Tiny effects from hundreds of common genes
- Deletions and duplications of large patches of DNA
- Ways in which a mother's genes affect the world she creates for her developing offspring

It's important to appreciate this complexity, especially when this only represents our current knowledge of the biological determinants of one particular mental health condition. Adding in the environmental effects, and how they can alter and influence the genetic factors, complicates the picture even more.

We're living in a world fascinated with technology, where doctors are using CRISPR and other biologic tools to alter specific genes in humans (Davis and Yeddula 2024). Yet our ability to tinker with biology often seems to exceed our contemplation of the implications and possible consequences of these manipulations. We're also living in a world where simplistic notions of the power of genetics, and mistaken ideas of race and character (Parker and Blum 2025), pervade the political realm. The Supreme Court even recently deemed it acceptable to use racial profiling (Lozano 2025) to target individuals for possible deportation. Our leaders need better education and awareness that it's not just a good gene or a bad gene that determines whether anyone is beautiful, athletic, greedy, cowardly, or murderous. Understanding more about the complexity of our genetic heritage can help us appreciate the diversity of humans and the multitude of forces that shape each of our individualities.

Section 2. Long COVID and ADHD

Our brains are vulnerable to injury in several ways, not just from physical trauma. The COVID epidemic demonstrated that infectious organisms have multiple pathways for invading our bodies and wreaking havoc with our brain function, as the following stories illustrate.

Jane's Story

Jane, thirty-five years old, works in sales. Her ADHD was well controlled by medications until COVID hit. During the early months of the pandemic, she felt more scattered and frequently became overwhelmed trying to conduct her job from home while simultaneously checking in on her three kids who were trying to navigate online learning. She and her doctor opted to increase her dose of Adderall, which provided some additional help for her worsened ADHD symptoms.

Joe's Story

Joe had mild ADHD symptoms his whole life but hadn't ever sought treatment. He felt that his job as a computer coder played to his strengths and largely avoided his weaknesses. But when he had to work from home during the COVID epidemic, without his coworkers around to reinforce the start to the workday, when to eat, when to go home, and whether he was staying abreast of his projects, he began to flounder. He had become accustomed to having ready access to the delicious lunches served in the tech company's cafeteria. That was his main sustenance for the day, and that too was gone. He sought an evaluation for ADHD and started treatment to get his life back on track.

Jim's Story

Jim, a fitness instructor, had never particularly displayed any signs of ADHD. Young and healthy, he hadn't felt a need to get vaccinated. He was blindsided by his first bout with COVID, which sent him to the hospital and had him briefly on an assisted breathing device. He was told that he had survived a "cytokine storm." But even more debilitating than the acute infection was its aftermath. He sought treatment for his shortness of breath, but he delayed seeking help for being "muddle-headed." It wasn't until a year after his initial infection that he began looking for a doctor who could help him with episodic headaches and problems with memory, attention, and sustained thinking.

Jill's Story

Jill lost her eighty-six-year-old father to COVID the same week that her own secretarial job was eliminated due to pandemic-related downsizing. She had a recurrence of depression. But this felt different from the depression that had followed the birth of her second son, decades earlier. She was alarmed that she had significant problems recalling events, went off-track mid-task, and felt unable to focus long enough to read to the end of brief, online news articles. She was worried that she had dementia, not just depression.

COVID deposited all these individuals, through differing pathways, onto different swaths of the ADHD spectrum. Jane's existing ADHD was exacerbated. Joe's subthreshold ADHD became full clinical ADHD. Jim had a new onset of

secondary ADHD. Case reports of individuals like Jim, with completely new onset ADHD, were also reported around the world (Victor et al. 2023). Others, like Jill, had depression or anxiety masquerading as ADHD symptoms.

We've become increasingly aware that even surviving acute infections with COVID doesn't mean the end of the story for suffering. Many people are disabled with long COVID that interferes with their lungs, heart, energy levels, or other bodily functions. But self-reports collected by the US Census Bureau indicate that a sizable majority of long COVID impairment is caused by attacks on the brain.

For the decade prior to the pandemic, the number of people in the US describing themselves as impaired or disabled was remarkably stable, at around 16 million. That number began rising abruptly in mid-2020, with an additional 1.7 million Americans identifying themselves as disabled by mid-2022 (Deitz 2022). Of that total, 1.3 million described their disability as based on "difficulty concentrating/remembering." While some of those individuals have recovered, the pandemic has left hundreds of thousands of Americans with brains that aren't working nearly as well as they were a few years ago. Similar effects have been observed around the world.

Some infectious disease experts estimate that 10 percent of individuals infected with COVID develop long COVID. At least half of Americans identify as having a COVID infection, and the number is undoubtedly higher, since many people had "silent," or asymptomatic, infections that went undetected, except by laboratory testing. But even asymptomatic coronavirus infections can lead to long COVID (Ma et al. 2023). Millions of Americans have become part of attention deficit world through the action of the coronavirus. Direct correlations between the coronavirus pandemic and rates of ADHD diagnoses have been observed in numerous countries (Ferrara et al. 2023).

What Is Long COVID?

Medical experts are still sorting out how to define and diagnose long COVID, which is the persistence of significant health problems months after being infected by the coronavirus (Pfaff et al. 2022). More than fifty different symptoms have been identified, affecting every major organ system of the body. Fatigue is present in 80 percent of cases (Davis et al. 2023). But the symptom cluster leading most frequently to functional impairment consists of the cognitive problems loosely labeled "brain fog" (Zayad and Rosen 2024). Brain fog includes problems with memory, attention, concentration, organization, and initiation of tasks. Measurable impairments on cognitive testing and abnormalities on brain scans are both associated with the self-reported symptoms of brain fog in people with long COVID (Li et al. 2023). Although only about 25 percent of those with long COVID report having brain fog or other cognitive challenges, this represents the majority of those who consider themselves severely impaired or disabled by their condition (Lopez-Leon et al. 2021).

Acute infection with the coronavirus is still considered primarily a respiratory condition, but long COVID symptoms can affect the lungs, heart, skin, brain, kidneys, digestive system, or combinations of these. To qualify as long COVID, symptoms have to be present at least twelve to sixteen weeks after an acute infection. Sometimes symptoms resolve after a few weeks, but in other cases they can persist undiminished for at least a few years. We don't yet know whether long COVID becomes a permanent condition for some individuals or whether it will resolve, albeit after years, for most of those who suffer from it.

While we have some general predictors of who may contract long COVID, there is a huge amount of individual variation. Factors that increase the risk of long COVID include:

- More severe acute infection
- Not having been vaccinated prior to infection
- Greater age
- Poorer overall health

Some, but not all, research suggests that earlier strains of the virus are more likely to lead to long COVID (Hernandez-Aceituno, Garcia-Hernandez, and Larumbe-Zabala 2023). Involvement of the central nervous system (loss of smell, delirium, coma, seizures) as part of the acute infection makes it more likely that someone will develop long COVID that affects their brain. Initial rashes and other skin reactions to the coronavirus may also predict later brain involvement. If that sounds surprising, consider that the skin and the brain share a common origin in the layer of the embryo that developmental biologists call the ectoderm.

Studies of those with long COVID brain fog have demonstrated measurable deficits in executive functions that correlate with individuals' experiences of problems with concentration, memory, and focus (Velichkovsky et al. 2023; Hampshire et al. 2024). Studies summarized by Zhitao Li and colleagues found that the types of memory problems displayed in long COVID patients during test-taking implicate frontal attentional circuitry and not just the involvement of hippocampal memory storage (Li et al. 2023). This pattern of deficits corresponds quite well to what is seen in many individuals with ADHD.

What's Causing Brain Changes?

How can a respiratory virus have such profound effects on the brain? Experts consider at least five potential pathways (Monje and Iwasaki 2022):

- Direct viral **infection** of the brain
- **Inflammation** of the brain or other parts of the nervous system
- Damage to the brain's **blood supply**
- Destruction from chronic **stress**
- **Psychosomatic** involvement, meaning mental factors cause or worsen symptoms

Infection

One of the classic symptoms of COVID-19 infection is the loss of smell, caused by damage to olfactory neurons at the back of the nose. In at least some cases, the virus propagates from these brain cells more deeply into the brain (Stein et al. 2022). We don't know how often neurons and supporting brain cells are infected in individuals with long COVID, but direct infection probably plays only a minor role in most individuals.

Neuroscientists are particularly fortunate that the British BioBank study began before the pandemic (Douaud et al. 2022). This means that for several hundred individuals, researchers had pre-coronavirus baseline MRI scans and neuropsychological tests that could be compared to their post-infection performance. These people could also be contrasted with a control group of individuals who didn't become infected with the virus. In both groups, the follow-up imaging and testing was done about three years after baseline data were collected.

Those who had been infected with COVID showed measurable shrinkage in a few brain regions directly connected to the olfactory cells at the back of the nose. But a subset of patients who were hospitalized with more severe COVID infections also displayed a reduction in the gray matter (nerve cells) in the frontoparietal cortex. Furthermore, this brain shrinkage was associated with diminished performance on memory, planning, and attention tasks.

Inflammation

Neuroinflammation appears to be the major culprit behind long COVID's attack on the brain (Braga et al. 2023). Acute infections with the coronavirus are notorious for causing "cytokine storms" and other expressions of extreme immune system activity in the body. Biochemical and anatomical signs of inflammation of brain tissue have been found in those with long COVID, including extensive scarring, called gliosis, in the frontal cortex.

Yale neuropsychiatrist Arman Fesharaki-Zadeh and his associates have marshaled evidence for the theory that the frontal cortex is particularly vulnerable to the coronavirus because it relies heavily on one type (NMDA) of glutamate receptors (Fesharaki-Zadeh, Arnsten, and Wang 2023). Glutamate, an excitatory neurotransmitter, is the most abundant neurotransmitter in the brain. Neuroinflammation and other toxic processes create chemicals that can damage the NMDA receptors, resulting in brain cell death, further inflammation, and disruption of critical pathways.

Blood Supply

The coronavirus also increases the propensity for blood clots and can cause inflammation of the lining of small blood vessels. The brain is one organ that is full of capillaries as well as small veins and arteries. When blood supply is cut off, brain cells die quickly. Evidence of multiple, tiny micro-strokes have been found in the brains of those with long COVID and are associated with impaired brain function.

Normally, the brain is somewhat protected from large molecules in the bloodstream by the semipermeable membrane called the blood-brain barrier. But acute infection with the coronavirus can disrupt this barrier, allowing potentially harmful molecules and the body's own inflammatory chemicals to more easily infiltrate the brain. In individuals with long COVID, researchers have found persistent, localized disruptions in the blood-brain barrier that are closely associated with the presence of brain fog and cognitive impairment (Greene et al. 2024).

Early in the pandemic, researchers discovered that brain blood vessels were damaged in individuals who incurred lethal COVID infections (Lee et al. 2020). Impairment in brain blood flow can be detected in individuals who survived severe COVID but whose brains appear normal by other types of testing (Qin et al. 2021). Other groups have documented decreased blood flow in parts of the brain in individuals with cognitive impairment from long COVID (Ajcevic et al. 2023).

Stress

Long COVID can produce long-term breathing difficulties, heart problems, rashes, and kidney damage. When a body fails to work the way it functioned before a COVID-19 infection, it can trigger the body's chronic stress reactions. Chemicals produced by the adrenal glands, and by neural circuits in the brain itself, can flood the body and brain with elevated levels of the hormone cortisol and the fight-or-flight neurotransmitters norepinephrine and epinephrine. At high levels and over prolonged times, each of these chemicals can be lethal to brain cells and disrupt neural circuits.

Psychosomatic

In the early weeks and months of the pandemic, the medical establishment often dismissed those who had cleared the virus from their body but who had persistent medical issues as having psychosomatic reactions. The strong implication was that their symptoms were "all in their head." Individuals were told that they really weren't tired, short of breath, or having trouble thinking. Instead, they were really just responding to the fear of living in the shadow of COVID-19, the anxiety of losing their job, the burden of having to work from home, the sadness of loved ones dying, or the confusion

and anger stirred up by political battles about COVID. We now know that many of those individuals, in fact, did have physical disruptions to their brains that were producing their symptoms.

Curiously, we seem to have completely flipped the script. Now that we know of at least four concrete, physiologic mechanisms by which coronavirus infection can damage the brain, I haven't read a single research article that addresses possible psychosomatic aspects of brain fog. Yet we continue to live with turmoil, confusion, hardship, and conflict, and it remains highly likely that psychological mechanisms are contributing to some of the brain problems observed in at least a few individuals with long COVID brain fog.

Although randomized controlled studies of treatment of ADHD caused by long COVID aren't yet available, clinics specializing in this field have been using the entire range of ADHD treatments to address symptoms of brain fog and executive dysfunction. These include stimulants (Ritalin, Vyvanse), non-stimulants (Wellbutrin, Strattera), guanfacine, amantadine, and N-acetyl cysteine as well as cognitive and behavioral therapy and neurofeedback approaches.

Feedback Loops

Not only did the early stages of the COVID pandemic contribute to attention deficit world, but long COVID also continues to create ADHD-like symptoms in many individuals. ADHD also makes it more likely that people contract COVID (Davoody et al. 2022). Distractibility, lack of attention to detail, impulsivity, and hyperactivity all increase the likelihood of viral exposure. People with ADHD are more likely to forget to wear a mask, wash their hands, or avoid touching their face. They are more likely to incorrectly estimate or ignore social distancing recommendations. They are less likely to attend to warning signs such as the person next to them coughing or sneezing, and they are less likely to follow through with protective measures if they do notice such behavior. When a person moves about more (hyperactivity being a symptom of ADHD), it increases the chance of entering into proximity with infected individuals.

Furthermore, the ADHD-COVID feedback loop intertwines with multiple other ADHD feedback loops. Sleep disruption decreases the efficacy of the immune system in fighting off infections. Being overweight, having low cardiovascular fitness, and smoking are all associated with ADHD, and all are risk factors for more severe COVID infections. COVID created more ADHD, and ADHD created more cases of COVID.

Section 3. ADHD and Plastics

Plastic pollution is a huge problem, as exemplified by the size of the Great Garbage Patch swirling amidst the Pacific Ocean. But it's also a tiny problem. The more we investigate, the more we uncover smaller and smaller plastic particles permeating not just our drinking water, soil, and air but also our bodies, including our brains (Nihart et al. 2025). Unless you sequester yourself in a (non-plastic) bubble, you can't avoid this exposure.

Maria's Story

Maria was a single mother and empty nester. She was considering retiring from her clerical job because she was finding it harder to concentrate at work and was making many more simple mistakes at home. Seeing a news story about the risks from toxins in black plastic cooking utensils drove her to wonder whether that might be causing her cognitive problems (Liu, Brandsma, and Schreder 2024).

When she came in for a consultation, we discussed that the risks from utensils had been overstated in the original study, and that research on the effects of plastics on the brain is still in its early stages. We reviewed other possible contributors to the cognitive issues she had noticed, including menopause and recent changes in her role in life, and outlined lifestyle changes that might be of help. She also scheduled an in-depth neuropsychological evaluation.

Background on Plastics

Much of the research on the biological impact from plastics has focused on their effect on hormones and fertility: androgens, estrogens, sperm counts, and deformed genitalia. But androgens and estrogens also influence brain development. Plastics, particularly exposure to phthalates and bisphenol B early in life, are associated with a greater risk of developing ADHD. ADHD-driven lifestyles increase the risk of exposure to these toxins.

The word “plastic” means “capable of being molded.” Now our very brains are being molded by our exposure to plastics. Dozens of studies link higher body levels of chemicals from plastics with a higher likelihood of developing cognitive deficits, ADHD, and autism (Minatoya and Kishi 2022; Kamai et al. 2021). Administering these same chemicals to mice interferes with neural development and replicates the hyperactivity and some of the other behaviors of ADHD (Ko et al. 2024). In particular, two classes of chemicals added to plastics—phthalates and bisphenols—harm developing brains.

Plastic Proliferation

Chemists developed petroleum-based plastics more than a century and a half ago. Early plastics were lighter (reducing transportation costs) and more easily shaped than most metals, glass, and wood, but were rigid and brittle. In the post-WWII years, the widespread addition of plasticizers, chemicals that increased the flexibility, durability, and transparency of plastics, kick-started the pervasive use of plastics in packaging, construction materials, and toys.

Manufacturers use phthalates to make polyvinyl chloride (PVC) and other plastics. Most PVC pipes, automotive plastics, wiring insulation, medical tubing, vinyl flooring, hoses, plastic sheets, and films used for packaging contain phthalates, as do many plastic toys. Phthalates are also added to adhesives, detergents, lubricating oils, soaps, hair sprays, and nail polish. The most prevalent bisphenol, bisphenol A (BPA), lines many of the cans for storing food.

During production, plasticizers are mixed in with, but don't chemically bind to, the plastic. That means phthalates or BPA can escape into the environment, or leach directly into people, during any of these stages: manufacturing, usage, recycling, and disposal. Although recycling in general is a good way to reduce the use of resources and conserve energy, recycling old PVC can lead to an increased release of phthalates and other plasticizers (Pivnenko et al. 2016).

Bodies also absorb phthalates through direct skin exposure, as well as from eating and drinking food and beverages wrapped or stored in plastic. BPA exposure occurs mainly through food consumption. The smaller the size of the particles, the greater access they have to various parts of the body. Even people living in remote, non-urban areas have at least some traces of these plasticizers in their bodies (Padha et al. 2022). Compared to some other classes of plasticizers, phthalates and BPA are not “forever agents”; rather, they decompose within hours or days. But most of us are constantly re-exposed, on a daily basis, because these chemicals are so prevalent.

Phthalates and BPA are also highly fat-soluble. Our bodies need to chemically modify them in order to excrete them in the urine. Being fat-soluble also means that they are particularly good at penetrating that large fatty organ, the brain. Average concentrations in the brain of several different types of plastic were found to be more than ten times higher than in the kidney or liver, and plastic levels have increased markedly just within the last decade (Nihart et al. 2025).

Plasticizers During Pregnancy

In one meta-analysis, 92 percent of published studies found an association between exposure to phthalates during pregnancy and the likelihood of a child developing ADHD (Rosi et al. 2023). Another review, examining a range of environmental pollutants, identified the three agents most strongly linked to later development of ADHD to be phthalates, BPA, and lead (Moore et al. 2022). Phthalates have been linked to impairments in a number of neurodevelopmental processes, resulting in conduct problems and poorer vocabularies. Bisphenol A exposure is particularly associated with subsequent hyperactivity, anxiety, and difficulties with emotional control and behavioral inhibition. Many studies have found connections between phthalate exposure and neurodevelopment problems at doses lower than what is considered “safe.” Also, most studies only examined a few types of phthalates, measured them at only a few points during pregnancy, and examined only a narrow range of brain or behavioral outcomes.

Biologists use the term “critical period” to indicate that the ability of outside factors to alter development may be restricted to certain periods of time. Critical periods in the nervous system usually occur when crucial neurons are forming, moving into position within the brain, or establishing connections with other brain cells. A chemical might have toxic effects during the critical period but have negligible effects earlier or later in development. Studying chemical exposure outside of the critical period could erroneously lead to the conclusion that the chemical had no negative impact. Some studies suggest that while fetuses may be particularly vulnerable to the effects of plasticizers, at least in rodents, exposure during adulthood can also lead to negative behavioral and cellular effects (Gaspar et al. 2023).

Not only is the time of exposure to toxins important in these studies, but when a behavioral outcome is studied can also determine the likelihood of finding an impact. Human brains continue developing long after birth. One study looking at the effects of maternal exposure to phthalates didn't detect a heightened rate of attention problems in their children until adolescence (Watkins et al. 2021). If they had stopped the study in childhood, this effect would have been missed.

Furthermore, studies looking for the effects of a single agent oversimplify reality, where almost everyone is exposed to multiple environmental pollutants simultaneously. Exposing pregnant rats to a combination of phthalates and other chemicals produced different negative neurologic effects compared to exposure to a single agent; the interactions can either worsen or mitigate some of the effects (Tanida et al. 2009).

Studies linking exposure of pregnant women to phthalates or BPA with higher rates of ADHD or autism in their children can at most show an association. However, when researchers intentionally expose test rodents to plasticizers and other rodents to placebos, and demonstrate biologic problems in those given the chemicals, we have a stronger case that plasticizers actually *cause* these negative health impacts (Ko et al. 2024).

Even with equivalent environmental exposure to phthalates and BPA, individuals with a genetic predisposition to ADHD might wind up with higher blood levels of these toxins (Stein et al. 2023). Glucuronidation, the biochemical system responsible for clearing the blood of phthalates and other contaminants, actually involves dozens of different enzymes, each focusing on binding glucuronic acid to one specific type of chemical. Stein's research also indicates that in those with ADHD, most of the glucuronidation system functions well, except for the very specific enzyme needed to clear phthalates from the blood, which is impaired.

How Might Phthalates Harm the Brain?

Having established the connection between phthalate exposure during pregnancy and behavioral problems in offspring, how might that process occur? Several possible mechanisms exist, any or all of which may be at play in any given individual. Phthalates have been shown to have these biologic effects, all of which impact the brain:

- Endocrine disruption—sex hormones affect the brain
- Lipid synthesis—brain receptors are embedded in lipid membranes
- Suppression of neurogenesis—fewer neurons are made
- Suppression of synaptogenesis—neurons don't connect to each other
- Thyroid disruption—thyroid hormones affect the brain
- Growth hormone—also affects the brain
- Inflammation—impairs neural communication, kills brain cells
- Epigenetics—which brain genes are methylated and turned on or off

Our current understanding is that these detrimental biological effects of phthalates and BPA all contribute to wiring the brain in a slightly atypical way. Exposure to these chemicals makes it more likely that someone with a high genetic risk for ADHD displays the condition. These forces may also push someone with subthreshold ADHD further along the ADHD spectrum and might propel individuals with low genetic risk for ADHD onto the spectrum.

Mothers vary in the extent to which they have been contaminated by phthalates or BPA, but very few escape all exposure, and recent generations face far greater plastic burdens than did previous generations. Even with equivalent exposure, some developing brains will be more vulnerable than others. The impaired glucuronidation pathway for eliminating phthalates, mentioned above, is one form of such increased vulnerability. But none of us lives in a bubble. And in this day and age, the bubble, made of either plastics or detergents, would probably contain phthalates. All of our brains probably have some degree of impairment, however slight, from our chemical exposures.

Although plastics have been around for more than a century, our use of them has dramatically proliferated in the last few decades, and their pervasiveness in our world has increased hugely in just the last decade. We know that they are affecting bodies, brains, and behavior, but we have yet to learn the size of their impact. It's unclear how many new cases of ADHD they are producing.

That will be hard to sort out because of feedback loops and confounding variables. Having ADHD, on average, reduces occupational choices and incomes and increases the likelihood of living in a neighborhood with higher exposure to toxic substances. ADHD also increases the likelihood of consuming more prepackaged food, further compounding one common and significant source of exposure to plastics.

Section 4. Loneliness and ADHD

We're awash amid seas of internet connectivity, yet we're often drowning in loneliness. Despite having ways to interact with others that our grandparents never imagined, many of us feel disconnected and isolated. Compared to members of past generations, we're much more likely to live far away from where we grew up. In his tenure as surgeon general, Vivek Murtha issued a health advisory on loneliness, declaring it a major public health issue and how, despite its impact, we have been neglecting it (Murtha 2023). Apparently, even loneliness feels lonely. He beseeched us to pay attention to how we are changing the ways we relate to one another, because we are causing serious harm to our bodies and communities. Loneliness kills people.

Much of the mental health impact of loneliness has focused on how it increases the likelihood of dementia in the elderly and the risk for depression across all ages. We've paid less attention to the fact that loneliness is associated with a deterioration in executive functions central to ADHD, including short-term memory, attention, impulse control, and emotion regulation. Our actions as individuals are changing our social environment in ways that potentially create millions of new cases of loneliness, and cases of ADHD. We are doing so without much awareness. If we want to avert this societal shift, we need to grasp more firmly the ways in which we are harming ourselves.

Marla's Story

Marla, a bookkeeper in her mid-fifties, hasn't been able to find new work since her job was downsized during the COVID pandemic. Her husband continues to be busy as a plumber and is in such demand that not only is he gone all day, but he also frequently responds to emergencies during evenings and weekends. She is estranged from her daughter, who lives in a far-off city, over political differences. Marla has been spending many of her hours playing Sudoku and word-finding puzzles. But she's finding it harder to concentrate and complete her games, too unsettled by the news to pay attention, and more scattered and inconsistent in attending to household tasks. She told her doctor that she didn't really feel depressed, but rather a mental foggy and sadness similar to what she had felt during menopause, a few years earlier. But this time the impairments felt more pervasive and inescapable.

Only the Lonely: Defining Loneliness

Social isolation describes the situation of having limited interactions with others. It can be measured in terms of the number of close contacts, the frequency of interactions, or hours a day spent with others. Loneliness, in contrast, is a *subjective* feeling that one's social connections are inadequate. Although social isolation and loneliness overlap substantially, some isolated people are content with their solitude. Others who appear to have extensive social engagements feel disconnected and lonely. Research indicates that loneliness and social isolation produce separable, distinct, negative impacts on physical and mental health (Cardona and Andres 2023). Yet current research methods don't generate an accurate portrait of either problem.

Psychologists usually measure loneliness by asking one, or at most a handful, of questions regarding one's subjective sense of inadequate connection to others. But loneliness, like ADHD, exists on a spectrum of severity. When we force people into an either-or response, some individuals with significant feelings of loneliness will be lumped in the wrong group, weakening findings based on such research.

Further compounding the inaccuracies, many studies collect data at just one point in time, comparing the presence of loneliness to some other variable of physical or mental health. At best, that research can show an association. For example, coronary heart disease is linked to loneliness (Xia and Li 2018). But simple correlations can't show cause and effect. Longitudinal studies, measuring loneliness at multiple points in time, and determining that loneliness precedes negative health outcomes, provide a stronger indication that loneliness might be a contributing cause. Such research reveals that pervasive loneliness appears more toxic to cognitive function than just feeling lonely at one point in time (Tao et al. 2022). Fortunately for individuals, but unfortunately for research, we do have a few randomly controlled trials of children in orphanages, some of whom were left in states of extreme loneliness and others adopted or fostered at various ages, which more clearly reveal the potential impact of severe loneliness early in life on physical, cognitive, and emotional growth.

In the 1950s, psychologist Harry Harlow used wire-frame mother monkeys to show that baby monkeys supplied with milk and physical warmth but deprived of maternal contact developed severe problems interacting with other monkeys as they grew up. Children left in orphanages, provided with adequate physical care but minimal intimate connections with humans, compared to those children who find foster homes, develop pervasive mental and physical health problems (King et al. 2023). Children who are adopted from such institutions at earlier ages have greater preservation of working memory and inhibitory control than those adopted at later ages (Dydenkova et al. 2024). The evidence that loneliness causes massive damage to emotional and cognitive health is so clear-cut that such “experiments” are no longer ethically permissible.

The COVID pandemic, and ensuing restrictions on previously normal patterns of interaction, provided another “natural” experiment on social isolation and loneliness. In general, those with ADHD tended to feel more loneliness during the pandemic than those without ADHD, and their isolation prompted more distress and dysfunction (Scriberras et al. 2022).

Why Loneliness Hurts

Humans have been social animals for millions of years. Group membership was essential for survival; humans couldn't ward off the big cats, woolly mammoths, and bears that wanted to eat us. Individuals faced big challenges in finding and gathering the diversity and volume of plants needed to survive. Catching enough game or fish to provide sufficient high-quality protein was easier as a cooperative venture. Solo humans simply died.

The necessity of remaining part of a group was built into our brains. Being lonely hurts. Pain from social isolation and from physical trauma share much of the same brain-pain circuitry (Zhang, Zhang, and Kong 2020). Pain provides important information and directs a response to that message. Pain tells the rest of the brain: This is really important! This is so bad! You need to do something to change this! In response, people pull their hand out of the campfire, stop walking on their broken ankle, or try to reconnect with the brother who just snarled at them.

Loneliness produces toxic effects that rewire the brain through both brain chemicals and patterns of brain activity. Brain chemicals include cortisol and adrenaline. In the short term, these provide useful information within the brain, motivating us to face a fear or run from it. But after prolonged exposure—the sort of stress induced by chronic loneliness—these chemicals act directly to kill brain cells and prune nerve cell connections.

Loneliness also damages the brain through the patterns of neural activity it induces. Nerves that fire together get wired together. By reducing interactions with others, social deprivation narrows our repertoire—we don't practice certain skills, so they shrivel. Even worse, we over-engage in rumination and worry about our lonely social status, which over-strengthens the default mode network. Loneliness reduces connectivity within attentional circuits in the brain and weakens executive functions (Layden et. al 2017). Loneliness degrades our brains.

How ADHD Causes Loneliness

Beginning at an early age, many individuals with ADHD recognize that their brains work differently than others, and that they are being treated differently than their peers. Inattention, hyperactivity, and impulsivity in those with ADHD can all contribute to social isolation and higher rates of loneliness than among those in the general population. This doesn't mean that all of those with ADHD are lonely. A sizable subset of those with ADHD are exceptionally gregarious and impervious to slights or negative feedback. Many with ADHD are well-adjusted individuals, valued by their friends for their spontaneity and their enthusiasm during social events.

Still, higher rates of loneliness among those with ADHD are seen in children (Smit, Mikami, and Normand 2020), adolescents (Jong et al. 2024), and adults (Stickley et al. 2017), as well as in both men and women. The association is only partly explained by other co-occurring mental health conditions; even with depression removed from the picture, ADHD is still associated with loneliness. The more severe the ADHD, the greater the likelihood of loneliness. Some of the susceptibility to loneliness appears to be under genetic control (Jami et al. 2022). But looking at group averages research shows that those with ADHD have a greater likelihood of the following measures, which are themselves associated with loneliness (Faraone et al. 2021):

- Relationship difficulties
- Poor relationship quality
- Being single
- Being divorced
- Feeling or acting suicidal

The ways in which neurodivergent individuals and the societies they inhabit interact with each other contribute to the greater prevalence of loneliness among those with ADHD in our modern world. Across different times and cultures, people often perceive differences as undesirable, subjecting those with ADHD to negative feedback, criticism, and rejection. In turn, this encourages many with ADHD to withdraw from, or restrict, their social interactions, contributing to loneliness.

Because of inattention, people with ADHD are more likely to miss social cues—they might not see someone's facial expression, they may fail to register who has higher status in the hierarchy, or they may not realize that it isn't their turn to speak. Breaking social norms causes conflict, which can in turn trigger resentment, confusion, social withdrawal, isolation, and loneliness. Of note, those with ADHD usually comprehend social communication when it's pointed out—they simply hadn't been attending to those details (Chan and Leung 2022). In contrast, a core symptom of those on the autism spectrum is difficulty processing social communication. Even when social cues are explained, the autistic individual still may not perceive them as meaningful, relevant, or reasonable. Furthermore, impulsivity and hyperactivity can lead to those with ADHD invading the personal space of others. Such behaviors include:

- Physically stepping on others' toes
- Bumping into others
- Fidgeting noisily without awareness of distracting others
- Standing too close while talking
- Cutting off others in conversation
- Being too candid or brutally honest in conversation

All of these behaviors contribute to the likelihood of social rejection by others, with consequent social isolation and loneliness.

Hyper-focusing, or becoming so absorbed in a task that a person is oblivious to the rest of their environment, is an additional ADHD trait that can lead to loneliness. If you're so busy coding that you don't even realize that all your coworkers have gone to lunch you will miss out on social connections. Others may mistake hyper-focusing as an intentional snub. Hyper-focusing can also drive excessive immersion in activities such as online gaming. Those with ADHD are substantially more likely to develop problems such as gaming addictions (Koncz et al. 2023) and excessive involvement in social media, which themselves are linked to loneliness. Those who adopt perfectionistic tendencies to compensate for their ADHD may also end up lonelier (Shafiq, Ali, and Iqbal 2023).

How Loneliness Worsens ADHD Symptoms

Few studies have been designed to determine whether loneliness specifically worsens ADHD, but numerous research projects demonstrate that loneliness is a predictor for the deterioration of cognitive and executive functions (Baumeister, Twenge, and Knuss 2002). While many of these studies were explicitly looking for the impact of loneliness on the development of depression or dementia (Cardona and Andres 2023), the executive functions they measured are the core components of ADHD. Loneliness precedes and is associated with (Sin, Shao, and Lee 2020):

- Poorer impulse control
- Poorer working memory
- Poorer planning and organization
- Poorer emotion regulation

A brain that marines in loneliness is practicing these ADHD traits. It is rewiring itself to continue to act more often in ADHD-like ways. And it is moving further along the ADHD spectrum of severity.

At the social level, more loneliness doesn't just mean more detached and unhappy individuals; it also means more impulsivity, more distractibility, poorer retention of information, and greater emotional volatility when these people do interact. Loneliness isn't just a result of individual decisions and actions; it also foments deterioration of the social fabric as well as deterioration of individual brains. Even if you aren't lonely, you're likely to have been deprived of connections with other people because of their loneliness.

Loneliness and ADHD interact in a toxic feedback loop. Loneliness adds to ADHD symptoms, and ADHD contributes to loneliness. Loneliness pushes brains further along the ADHD spectrum. Those who already have ADHD will demonstrate more severe problems. Some with mild symptoms will be pushed into clinical ADHD. Many more will suffer from additional episodes of inattention, distractibility, and frustration.

The loneliness-ADHD loop is compounded by additional factors. Loneliness is associated with less healthy eating patterns, overuse of social media, disturbed sleeping patterns, and less exercise, all of which themselves worsen ADHD symptoms. Loneliness has already scarred many of us; as Surgeon General Murtha pointed out, this is not just a personal but also a social catastrophe. Loneliness causes brains and societies to wither. Unless we start paying attention to the ways we are ruining our lives, we can't alter them. The longer we wait, the less collective ability we have to collaborate and focus on what we need to change.

Section 5. Additional Information on Sleep and ADHD

Sleep problems are associated with a broad range of mental health conditions, and the connection is particularly strong among those with ADHD. Those with ADHD are more likely than the general problem to have erratic sleep patterns and to have trouble both falling asleep at bedtime and waking up in the morning. In addition, sleep deprivation and sleep disruption in individuals with clinical ADHD can powerfully worsen symptoms, and can create symptoms resembling ADHD in those not previously on the ADHD spectrum. Sleep disruption has both immediate and chronic effects undermining executive functions.

Stimulants and Sleep

Some people worry that taking stimulants, even if just a dose in the morning, will rev them up and make it harder to sleep at night. This indeed is one of the more common side effects of these medications, particularly in the first few days of use. It is often an indication to reduce the dosage, take the pill a few hours earlier in the morning, or take a shorter-acting version of the medication. But research shows that, rather than disrupting sleep, those with ADHD often experience an improvement in nighttime sleep after they start taking stimulants (D'Aiello et al. 2025). While the fact that stimulants can improve sleep may seem paradoxical, there are several possible explanations: the medications may help strengthen circadian rhythms and provide the brain with a clearer signal to fall asleep at night; being more productive and alert during the day can increase fatigue by evening; and having accomplished more tasks and having greater social harmony during the day due to the stimulant decreasing ADHD symptoms can allow for greater relaxation at the end of the day.

A subset of individuals with ADHD and insomnia actually benefit from taking a small dose of stimulants right at bedtime. Most often these are individuals who describe their thoughts as jumping inside their heads and that they're unable to quiet their minds. These are not usually individuals with high levels of anxiety and worry driving their bedtime thoughts. The low-dose stimulant allows those with non-worry-related, rapidly ping-ponging brain activity to corral their thoughts and turn off their arousal so sleep can arrive. This is an approach that should only be tried with caution, starting with a very low dose, because stimulants late in the day do increase the level of arousal for many.

Sleep Medications

Most of our older sleep medications are sedatives that just strengthen the signal to sleep. This includes barbiturates; benzodiazepines like Restoril, Halcion, Xanax, Valium, Klonopin, and Ativan; and "z-drugs" (Ambien/zolpidem, Lunesta/zopiclone, and Sonata/zaleplon) that work on benzodiazepine receptors but have a different chemical structure. These medications tend to work better in the first few days and weeks than they do after months or years. In addition to the problem of tolerance, they can cause addiction and bizarre behaviors during states of partial sleep. Fundamentally, they're working on a part of the system (strengthening sleep) that isn't the source of most insomnia. Most insomnia is from the failure to shut off daytime arousal, not because nighttime sleep systems are broken. All of the above mentioned medications should be used sparingly, if at all; only in consultation with medical professionals; and only after systematic sleep hygiene and cognitive behavioral approaches have failed.

Some other medications (Rozerem/ramelteon and melatonin) appear to work primarily by increasing the circadian signal for sleep onset. In contrast, the newest class of sleep agents, called dual orexin receptor antagonists (DORAs) (Belsomra, Dayvigo, Quviviq), work to shut down excessive daytime arousal that is inappropriately still turned on at bedtime. They're not directly sedating, but they help with sleep. Whether these options really are safer and outperform our older sleep medications in the long term has not yet been clearly demonstrated.

Naps and Siestas

I usually don't recommend napping because most of the naps described by my patients are a response to feeling tired from not getting sufficient sleep the previous night. Napping midday then disrupts the fatigue factor, one of the primary forces influencing sleep at night. Napping thus encourages another night of insufficient sleep, which reinforces continued daytime napping and more problems with nighttime insomnia. However, there are some individuals who do manage to use strategic, short daytime naps to improve cognitive performance without disrupting nighttime sleep.

Siesta time is a phenomenon that American culture has persistently failed to address. If they think of it at all, Americans tend to dismiss siesta time as an indulgence practiced by relaxed inhabitants of warm climates. Yet humans show a real, biologic decrease in alertness, and an increased propensity to sleep, in the early afternoon. This is a true innate circadian rhythm, not just a pattern induced by having a big midday meal. Curiously, many of the individuals with ADHD whom I work with are not aware of having any siesta time lull in alertness until after they have begun treatment with medications. This newfound awareness might stem from increased ability to track and recall their own bodily sensations. Or it could arise from their circadian clocks working in greater synchrony with each other, making the midday lull more distinct. Or it may simply be that medications make some individuals more productive in the mornings than they customarily were, and consequently more fatigued by midday.

The first step in dealing with the siesta lull is understanding that this is a normal, biologic pattern of humans. Next, I encourage respecting the fact that at certain times of day humans are less productive. In response to siesta time, it may make sense to schedule a midday walk or work break or to opt for focusing on tasks that are less reliant on attending to fine details. For some individuals an adjustment in the timing of medications is important to account for this midday lull. However, I usually discourage using medications to try to blast through the entire day at "full force."

Section 6. Perfectionism and ADHD

One of the ironies of our imperfect world is that many individuals make themselves—and often those around them—miserable by struggling for perfection. After all, there are only seven perfect people on the planet.

What? Huh? Who? Oh!

I always word it that way when talking with patients. It makes people think about the topic. In contrast, the phrase “nobody’s perfect” is so trite that it tends to be dismissed without thought or automatically rejected with the counterclaim, “I’m not trying to be perfect.”

Psychologists define perfectionism as straining compulsively for unattainable goals or striving to be in a flawless state, devoid of any errors or mistakes. Perfectionism is unattainable, and our inability to achieve perfection is fuel for a range of miseries. Many insist it’s “just the way I am” or “part of my personality” so it can’t be changed. But plenty of research indicates that for many, perfectionism can be reduced, and that doing so leads to healthier, happier lives.

The Two Types of Perfectionism

There’s a close connection between perfectionism and measuring self-worth according to productivity and accomplishments. Perfectionists tend to see their value as tied to the tasks they’ve completed and how highly those achievements are rated. Being harshly self-critical has a strong association with perfectionism and is a predictor of reduced overall life satisfaction (Fekih-Romdhane et al. 2023).

Some research distinguishes between self-oriented perfectionism (the pressures we place on ourselves) and socially prescribed perfectionism (perceived external pressures) (Powers et al. 2011). Self-oriented perfectionism is based on internal standards, not on the expectations of others. This generates internal motivation to complete a task, rather than the external motivation promoted by socially prescribed perfectionism, which is strongly associated with insecurity and negative self-views.

Researchers generally conclude that socially prescribed perfectionism is maladaptive but concede that self-oriented perfectionism may have some positive attributes because it encourages individuals to exert meaningful effort to achieve goals. However, particularly outside the laboratory situation, many individuals with one type of perfectionism often score highly on both measures (self-oriented and socially prescribed perfectionism). In everyday life, exploration of the underlying motivation for sustained, excessive effort on a particular project often blurs and diminishes the distinction between these ostensibly different types of perfectionism.

Genes have been shown to contribute to perfectionism, with the impact slightly higher for women than for men (Iranzo-Tatay et al. 2015). Somewhat surprisingly, genes have a larger role in socially prescribed perfectionism than for self-oriented. One study found heritability of self-oriented perfectionism to be about 25 percent and that of socially prescribed about 40 percent. For reference, more strongly genetically determined traits like height, or ADHD, have heritability closer to 80 percent. As with most other mental health conditions, the hereditary component is polygenic, which means that hundreds of gene variants each contribute a tiny bit to the likelihood of developing that trait. There’s no single “perfectionism gene.”

Some evidence indicates that those who pay attention to details, or what is called high-frequency spatial information, versus those who pay attention to the whole picture (low-frequency spatial information) are more prone to perfectionism (Kauffmann, Ramanoël, and Peyrin 2014). But in this association, it isn’t clear whether a certain visual style results from perfectionism or contributes to perfectionism, or both. Similarly, left-brain processing, being detail-oriented, is also associated with perfectionism, in contrast to more holistic right-brain processing (McGilchrist 2009).

Environmental Impacts on Perfectionism

Childhood environment plays a larger role than genes in contributing to perfectionism. In particular, exposure to highly critical adults—usually parents, but also other important individuals such as other family members, teachers, or coaches—can boost the likelihood that one grows up with perfectionistic tendencies. The theories propose that if a child continually receives the message that they're not good enough, they develop the thought that if they could only perform better, then they might still be loved. This can lead to obsessively focusing on being the “best little boy or girl” who does everything perfectly and pleases others.

There is undeniable logic to the approach that working harder might make one more appealing to others. But ultimately it is ineffective because nobody can be perfect. Furthermore, becoming “better,” or even perfect, ignores that the feelings of imperfection aren't a reflection that the individual person truly lacks enough good qualities to be appreciated and even loved by themselves and others. In the long term, obsessive striving actually tends to pull the individual away from interactions with others, leading to greater loneliness and feelings of isolation and rejection (Binder, Woodfin, and Hjeltnes 2022).

The Pitfalls of Perfectionism

Failure to achieve perfectionistic goals (whether internally or externally motivated) can lead to depression and anxiety. Both suicidal ideation and actions bear an association with perfectionism. And a number of mental health conditions demonstrate strong associations with perfectionism, including:

- Eating disorders
- Narcissistic personality disorder
- Obsessive-compulsive personality disorder
- ADHD

Individuals who are overly concerned with getting everything right, and controlling their bodies, have high rates of developing eating disorders, particularly anorexia. The core features of narcissism are feelings of inadequacy, which can make individuals strive to get everything right and present themselves as perfect to others. Obsessive-compulsive personality disorder is defined as a persistent pattern of preoccupations with orderliness, perfectionism, and control, leading to distress and deterioration of social connections.

ADHD may appear incompatible with perfectionism, in that those with ADHD tend to make mistakes through inattention, procrastination, blurting out comments at inopportune times, and tardiness. However, perfectionism, and needing to have everything “just right” before one starts a task, is prevalent among those with ADHD. In at least one survey of adults with ADHD, perfectionism was the number one distortion in thinking leading to dysfunction (Strohmeier et al. 2016). In some individuals with ADHD, perfectionism may be an attempt, conscious or otherwise, to compensate for past ADHD-driven errors.

Changing Perfectionism: A Choice of Therapies

When perfectionism is viewed as being determined by biology, or a fixed part of one's personality, it can increase barriers to change. But at most, genetics predispose an individual to be restricted to one section of the range of perfectionistic thoughts and behaviors. Moving from the more-perfectionistic end of the spectrum to the less-perfectionist end can result in a meaningful difference in how one lives life. Through experience or therapy, an individual may also be able to move

beyond the range of perfectionism promoted by their genes. Numerous studies indicate that therapy can reduce perfectionism. Successful approaches include:

- Cognitive behavioral therapy
- Interpersonal therapy
- Exposure and response techniques
- Acceptance and commitment therapy

Cognitive behavioral therapy involves becoming aware of errors and distortions in your thinking and learning more accurate alternatives. Changing how you think can change how you act and how you feel.

Interpersonal therapy addresses that an important driver of perfectionism is either actual or imagined rejection by powerful figures in your life. This form of therapy can help you learn that you are okay as you are and don't have to be perfect to be accepted and loved.

Exposure and response techniques challenge an individual to defy their fears, try an action that they are convinced will result in disaster, and view the actual results. When they see that turning in imperfect math homework or cooking an imperfect meal for a party still results in acceptance and approval, then they become less worried about needing to do things perfectly.

Acceptance and commitment therapy entails accepting what you can't change (including being an imperfect human being) and taking decisive steps to improve what can be altered.

Practical Tips and Tools

The following suggestions largely entail challenging patterns of perfectionistic thought. They contain redundancy and overlap, because hearing a message in multiple ways increases the likelihood that at least a few of them will penetrate resistance to change. Some of these reminders are more directed at socially prescribed perfectionism, and some at self-directed, but most of them apply to both.

Learn to set realistic goals. This involves knowing what your overarching goals are, evaluating your own capabilities (not those of a professional or an expert), and remaining aware of your time frame. At least initially, you won't be perfect at self-assessment. But that's okay, because as long as you're alive, life will keep giving you new chances.

Your calendar is your friend. Your schedule will let you know what your existing commitments are and how much time you really have available to work on a project. Life creates time constraints—including mortality itself. A nearly completed, almost-perfect project doesn't get counted if it misses the deadline. A schedule can keep you from becoming overcommitted and also teaches you how much time you actually require to complete tasks.

Consultation can help. Asking those with more experience what is a reasonable scope for your project, or what is an attainable timeline, can aid in setting realistic goals.

Delegate decisions about what's good enough. Your manager, your team members, and your audience can decide whether your efforts are adequate. That doesn't mean you can't try harder or work later on improvements. But what you do at work, or as art, or in a sport is a human task. Keep in mind that you have a common goal with your company, or your fan base, or your community of peers and that they are invested in your success, which usually doesn't require a perfect project.

You can revise your commitments. If you bite off more than you can chew, tell someone, preferably sooner rather than later. People are allowed to back off, particularly if they do so with enough time to enable someone else to take over or help.

Flexibility is the best predictor of success. Perfectionism entails rigidity. It can be hard to let go of your idea of what is right or perfect, but mental flexibility is actually much more associated with success than is perfectionism (Archer et al. 2024).

Performance is almost always on a spectrum. Everything short of perfectionism isn't a failure. Even "perfect" accomplishments can usually be improved upon. Usually your criteria for "perfect" are in fact, arbitrary, artificial, and not terribly useful.

Perfect is not attainable. Any project can be improved upon. Failing to see that demonstrates a lack of imagination or vision.

You're not a perfectionist; you have perfectionistic tendencies or behaviors. Genes and early life experiences can strongly push an individual in a particular direction, but there are always options for behavior. Knowing you can change perfectionistic behavior is the first step in changing it.

Perfectionism is only part of you. Even if one part of your brain wants things to be perfect, the other parts know that this is unattainable and that there are usually plenty of other acceptable options. The whole of your brain is stronger than just the perfectionistic part.

There are only seven perfect people on the planet. Okay, nobody's perfect.

Find an imperfect role model. All role models are imperfect. Appreciate them for what you think is great about them but also take note of their imperfections. Sports heroes who are endowed with natural strength or grace or speed are paid hundreds of millions of dollars and practice for hours a day yet they still make mistakes. Even the greatest of all time (GOATs). The same is true in art, business, politics, science, and any field of endeavor.

The perfect is the enemy of the good. Striving until a task is in perfect shape often results in producing nothing; perfectionism blocks ever quite finishing.

A single mistake seldom derails a career or friendship or romantic relationship. Your enemies already dislike you—a mistake may reinforce that but doesn't establish or cement their opinion. Your friends already hold you in positive regard—they'll cut you some slack and put any mistake in perspective because they already have a positive impression. As for the people who don't know you—most of them will keep on not knowing you. Your "failure" generally won't register with them.

You can't control what others think. Your task is to manage your own thoughts, feelings, and behaviors. What you do can influence others, but ultimately their thoughts, feelings, and behaviors are up to them.

Quest, not test. Be mindful of your quest, your overarching goal; don't make a test out of any particular approach to your goal. If you're thwarted, blocked, or failing at your current approach, there are almost always other options for moving toward your goal. If you're on the ADHD spectrum, use your nonlinear thinking to come up with alternative paths to your goal.

Don't delay getting started. Waiting until conditions are optimal, or the perfect inspiration strikes, is not nearly as effective as getting started and seeing what happens. I've written about my SPWN approach to confronting procrastination in Section 7 of this online tool; SPWN involves **s**cheduling, **p**reparing ahead, getting in touch with why you **w**ant to do the task, rather than why you should or need to do it, and not engaging in **n**egative self-talk before starting.

Perfectionism is a form of anxiety. Perfectionists worry about how they or an imagined audience will rate or evaluate their performance or product. Anxiety is almost always an attention problem, so redirect your attention from evaluating the project to actually engaging in and working on the project. Do rather than judge.

You say tomato, I say to-motto. I didn't choose my alma mater, the University of Rochester, because of its motto, but people have chosen schools for worse reasons. Rochester's motto, "Meliora," often translated as "ever better" (it's the source of our English word "ameliorate") is a pretty good antidote to perfectionism. It's fine to keep striving to improve whatever you do, just remove the expectation or desire that it's possible to upgrade to perfect.

Section 7. The SPWN Approach to Procrastination

My approach to procrastination, which I've adapted from cognitive behavioral therapy (CBT) and other therapies, has helped many of my patients with ADHD procrastinate less often and for shorter intervals. I refer to it as the SPWN remedy for procrastination, because it helps spawn good work habits, and the letters stand for **S**chedule, **P**repare, **W**ants, **N**o Negatives. Fortuitously, these initial letters also spell out **S**top **P**rocrastinating! **W**hen? **N**ow!

The SPWN approach has worked in the real world, with hundreds of individuals across thousands of types of tasks. Both avoidant procrastinators (those trying to delay or put off a bad outcome) and arousal procrastinators (those who feel a rush of stimulation by waiting until the last moment) have achieved success with this method. As with any new habits, the more you practice, the better you will become. So don't worry about not being perfect from the beginning—life will deliver many more opportunities to either procrastinate or to take care of business.

S Is for Scheduling

The first step is scheduling the activity. Telling yourself that you'll do it "later today" or "sometime this week" doesn't work. Such statements always leave time to take care of it later. But "later" never arrives. You need to write down a specific time and date for the task. Scheduling doesn't guarantee that you'll engage in an activity, but it substantially increases the likelihood of doing so. Schedule a time with a starting point and duration that make sense both for you and for the task.

P Is for Preparing

You want to be ready to start working when the scheduled time arrives. Assemble any equipment, clothing, worksheets, ingredients, phone numbers, or whatever you need for the task ahead of time. If you set aside an hour to go power walking at 4:00, but you take thirty minutes to find your walking shoes and leggings, then you've already squandered half of your allotted time before you even started. Some tasks require no prep work. Some may require so much that it makes sense to schedule the prep work as a separate task, to be completed before the actual designated task.

One part of prep work is readying your environment. The procrastinating mind relishes distractions. Eliminate or minimize them *before* your scheduled time. In addition to making sure that your work tools or ingredients are available and ready to be used, clear other objects out of your workspace. Close any unnecessary windows and tabs on your computer. Unless you need it for your task, turn your phone off and place it out of sight. To reduce the temptation to multitask, it may be helpful to print out instructions, rather than having phones or computers open and beckoning.

W Is for Wants, and Getting in Touch with Them

You're ready to work, and the clock strikes the appointed hour. We're at the pivot point of the SPWN approach, transitioning from thinking and prepping to actually doing. What's going to help you get started?

First, respect your calendar. If your house is on fire, if the river is rising and floodwaters are at your doorstep, if an armed intruder is brandishing a gun—those are real emergencies. Forget the schedule and get the heck out of there! But *anything* else is a distraction. You might think it would be more fun/easy/rewarding to go out to lunch with the buddy who

just called, or play another hand, or two or seventeen, of solitaire, or look at just one more puppy on a surfboard video. Don't!

Remember that it was the smartest, kindest part of you that put the task on the calendar for this moment. The part of you that tries to align what *you* do in the moment with *your own* lifelong goals, values, and ethics. It's time to start listening to your best self and respect the part of you that places items on your schedule.

You're about to buckle down and start work. What's going through your mind? Usually a lot of negative thoughts and excuses: "I'm not really sure how to start this." "I don't really know what my boss wants of me." "This is going to be too hard." "I didn't sleep well enough last night." "I'm too hungry, tired, or upset to do a good job." For some people, those negative thoughts stop them right there, and they peel off into feeling defeated or jump into distraction land.

More often, people are aware of their negative reactions and attempt to counter them: "I really need to do get this done." "I have to do it." "I ought to do it; the team's counting on me." "I should do it, or I'll look like a loser." But needs, have-tos, oughts, and shoulds were true all along; even when we tell ourselves these are mandatory orders, they're not particularly motivating. If they were really that compelling, you would have already done the task.

Have you eaten Brussels sprouts in the last year? If you did, you almost certainly ate them because you *liked* them, or they seemed enticing enough to at least to *want* to try them. Adults do things that they *want* to do or *like* to do. Having those wants and likes uppermost in your mind as you start the task is crucial for beginning. For most of us, very seldom do the wants and likes spontaneously arise at crunch time. Visual reminders can provide a huge support here. Usually, when you scheduled the task, you were in touch with why you wanted to complete it. Jot those reasons down on the calendar. Then you'll be able to read, in your very own words, at the very moment you most need it, your positive motivation for doing the task. Wanting to do something is more powerfully motivating than knowing that you have to do something.

The wants and likes could pertain to how you feel while engaged in the activity. They could be how you think you'll feel later that day. They could be the long-term success you imagine accruing from this task. They can be your pleasurable sensory experiences while doing the task. They can be the sense of satisfaction or reward you anticipate on completing the task. They can even be the relief you will feel from not having to worry about this task and the elimination of guilt from previously neglecting the task.

You can use other explicit, visual reminders. Put a sticky note on your gym clothes or your computer about how you enjoy the way your muscles feel during a hard workout. Or if your motivation is admiring all of the other hot, trim exercisers you'll see at the gym, write that reminder on your note. Or if the anticipation of your own body becoming stronger or sleeker inspires you, make that your motivational note. Images are even more potent reminders than written messages. Place a photo of a delicious breakfast or a scenic landscape next to your alarm clock to remind you of why you want to get out of bed or go for a walk. Immerse yourself in *why* you want to do a task, and it will be easier to start.

N Is for No Negatives

We have plenty of good arguments provided by cognitive behavioral therapy to talk back to the distractions and excuses we use to procrastinate: Remind yourself that you've successfully completed very similar tasks in the past. That you know that once you've started, your path forward will become clearer. That the work will get easier once you're into the flow. That you've done harder things in the past when hungry, tired, or preoccupied.

But *now* is *not* the time for such a discussion. Tell your brain that you can review and argue about your own objections and resistance *after* you complete your task. If you spend a half hour arguing with yourself, then you are likely to sacrifice the time slot that you allotted to get the task done. You've reinforced the habit of ignoring what your own calendar says. The schedule that the wisest, nicest, most nurturing part of you designed.

Remember, the calendar doesn't commit you to anything beyond the hours you've designated for tasks today. If you learn that a certain hour is a lousy time to go the gym, or write a report, or call a colleague, you won't schedule it at that time in the future. Respect the calendar in the moment, but also know that it is a living, working, breathing, growing tool

to help you sort out what is effective for *you*. Learn from your calendar, and on future days and weeks, modify it accordingly.

So if you want to avoid procrastinating: schedule your tasks, prepare ahead, get in touch with your wants, and turn off your negative thoughts. If you didn't achieve complete success, go back and examine the SPWN steps. You'll be able to refine and improve on what you attempted today. Life will continue to provide you with opportunities to practice this approach. The more you do it, the better you will get.

It may often feel like you're swimming upstream, but fish around for opportunities. With the SPWN approach, you can scale almost any challenge. You can spawn new habits, and you can do it today!

Section 8. An Overview of Medications and ADHD

What ADHD Medications Do

In the broadest sense, a stimulant is any agent that arouses and stimulates, anything from caffeine to methylphenidate (Ritalin) to cocaine. Most stimulants have at least some ability to decrease symptoms of ADHD. Another term used interchangeably with this general use of “stimulant” is “sympathomimetic,” which refers to a substance that mimics the sympathetic fight-or-flight response. Either directly or indirectly, medications that help with ADHD enhance the activity of dopamine, norepinephrine, or both in the prefrontal cortex. This enhanced neurochemical activity increases the efficiency of circuits controlling executive functions. Most effective ADHD medications appear to improve the performance of at least several different executive functions. Whether some medications more effectively enhance some executive functions than others remains inadequately studied, although recent research indicates that the traditional stimulants may be activating arousal and motivational circuits more than they enhance attention directly (Kay et al. 2025). In particular, it has been hard to disentangle the benefits of improving motivation from that of enhancing focus, concentration, or the ability to initiate and organize tasks. Regardless of the direct effects of stimulants, most of our executive functions interact with each other, both in positive, reinforcing and negative, destructive ways, so don’t ignore or minimize the indirect effects that medications can have on executive function circuitry.

Within psychiatry, and particularly regarding ADHD treatment, the term “stimulant” is used in a much more narrow sense to refer to amphetamine-based products (Adderall, Vyvanse, Dexedrine, etc.) or methylphenidate-based products (Ritalin, Concerta, Focalin, Jornay). All other ADHD medications, whether arousing (atomoxetine/Strattera, bupropion/Wellbutrin, modafinil/Provigil) or not (guanfacine/guanfacine), are referred to as “non-stimulants.”

The most common method for directly enhancing dopamine and norepinephrine activity is reuptake inhibition. Neurons using dopamine or norepinephrine as neurotransmitters release the chemical into the small cleft, or synapse, between nerve cells, where the neurotransmitter can bind to receptors on a second neuron. The signal to the second neuron is usually turned off when the neurotransmitter diffuses back into the synaptic space, binds to a transporter molecule on the releasing neuron’s surface, and is taken back up into that first cell. It may then be repackaged for later use or inactivated by enzymes that break down neurotransmitters. Stimulants like dextroamphetamine and methylphenidate, as well as non-stimulants like atomoxetine, duloxetine, and bupropion, all act by blocking the reuptake of norepinephrine, dopamine, or both. This reuptake inhibition allows the original amount of neurotransmitter released into the synapse to act for a longer time, resulting in a longer, but not bigger, signal to the receiving neuron. In addition to their reuptake action, amphetamines also cause a *greater amount* of dopamine and norepinephrine to be released, resulting in a bigger signal. It almost certainly accounts for why amphetamines are the most potent drugs for reducing symptoms of ADHD, as well as why they possess certain unique side effect risks.

It’s not at all clear whether methylphenidate also causes the release of an extra-large amount of dopamine or norepinephrine. Older pharmacologic studies claimed that it did, but more recent assessments describe no to minimal boosting of the amount of neurotransmitter released (Volz et al. 2008; Jîtcă et al. 2025). If it does occur, it is substantially less than what amphetamine evokes. This difference is consistent with what a multitude of studies reveal about benefits for ADHD. The cumulative data show that amphetamines outperform all other agents for ADHD. This is true in both adults and children with ADHD. The reason that first choice medication recommendations from professional groups indicate amphetamine products for adults but methylphenidate for children is not because of less efficacy of amphetamine in

children. It's simply that side effects of amphetamine are more prominent in children, so the cost/benefit ratio favors methylphenidate in that group.

The effects of methylphenidate on ADHD symptoms tend to register well below those of amphetamine. Methylphenidate may perform at the top of the non-stimulants, but in terms of the magnitude of ADHD symptom reduction, methylphenidate is more similar to non-stimulants than it is to amphetamine. For most purposes, methylphenidate may be more aptly considered a non-stimulant than a stimulant. In particular, some recent studies indicate that psychosis, one of the rare, severe side effects of amphetamine, does not appear to be associated with methylphenidate intake (Hollis et al. 2019; Zarchev, Bouter, and Grootendorst-van Mil 2023).

Caffeine

Caffeine is the mostly widely used psychoactive substance on earth. It directly interferes with the accumulation of adenosine, decreasing sleepiness and indirectly boosting dopamine. Most conventional use of coffee or tea employs fairly low doses. But when boosted to levels where it is having a stimulating effect comparable to prescription medications, caffeine seems to pose a greater risk for tremor, anxiety, and cardiac problems than do controlled medications. Some clinicians recommend avoiding all caffeine for their ADHD patients, not only because of side effects but also because in most situations it is harder to know what dosage one is receiving. For individuals unwilling to stop caffeine consumption because it is so embedded in their daily lives, it is important to adjust for the presence of this alternative stimulant when taking additional prescription ADHD medications.

Common Side Effects of ADHD Medications

The most common side effects of ADHD medications are associated with their sympathomimetic action—they overactivate people, which can show up as tremors, overall restlessness, feelings of anxiety, and problems falling or staying asleep. They can produce excessive sweating and dry mouth. Some individuals have digestive system discomfort and many experience reduced appetite. Most of these side effects are proportionate to the dosage, so if they are too intense, decreasing the dose usually eliminates these side effects or makes them more tolerable. For most people, these side effects subside within days or weeks.

Both stimulants and non-stimulants tend to increase blood pressure and heart rate. At a group level, the increases are usually pretty small—less than five beats a minutes for heart rate and less than five points for blood pressure. But those group averages hide that a large majority of users experience a smaller change in these variables or no change at all; yet for 15 to 20 percent of individuals, the changes are larger. People with preexisting hypertension may need to increase the dosage of their hypertension medication. Some people who did not previously have high blood pressure become hypertensive from their ADHD medications; in these cases, the elevated blood pressure usually responds to antihypertensive medications. Guanfacine, an FDA-approved medication for ADHD whose original use was as an antihypertensive, is an exception in that it does not tend to increase blood pressure.

Uncommon and Rare Side Effects of ADHD Medications

Pharmacologists define uncommon side effects as those that affect less than 1 percent of those taking a medication. Rare side effects occur in less than one out one thousand individuals taking a medication. However, some uncommon and rare side effects are serious enough that even though they occur infrequently it is important to provide warnings about the low likelihood of very bad outcomes.

Cardiovascular Effects

Beyond immediate effects on blood pressure and heart rate, long-term use of ADHD medications seems to slightly increase the likelihood of more serious cardiovascular conditions. However, the absolute risk appears quite small; even after a decade and a half of use, fewer than 1 percent of individuals on stimulants develop a cardiovascular condition, although this is slightly higher than the percentage of those with ADHD who never took stimulants. Almost all of the serious cardiovascular problems are classified as “arterial disease,” rather than life-threatening heart attacks, arrhythmias, or strokes (Zhang et al. 2023). Given the propensity of most non-stimulant ADHD medications to elevate blood pressure and pulse, it is not clear whether they pose less long-term cardiovascular risk.

Stimulants can provoke acute, dangerous electrical rhythms in the heart. Every year a high school or college athlete suffers cardiac arrest, at practice or a game, in conjunction with prescription or street stimulant use. These almost always occur in individuals with genetic conditions affecting the neural wiring to the heart. Often other family members have had heart attacks at young ages (in the absence of stimulants) or the individual has had earlier warning events. Even cardiology organizations have not advocated that everyone starting on stimulants get an EKG to measure heart rhythms because these conditions are extremely rare in the general population. But if a careful family and personal history suggests the presence of heart conditions, then an EKG is warranted.

Addiction

The most common dangerous side effect of stimulants, which is absent from non-stimulants, is addiction. Rigorous data is hard to find on how likely this is, with most experts citing that less than 2 to 4 percent of children on amphetamine or methylphenidate become addicted to that substance. Studies claiming higher rates are almost always including “misuse” with abuse/addiction, and usually define misuse as any departure from the written directions on the prescription. Given that those with ADHD frequently forget to refill prescriptions on time, miss doses, or double up on doses on occasion, all of which qualify as “misuse,” inclusion of cases of misuse does not necessarily reflect behaviors that are abusive or addictive. However, because millions of individuals are prescribed stimulants, even a small percentage becoming addicted is a tragedy we need to work on reducing. Warning individuals and families of potential risks in advance of prescribing, monitoring for dangerous modes of taking drugs (inhaling and injecting) and rapid escalations of dosages, and reinforcing the risks of sharing medications can help avoid some disasters.

Two additional factors need to provide context for any discussion on addiction risks. One is that ADHD itself isn't trivial; it isn't just “there's a squirrel”: It kills people. Rates of fatal accidents and suicides are both substantially higher among those with ADHD, and life expectancy is substantially reduced by the presence of the condition. Numerous studies document stimulants reducing many of these serious consequences of ADHD. Secondly, substance abuse problems are common in modern industrialized societies. About 20 percent of Americans will develop a substance abuse problem. The risk is almost doubled in those with ADHD, close to 40 percent, due to impulsivity, inattention, discounting negative long-term outcomes, and being less aware of the risks and how they might apply to oneself. Yet among those with ADHD, starting stimulant medications, particularly before middle school years, dramatically reduces the likelihood of later developing a substance abuse disorder, back down to the rates seen in the general population (Chang et al. 2013).

Psychosis

In my experience, amphetamine-induced psychosis is the most underrecognized of the severe, horrible outcomes of stimulant use. Some discussions blur the distinction between addiction and psychosis (Schwarz 2017). Most individuals addicted to stimulants don't become psychotic, and psychosis can certainly develop without any addiction. Paranoid delusions are the most prominent symptom of amphetamine-induced psychosis, where individuals feel that they are being

surveilled, harassed, and harmed by others. Although there may be an element of narcissistic importance to these delusions, the grandiose, expansive thoughts of mania are seldom a feature in the cases I have seen. I also have not seen those with amphetamine-induced psychosis display the bouts of silliness, wordplay, and positive mood that characterize manic episodes.

Lots of substances can cause psychosis. When someone is really, really drunk, they often lose touch with reality and even hallucinate. But this is an intoxication state. The drunk person will fall asleep, wake up the next day with a headache or full hangover, and be sullen, but they're no longer delusional. In contrast, amphetamine-induced psychosis often persists for days, weeks, or months after the substance has left the body. This means the medication has changed their brain for the worse; the symptoms aren't just a direct response to the presence of the drug. Even worse, a few recent studies that have followed these individuals for fifteen to twenty years after a single episode of amphetamine-induced psychosis find that 15 to 20 percent of them are in a permanent schizophrenic-like state (summarized in Murrie et al. 2020).

It's hard to study rare events, but some recent studies suggest that one in five hundred individuals taking prescription amphetamine products develop psychosis (Moran et al. 2019). Some studies fail to find an association with methylphenidate and psychosis (Hollis et al. 2019), again raising the question of whether Ritalin is "really" a stimulant. Methamphetamine (street names: speed, crank, ice) appears to pose a substantially greater risk than amphetamine itself. Prescription methamphetamine is available in the US under the brand name Desoxyn, for either ADHD or obesity, but only a few thousand individuals are taking it. High doses of amphetamines may present a greater risk than low doses. Past history of any psychotic episode or a family history of psychosis also appears to substantially increase the risk of psychosis emerging after taking stimulants. When psychosis appears, stopping the stimulant is essential, but it is seldom sufficient; starting an antipsychotic as soon as possible helps end episodes.

Medication Myths

Doctors have been using stimulant medications to treat ADHD for more than half a century, but many myths persist about these medications. People are increasingly obtaining medical information online, yet studies show that the majority of claims about ADHD made on popular sites are inaccurate (Karasavva et al. 2025). Regarding stimulants and other medications, false information continues to circulate about both their benefits and their potential harms. Unfortunately, many individuals are making important decisions about their mental health based on misinformation. I address some of the most prevalent myths below.

#1: Stimulant Response Reveals Who Has ADHD

Many assume that an individual's response to stimulants is a way to ascertain the presence of ADHD. But with the right dosage, almost everybody will become more focused and attentive on a sympathomimetic medication. If the dose is increased too much, they will eventually become too revved up, physically agitated, anxious, sweaty, and tremulous. While it is true that, on average, those with ADHD require a higher dosage of a medication to get into an optimally functional space, there is a great deal of overlap between those on the ADHD spectrum and those not, so medication response is not particularly effective as a diagnostic tool.

Related to this, if circumstances are contributing to a state of sympathetic system overdrive, and an individual is already feeling anxious or wired, then their regular ADHD medication dosage can push them into a state of too much. When someone is in a state of increased anxiety from situational factors, backing down on the dosage of any medication that is further activating the sympathetic nervous system usually makes sense.

In the bigger picture, this is a reminder that we should focus on how a given drug affects a given body and brain, both in terms of benefits and adverse effects, rather than becoming overly focused on how many milligrams the individual is taking. The FDA explicitly states that its recommendations are simply that, not rigid restrictions, and that there will be

some individuals who obtain benefits at lower levels and some who will require going higher before they register benefits and can do so without incurring side effects.

#2: Stimulants Cause Brain Rot

In addition to the fear of addiction, many parents voice concerns that long-term prescription use of stimulants might damage the brains of their children with ADHD. They worry that exposure to these drugs, especially at an early age, may alter the brain in detrimental ways and may perpetuate, or even worsen, symptoms of ADHD. These worries aren't completely unwarranted. Stimulants of abuse, including both cocaine and methamphetamine, have been associated with damage to neurons in the brain, particularly dopamine pathways (Kim, Yun, and Park 2020). Furthermore, some studies in rodents also found destruction of nerve cells and signs of brain inflammation after treatment with stimulants (Senior et al. 2023).

Fortunately, a wealth of human data with prescription stimulants leads to a different conclusion. A 2013 meta-analysis of more than two dozen studies compared kids with ADHD who were on stimulants to those with ADHD who had not received such treatment and found no brain damage associated with medications (Spencer et al. 2013). Furthermore, in almost all the studies examined, ADHD brains exposed to stimulants, in terms of structure, connectivity, and neural activation, more closely resembled individuals who never had ADHD than they did the brains of untreated individuals with ADHD. Dozens of subsequent studies have replicated and bolstered these results. That turns the common concern on its head, because it suggests that withholding stimulants from some youth with ADHD may actually consign them to a potentially avoidable lifetime of significant ADHD symptoms.

So why the difference between the research with street stimulants and with rodents, compared to the findings of youth treated with prescription stimulants? The two sets of studies differ in several critical ways:

- Substances
- Dosages
- Delivery systems
- Patterns of delivery

The difference between methamphetamine and amphetamine is a simple methyl group—a carbon atom with three hydrogen atoms stuck on it—which might not seem like much. But cocaine and meth cause greater release of neurotransmitters than do amphetamine or methylphenidate.

With stimulants, improvement in focus and attention usually occurs at lower doses than that causing mood elevation. Street stimulants are most often taken for their euphoric effects, which means that they are usually consumed at higher equivalent doses than what is prescribed for ADHD. In rodent studies, stimulant dosages (by body weight) are often ten or more times higher than doses of prescription stimulants administered to humans. Part of the rationale is that these smaller mammals have higher rates of metabolism, but even so, these dosages generally greatly surpass the equivalent of what ADHD patients are exposed to.

Furthermore, the effects of stimulants reflect not just the concentration of the drug at the dopamine and norepinephrine receptors but also how quickly the level of drug changes in the brain. This is a large part of why injecting or snorting the same dose of a stimulant has a bigger effect than swallowing it. Excitotoxic damage is much more likely when a huge flood of dopamine is released immediately than when the same amount is released more gradually. The rodent studies showing brain damage occurred after injecting high doses of the drug into the abdominal cavity, where the drug entered the blood supply and was delivered to the brain quickly. The same doses, when delivered inside the rodents' digestive system, requiring gradual absorption before entering the blood, resulted in no signs of brain damage.

Finally, taking a regular dose of a stimulant on a daily basis appears less likely to result in damage to neurons than does the binge pattern typical in those with substance abuse. In the latter case, not only is each dose large, but the pattern of ingesting several large doses in quick succession followed by periods of abstinence is much more likely to overwhelm the brain's neuroprotective systems.

Although the evidence to date does not indicate that prescription stimulants commonly cause new cases of ADHD, a number of substances of abuse, including street stimulants, but also marijuana and even opioids, after years of abuse, can result in patterns of increased impulsivity and hyperactivity, decreased concentration and focus, problems with organization and planning, and states of low motivation, all of which can push individuals onto the ADHD spectrum.

While the US opioid crisis early in the twenty-first century has been subsiding in the 2020s, illicit stimulant use appears to be rising. As previously discussed, ADHD itself contributes to the likelihood of substance abuse, but there may well be a feedback loop here, in that illicit stimulant use may push individuals further along the ADHD spectrum. The substance abuse feedback whorl also interacts with other ADHD feedback loops, particularly because substance abuse increases the risk for head trauma, chronic infections, and PTSD, all of which can worsen ADHD symptoms.

#3: Non-stimulants Work Slowly

For years, many prescribers have claimed that non-stimulant medications for ADHD work slowly, because many of them are antidepressants, which tend to take weeks before they produce benefits for depression or anxiety. This makes little sense at either a neurochemical or a clinical level. Most of these non-stimulants block norepinephrine or dopamine reuptake within minutes to hours, just as amphetamine and methylphenidate do. Thus, we should expect them to have benefits for ADHD in humans almost immediately. And if you ask patients, as long as you start them at an effective dose of the medication, they will report that within hours of taking bupropion, duloxetine, or modafinil, they experience improvement in their ADHD symptoms. There's nothing particularly unusual about a medication that has immediate, direct effects that are distinct from the same medication producing gradual, indirect effects. A drug can be a fast agent for ADHD and also treat depression at a longer timescale.

Strattera/atomoxetine, the first approved non-stimulant medication for ADHD, has been a major factor contributing to the slow-acting myth. Most individuals can't tolerate side effects of atomoxetine. They need to start at very low doses and then take weeks to gradually titrate up to a therapeutic level. ADHD symptoms respond slowly to atomoxetine because it takes a long time to get to an effective dose. Also, many prescribers won't see a patient back for two to four weeks after starting a non-stimulant medication. If the patient reports at the follow-up appointment that their condition has improved, the doctor may not inquire about whether the benefits gradually accrued or were present from early on, and instead make assumptions about the timing of the appearance of benefits based on their own expectations.

Guanfacine is one ADHD medication that does appear to work slowly and indirectly. Guanfacine has immediate effects on a subset of norepinephrine receptors in the prefrontal cortex, and activation of these receptors works slowly to instigate forming new synaptic connections and strengthen communication between neurons. Unlike most ADHD medications, guanfacine's most common immediate side effect is sedation. Although guanfacine is approved as a stand-alone agent for ADHD, it's more commonly used for those who can't tolerate stimulants because of excessive arousal. Once they are stabilized on guanfacine, if they need further symptomatic help, they are usually more tolerant to restarting the stimulant.

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