

Early Release

Attention Deficit Hyperactivity Disorder: From Behavioral Treatment to Animal Models

Jonathan M. Slezak^{1,2}

Kwadwo Britwum

Dinu Y. Ratnayake

Attention deficit hyperactivity disorder (ADHD) has been described in literature for over 200 years (Lange et al., 2010), and the modern conceptualization continues to evolve (Sonuga-Barke et al., 2023). Contemporary views place ADHD within a neurodivergence framework. Behavioral symptoms can be viewed as variations along a continuum of everyday behavior, with fluctuating patterns of symptom remission and recurrence across the lifespan (Sibley et al., 2022; Van Meter et al., 2024). In addition, there is greater consideration of how symptoms can be viewed in context as strengths, and of environments that support behavioral variation, which are fruitful directions for research (Sonuga-Barke et al., 2023). In this chapter, we outline the clinical features of ADHD and highlight the condition's multifaceted nature, which has hindered understanding of its etiology and pathophysiology. We then discuss personalized medicine approaches used in Applied Behavior Analysis (ABA), which remains relatively agnostic about pathophysiology and instead focuses on environmental variables that maintain the ADHD behavior of interest. Finally, we discuss the importance of modeling ADHD in animals and its translational significance to understanding ADHD-related behavior.

Background: Clinical Presentation and Associated Risks

ADHD remains one of the most common conditions of childhood and adolescence worldwide (3-8%) with estimates likely varying due to methodological disparities (Ayano, Demelash, et al., 2023; Polanczyk et al., 2007, 2015). ADHD can persist in adulthood or be diagnosed as late onset, with overall prevalence estimates at 3-5% (Ayano, Tsegay, et al., 2023). The average age of diagnosis is seven years old, but symptoms typically begin to

¹ The authors thank Dr. Jonathan L. Katz for his helpful comments on earlier drafts of this chapter.

² Portions of the research discussed were supported by the National Institute of Mental Health (NIMH) through a Ruth L. Kirschstein National Research Service Award (NRSA) postdoctoral fellowship (F32MH094065) awarded to the first author.

appear around preschool age. The diagnosis includes symptoms of inattention and/or hyperactivity-impulsivity that are present in at least two settings (e.g., home, school, or work) and interfere with social, academic, or occupational functioning (Faraone et al., 2021). ADHD-diagnosed youth can have persistent academic struggles, including lower standardized test scores, more frequent grade repetition, and a higher need for special education services (Loe & Feldman, 2007). These challenges often continue into adulthood, where individuals with untreated ADHD finish fewer years of education and are less likely to earn a college degree (Barkley et al., 2006). Employment outcomes are also negatively affected since adults diagnosed with ADHD are less likely to secure and maintain full-time work and are more than twice as likely to experience job loss or unstable employment (Biederman et al., 2006).

Social relationships often suffer because children with ADHD frequently face peer rejection due to the associated behavior, and adults commonly report greater conflict in romantic, family, and other social relationships (Bagwell et al., 2001). Physical safety concerns are notable as well because ADHD is linked to higher rates of injuries, more emergency room visits, and about twice the risk of motor vehicle accidents in adolescents and young adults (Merrill et al. 2009; Barkley & Cox, 2007). Finally, untreated ADHD may reduce life expectancy by approximately 4.5 to 11 years because of the combined effects of mental health issues, substance use, and physical risks (Dalsgaard et al., 2015). These findings highlight the importance of early identification and timely intervention for individuals with ADHD.

Biomarkers

As with other mental health disorders, there is a continued research emphasis on identifying biological markers to aid prevention, diagnosis, and treatment per the National Institute of Mental Health's Research Domain Criteria (Musser & Raiker, 2019; Pacheco et al., 2022). Currently, diagnosis relies exclusively on descriptive data utilizing DSM-5 criteria and parent/self-assessment questionnaires (Faraone et al., 2021). There are no biological indicators via blood screens, neuroimaging, or neuroactivity to aid/refine diagnosis despite the years of research dedicated to this endeavor. Mental health disorders are likely to exhibit changes in physiological pathways before observable symptoms appear. As an extreme example, the neurodegenerative condition of Parkinson's disease can result in about 50-80% dopamine depletion in the substantia nigra before clinical symptom onset (Heng et al., 2023). Identifying individuals at risk for ADHD could provide a means for early intervention before clinical onset.

One novel area of investigation into prevention and diagnosis is the epigenetic alterations that underlie ADHD. Epigenetics involves the interplay of the environment (e.g., maternal smoking or stress) and gene expression (e.g., DNA methylation or histone modification) that can determine whether a gene is expressed or not. Cecil and Nigg (2022) have recently elaborated on the promises and challenges of epigenetic biomarkers associated

with ADHD and the potential to personalize treatment/prevention measures. However, multiple factors, including heterogeneity of clinical presentation, genetics, co-morbidity, and environmental risks, have all contributed to the limited understanding of the causes and biological mechanisms of ADHD (Cortese, 2012; da Silva et al., 2023; Koriala et al., 2024).

Factors Complicating the Discovery of Etiology and Pathophysiology

ADHD is considered a heterogeneous condition as symptoms can be diagnosed across three subtypes (inattentive, hyperactive-impulsive, and the combined subtype) that tend to co-vary with developmental period and sex. For example, the diagnosis rate among male patients can approximate twice that of females during childhood (Franke et al., 2018). Males have a higher diagnosis rate of the hyperactive-impulsive subtype with a diminishing difference in late adolescence. The inattentive subtype appears to be more common among females, which could be overlooked clinically and partly accounts for the lower diagnostic rate (Mowlem et al., 2019). Thus, clinical presentation of ADHD symptoms may depend on the developmental period, subtype, and sex of the patient.

ADHD also has one of the highest heritability rates of all mental health conditions, estimated at around 70%-80% (Willcutt, 2012). However, there are no large-effect genes driving the high heritability, unlike Huntington's disease, which is entirely accounted for by a mutation in the huntingtin gene. Instead, ADHD is considered polygenic, with many small genetic associations identified through candidate gene and genome-wide association studies, including those related to dopamine, noradrenaline, neurotransmitter signaling genes, and transcription factor genes involved in DNA-to-mRNA transcription (Klein et al., 2017). Thus, insights from genetics will be multifaceted and likely modifiable by various environmental factors, such as prenatal alcohol or tobacco use, low birth weight, family adversity, pesticide exposure, and lead exposure (Thaper et al., 2007).

Further complicating efforts to identify pathophysiology is the high degree of comorbidity. A Danish study over 30 years indicates more than 60% of ADHD patients have at least one comorbidity (Ottosen et al., 2019). For example, depression and anxiety are reported as occurring in 18%-50% of adult ADHD-diagnosed individuals (Biederman et al., 2006; Fu et al., 2025). The likelihood of developing a substance use disorder is also higher, with approximately a quarter of adolescents and adults affected, often coping with untreated symptoms (Lee et al., 2011; Wilens, 2004). Such complexity, from genetics to clinical presentation, indicates that diagnosis and treatment of ADHD would benefit from a personalized medicine approach that is data-driven and tailored to the individual needs of a patient.

Personalized Medicine

Personalized medicine is found in the field of pharmacogenomics, where research is growing to understand how medication responses vary based on individual genetic makeup.

The goal is to better understand how a given drug moves through and interacts within the body (i.e., pharmacokinetics and pharmacodynamics) to tailor specific drugs and doses that optimize therapeutic efficacy while limiting side effects in individuals. For example, current research is aimed at alterations in a sub-cohort of ADHD individuals with genetic modifications in metabotropic glutamate receptors that could be targeted with specific compounds (e.g., the metabotropic glutamate receptor activator fasoracetam (NFC-1), aimed at this receptor pathway (Connolly et al., 2015; Mamiya et al., 2021). Another form of personalized medicine is the development of diagnostic and treatment plans within the field of Applied Behavior Analysis (ABA).

ABA offers a personalized medicine approach that aligns with the Research Domain Criteria (RDoC; Auerbach, 2022) framework, focusing on identifying specific behavioral markers and the contextual variables associated with them. The approach is multimodal and starts by operationalizing core behavioral features (such as academic failure, inattention, impulsivity, etc.) and identifying environmental events around these markers (like antecedents and consequences), with the primary goal of improving the life circumstances for individuals with an ADHD diagnosis (Neef et al., 2013).

ABA ADHD Assessments and Treatment Methods

Applied behavior analysis (ABA) interventions targeting behaviors that impede functioning in ADHD typically begin with functional assessment (Neef & Northup, 2007). The assessment process includes indirect methods (e.g., caregiver/teacher interviews and standardized checklists) and direct methods (e.g., descriptive assessment and, when indicated, experimental functional analysis) to identify antecedent events that reliably occasion the target behavior and the consequent events that maintain it. These maintaining consequences may be socially mediated (e.g., attention, escape from demands or other environmental events, access to preferred items/activities) or automatic/nonsocial in origin.

Several studies have conducted descriptive or antecedent assessments of associated ADHD behavioral concerns (e.g., Anderson et al., 2006; Ervin et al., 1998; Flood & Wilder, 2002; Hawkins & Axelrod, 2008). For example, Anderson and colleagues (2006) used a structured descriptive assessment (SDA) to evaluate the circumstances surrounding the behavior of children with various behavioral needs, such as ADHD-related disruptive behavior. Results showed that the SDA effectively identified distinct behavioral patterns (i.e., behaviors that occur more frequently in the presence of certain antecedent environmental events), which are often overlooked by traditional assessment methods. It highlighted the nuances in children's behavior, suggesting that implementing structured assessments of ecological variables using SDAs could lead to more tailored and effective educational strategies for children with ADHD and related challenges.

Other studies have experimentally manipulated antecedents and consequences associated with specific ADHD behaviors to determine which events reliably influence these behaviors, and to improve them (e.g., Athens & Vollmer, 2010; Boyajian et al., 2001; Northup et al., 1995). This direct assessment process is known as a functional analysis (Iwata et al., 1994). In one such example, Boyajian and colleagues (2001) conducted a series of brief functional analyses within the preschool classroom environment to address specific disruptive behaviors among children diagnosed with different ADHD subtypes. The analysis used procedures from Northup et al. (1991), with functional analysis sessions lasting 5-to 10-minutes, with brief 1-to 2-minute breaks between sessions. The analysis identified high rates of inappropriate behavior during the contingent attention, access to tangible, and escape conditions for the preschoolers in the study. More importantly, applying these findings led to the development of targeted behavior interventions that significantly reduced off-task and inappropriate behaviors in the classroom. The findings suggest that early interventions based on functional analysis not only address immediate behavior issues but also contribute to overall educational and social skills development among preschoolers with ADHD.

Functional analyses have also been conducted to evaluate how medications affect behavior by altering the motivational functions of some behavioral consequences (e.g., Carlson et al., 2012; Cox & Virues-Ortega, 2016, 2022; Dicesare et al., 2005; Neef et al., 2005). In one such example, Dicesare and colleagues (2005) investigated the effects of methylphenidate on disruptive behavior in an 18-year-old man with ADHD. The functional analysis involved exposing the adult to different environmental conditions in which antecedents (i.e., motivating operations and discriminative stimuli) and consequences were manipulated for various reinforcers (e.g., socially mediated reinforcers such as attention, escape from some environmental event, and access to some items or activities) to determine which maintained disruptive behavior. Under these conditions, the adult received varying doses of methylphenidate and then underwent functional analysis to assess the medication's effects on behavior. Results indicated that the adult displayed lower levels of disruptive behavior when given methylphenidate; however, in the absence of methylphenidate, high rates of disruptive behavior occurred in the attention-reinforcer condition. These results suggest that methylphenidate decreased disruptive behavior maintained by attention. This implies that methylphenidate may have decreased the reinforcing effects of social attention for this individual. Overall, this study demonstrates the utility of combining functional analysis with pharmacological interventions to better understand and treat disruptive behavior associated with ADHD.

Functional Assessment-Based Interventions

As discussed in the previous section, the results of functional assessments offer ways to address ADHD-related behaviors that enhance learning opportunities. This has been supported by research using functional assessment-matched intervention strategies, including procedures that manipulate antecedent (i.e., motivating operations and discriminative

stimuli) and consequences (i.e., attention, escape from some environmental events, and access to some items or activities) assessed to evoke and maintain ADHD behavior reliably.

Antecedent-Based Interventions. Once the functions of ADHD-related behaviors are identified, antecedent strategies focus on reducing the need for behaviors that generate specific reinforcers before they happen (e.g., Kodak et al., 2003; Jones et al., 2000). For example, Jones and colleagues (2000) evaluated whether providing noncontingent peer attention could effectively reduce disruptive behaviors, specifically in an 8-year-old child diagnosed with ADHD. The researchers first conducted a functional analysis to identify the variables maintaining the participant's disruptive behavior. Through this process, they reliably identified that peer attention significantly reinforced the child's behavior. Then, using a reversal design, they evaluated conditions in which the child received noncontingent peer attention at specific 90-second intervals. Results indicated a marked decrease in disruptive behavior during the noncontingent peer attention condition, showcasing the potential effectiveness of this antecedent intervention strategy.

Consequence-Based Interventions. Other studies have manipulated functional consequences associated with ADHD-related behaviors, and provided them for functionally equivalent appropriate behavior, while withholding them for previously reinforced inappropriate behavior (e.g., Flood et al., 2002; Grauvogel-MacAleese et al., 2010; Hagopian et al., 2005). Grauvogel-MacAleese and colleagues (2010) evaluated the effectiveness of peer interactions in a structured work context in improving on-task behavior in children diagnosed with ADHD. Before the intervention, a functional analysis was conducted, which determined that off-task behaviors were maintained by access to peer attention. Next, during the intervention phase, peers provided praise and help when participants were on task. If they were off task, the peer discontinued praise and help until they were back on task. Results indicated that the peer-delivered contingent attention intervention significantly reduced off-task behavior and improved on-task behavior. Moreover, the implications of these results resonate with broader literature on ADHD interventions, which emphasize the importance of both direct skills training and the social environment supporting positive outcomes for children diagnosed with ADHD.

When functional assessments of ADHD-related behaviors have not been feasible, penalty- or punishment-based procedures have been added to reduce the occurrence of the impeding behavior (e.g., DuPaul et al., 1992; Fabiano et al., 2004; Northup et al., 1999). This approach is utilized when ADHD related behaviors produce severe risks for the behavior and others in the learning environment. For instance, Northup and colleagues (1999) investigated the separate and interactive effects of methylphenidate (MPH) and standard classroom punishment-based contingencies on disruptive and off-task behavior among children diagnosed with ADHD. The researchers used analogue conditions with different contingencies, such as contingent teacher reprimands, brief time-outs, no interaction, and an 'alone' condition, all conducted in a multi-element design. The experimental design rotated

between MPH and placebo days, enabling the researchers to assess the effects of medication alongside various behavioral strategies used in classrooms. This careful multi-element setup allowed a thorough analysis of individual differences in responses to both medication and behavioral interventions. Results revealed that both MPH and classroom contingencies had significant individual and combined effects on reducing disruptive behaviors. Specifically, MPH was found to be effective on its own, but its effectiveness was enhanced when combined with specific classroom contingencies. This interaction effect of MPH with behavioral strategies suggested that the combined approach provided greater reduction in off-task and disruptive behavior compared with either treatment alone, thereby underscoring the benefits of the multimodal educational strategy.

Skill-Based Interventions. In many cases, children and adolescents with ADHD display behaviors that result in academic impairment. For instance, DuPaul and Langberg (2015) suggest that preschoolers and children with ADHD have lower literacy skills, making it essential to address behavior associated with ADHD in learning contexts. In some of these cases, non-function-based antecedent interventions have been used to build skills that facilitate learning. For instance, some of these interventions have included the use of white noise (Cook et al., 2015; Lin, 2022; Rosalez et al., 2020), added physical activity (Kercood et al., 2012), targeted instructions to use during schoolwork completion (Bicard & Neef, 2002), and inclusion of choice-making opportunities (Kern et al., 2001; Powell & Nelson, 1997), all of which have produced good outcomes for individuals.

Attention Training. ADHD-associated behaviors may result in inattentive behavior, resulting in significant impairment for the individual who displays these behaviors. According to the National Institute of Mental Health (NIMH, 2024), inattentive ADHD behavioral markers are commonly addressed with medications that elevate levels of thinking and attention-stimulating catecholamines (e.g., dopamine and epinephrine). However, these treatments alone may not be effective in establishing adaptive skills for the individual with an ADHD diagnosis. In some of these cases, contingent-reward interventions that involve physical activity have been used to teach attention skills (Azrin et al., 2006, 2007).

For instance, Azrin et al. (2007) explored the effectiveness of physical activity as a reinforcement strategy to promote calmness and shape learning readiness in children with ADHD in a classroom setting. This study used a pre- and post-intervention design, and a shaping procedure was employed to gradually increase participants' duration of calmness and classroom engagement. Results indicated a positive correlation between contingent engagement in physical activity and the levels of calmness and classroom engagement observed among children with ADHD. Specifically, structured physical activity periods led to significant reductions in hyperactive behaviors and improvements in attentiveness, supporting the hypothesis that physical activity can serve as an effective behavioral reinforcer.

A complementary line of research also shows that gamified, app-based “digital therapeutics” can instantiate ABA principles by programming antecedent cues (i.e., structured, stimulus-controlled tasks with dynamic difficulty) and contingent consequences (i.e., immediate feedback and in-game rewards) to shape attention and on-task behavior (Kollins et al., 2020; American Psychiatric Association, 2020). In this way, game-based interventions operationalize the same functional relations targeted by other ABA antecedent-and-consequence procedures, while also serving as a skill-building, attention-training strategy that can be layered with classroom contingencies or medication as part of a multimodal plan (Kollins et al., 2021). Early large trials using this approach report objective gains in sustained/selective attention with minimal side effects (Kollins et al., 2020; Kollins et al., 2021).

As an example, Kollins et al. (2020) evaluated the video-game-based intervention AKL-T01 (Akili Interactive Labs, Boston, MA, USA) in the Software Treatment for Actively Reducing the Severity of ADHD (STARS-ADHD) randomized, double-blind trial (n=348; ages 8-12). The intervention used a video-game interface with two tasks: a perceptual discrimination task in which users respond to instructed stimulus targets while ignoring distractors (similar to a Go-No-Go task), and a sensory-motor navigation task in which users continuously adjust their position to interact with and avoid positional targets. The control was designed to match AKL-T01 in expectancy, engagement, and time on task and comprised a digital word game. The intervention group was instructed to use the intervention for approximately 25 minutes per day, 5 days per week, over 4 weeks. Results showed that the AKL-T01 intervention produced significantly greater improvements on the Test of Variables of Attention (TOVA) Attention Performance Index (primary endpoint), with high adherence and no adverse effects. Subsequent research using STARS-Adjunct by Kollins et al. (2021) found that adding the same intervention to usual care led to significant reductions in ADHD-related impairment for children both on stimulant medication and not on medication, supporting its utility as an adjunct within multimodal treatment. Reflecting this evidence base, in June 2020, the U.S. FDA authorized marketing of AKL-T01 as the first prescription, game-based digital therapeutic to improve attention function in pediatric ADHD, alongside clinician-directed therapy, medication, and educational supports (American Psychiatric Association, 2020).

Self-Management Training. Self-management skills have also been taught when ADHD related behaviors result in inattention (e.g., Davies & Witte, 2000; Hoff & Ervin, 2013; Harris et al., 2005; Gureasko-Moore et al., 2006). Self-management programs teach individuals to arrange environmental variables (i.e., antecedents and consequences) to modify aspects of their own ADHD related behavior. In essence, these programs help individuals to be aware of their ADHD related behavior through some or all of the following: (a) goal setting, (b) self-instruction, (c) self-monitoring, (d) self-evaluation, and (e) self-reinforcement (Erhard et al., 2022). This approach to skill building increases autonomy by minimizing

others' involvement in intervention delivery and maintenance, while creating an optimal and compassionate teaching environment (Scallan & Rosales-Ruiz, 2023).

Gureasko-Moore and colleagues (2006) investigated the impact of self-management strategies on the organizational skills of three seventh-grade males diagnosed with ADHD. All participants received methylphenidate to help alleviate the symptoms of ADHD, and each participant was taught specific self-management strategies through coaching from the researcher. The skills taught included self-monitoring of organization, goal setting, and self-reinforcement. The results showed a statistically significant improvement in participants' organizational skills following the implementation of self-management strategies. Specifically, there was a marked improvement in areas such as task completion and time management. Teachers also reported fewer instances of disorganization among participants, which aligned with objective measures of organizational skills observed during classroom activities after participants acquired self-management skills.

Self-Control Training. In other cases, ADHD related behavior has resulted in what has been described as “impulsive choice making” requiring structured skills-based interventions to teach self-control (Neef et al., 2001). Impulsive choice making occurs when an individual chooses to respond to a smaller, more immediate reinforcer. The alternative, which involves the individual responding for/or selecting a larger, more delayed reinforcer, is considered a “self-controlled choice” (Neef et al., 2001; Neef et al., 2005; Schweitzer & Sulzer-Azaroff, 1988).

Assessments have been developed to measure the extent to which the value or effectiveness of a consequence is a function of its immediacy relative to other possible dimensions (such as quality, rate, magnitude, probability, or effort, Neef & Lutz, 2001; Neef et al., 2001). The structure of these assessments involves arranging choices in which response options are between those that result in immediate consequences that are less favorable with respect to another dimension (e.g., an immediate low-quality reinforcer) and delayed consequences that are more favorable with respect to the same alternative dimensions (e.g., delayed high-quality reinforcer, Neef & Northup, 2007). These resulting choices are then examined through evaluation of the percentage of choices that are made between the options and resulting response patterns. For instance, if an individual reliably selects the response options that result in immediate reinforcement, despite the quality, magnitude, rate, or effort necessary for reinforcement relative to the alternative, then their choices will be characterized as “impulsive choice making” (Neef et al., 2001). However, if the individual's response pattern changes relative to other dimensions of reinforcement, and not just immediacy, then their choices may be characterized as “self-controlled” (Neef & Northup, 2007).

ABA studies have used singular and combined intervention strategies to increase self-control skills with individuals with ADHD (Binder et al., 2000; Dixon & Holcomb,

2000; Dixon & Cummings, 2001; Neef et al., 2001, 2005; Schweitzer & Sulzer-Azaroff, 1988). For instance, Schweitzer and Sulzer-Azaroff (1988) taught six children whose behavior produced outcomes identified as impulsive to wait for delayed reinforcers. All six of the children were assessed to display behaviors associated with an ADHD diagnosis. The children were exposed to gradually increasing delays between choices and receiving a larger delayed reinforcer over a smaller immediate one. Results indicated that this progressive delay procedure successfully enhanced the participant's self-control skills.

Neef et al. (2001) assessed the use of a combined approach consisting of reinforcer dimension manipulation and delay fading to promote self-control skills with three children diagnosed with ADHD. An initial assessment was implemented in this study to evaluate the influence of reinforcer dimensions (i.e., rate, quality, immediacy, and effort) on participants' time allocation between concurrently available sets of math problems. Next, a self-control training was implemented, in which immediacy and other reinforcer dimensions and delays associated with the higher rate or quality reinforcer alternative were gradually increased. Results of this training indicated that self-control or sensitivity to different dimensions of reinforcement emerged for all participants in this study. Illustrating the effects of this procedure on self-control skills.

Self-Control and Verbal Mediation Training. Some self-control studies have employed verbal mediation strategies in addition to delay fading and direct reinforcement strategies described above (Binder et al., 2000; & Dixon & Cummings, 2001). For instance, Binder and colleagues (2000) evaluated the use of a progressive delay procedure combined with verbal mediation to teach self-control to three children with ADHD. An initial natural baseline was conducted in which two preferred items of different quantities (one large and one small) were placed in front of each child. Next, each child was asked to choose an item and then wait as long as possible before eating it. A choice baseline was then implemented, during which each child chose between a smaller immediate item and a larger delayed item. During the self-control training, if the child selected the smaller item, it was delivered immediately; however, if the child selected the larger item, incremental delays along with two types of alternating verbal activities were implemented. In the first verbal activity, the child repeated the self-rule, "if I wait longer, I will get the bigger one," and another activity involved the child naming pictures of objects depicted on a flash card. Results indicated that both intervening verbal activities were successful, as all participants demonstrated self-control regardless of the content of the verbal activities. Future research is necessary to continue to explore the role of verbal behavior in conditioning and mediating choices of reinforcers in individuals with ADHD.

While these behavioral strategies show promise when effective, understanding the underlying mechanism of ADHD requires deeper exploration across the various domains of behavioral science (Moore & Cooper, 2003). Animal models of ADHD provide a valuable framework for investigating the neurobiological foundations of impulsivity and attention

deficits. By simulating ADHD-like behaviors in controlled settings, these models allow researchers to test interventions, examine brain function, and refine treatments that may ultimately enhance outcomes for individuals with ADHD.

Establishing Animal Models of ADHD

Animal models are approximations of clinical disorders and rarely capture the full spectrum of a human condition. A primary goal of animal modeling is to isolate the biological or behavioral mechanisms in controlled settings. Aspects of learning history, environment, and biology can all be carefully studied to illuminate contributing factors of the condition that could be further investigated in the clinical population. Ultimately, we want our animal models to have some translatable significance that can lead to improvements in the human population. For example, from a pharmacotherapy perspective, we could work on ways to understand or reduce side effects of current treatments, develop novel primary or adjunctive treatments, increase treatment adherence (e.g., via route of administration or duration of effect), decrease the abuse potential of a current treatment (e.g., prodrugs that metabolize into the active ingredient after administration), or understand the interaction between clinical drugs and the underlying mechanisms. Alternatively, focusing exclusively on physiological or behavioral mechanisms could allow for earlier detection, preventative care, and expanded non-pharmacological treatment options. The utility of animal models depends on their effectiveness in predicting clinical outcomes from the laboratory findings. In general, there are three categories of animal models (Kantak, 2022; Kim et al., 2024; Regan et al., 2022; Wickens et al., 2011) that have been studied in relation to ADHD: 1) genetic (e.g., Spontaneously Hypertensive Rats, dopamine transporter knockout mice), 2) environmental (e.g., prenatal alcohol or nicotine exposure), and 3) procedural models (e.g., delay-discounting or serial reaction time tasks). The process of validating an animal model primarily focuses on face, predictive, and construct validity (Katz & Higgins, 2003; McKinney, 1989; Willner, 1986).

Face Validity. The concept of face validity concerns the resemblance of the clinical condition by the appearance of symptoms and outcomes. For example, researchers may try to approximate hyperactivity in a familiar environment. Children and adults will generally explore novel environments when at a new park or when exposed to new toys or games, but over time, habituation sets in with continued exposure. This is less the case with ADHD, and therefore, we may look for an animal model that shows excessive locomotion in a familiar environment compared to a control group. Face validity, thus, could entail a model showing parallels in behavioral symptoms, so it “looks like ADHD.” However, there are limitations to relying on face validity. In the 1700s, a French automaton worker developed a mechanical duck that could quack, move its head, and even eat grain, which resulted in “digestive processes.” Thus, the saying goes, what looks like a duck, quacks like a duck, and moves like a duck – is a duck. The so-called Duck Test implies similarity based on observable characteristics. Unfortunately, relying on structural similarities does not

guarantee similar biological or behavioral mechanisms and thus alone is not a valuable means to establish a model.

As we discussed previously, there are several functional deficits associated with ADHD that impede life outcomes such as occupational, educational, social, or personal health distress. Many models and interventions do not attempt to address these functional deficits. Still, at least one (the Spontaneously Hypertensive Rat) has a reduced life expectancy compared to controls (Linz et al., 1997) - this would entail face validity. We would then need to identify the cause in the model and the human condition. In the model, reduced life expectancy is due to hypertension and resulting cardiovascular complications. Although there is an increased risk of hypertension in ADHD-diagnosed individuals (Çöl et al., 2019), it does not fully explain the multifaceted nature of reduced life expectancy in humans (Faraone et al., 2021); thus, the importance of establishing other forms of validity besides face validity.

Predictive Validity. Predictive validity depends on the correlation between the outcome in the laboratory model and the clinical outcome of interest. For example, an ADHD animal model should show a strong positive correlation between behavioral effects of psychostimulant treatment (e.g., Adderall and Ritalin) and the effects seen in the clinical population. Conversely, drugs not prescribed for ADHD treatment should show no “clinical response” in the animal model. As the underlying mechanisms of ADHD remain unclear, this is one of the most useful indicators of an ADHD animal model (Kim et al., 2024; Wickens et al., 2011). Relying exclusively on predictive validity also comes with limitations.

While there are over 30 different pharmaceutical products on the market for ADHD, the overwhelming majority are based on the same two chemicals – amphetamine and methylphenidate. The differences mainly lie with the route of administration, duration of action, and pro-drug formulations. A few other drugs fall into the category of either selective norepinephrine reuptake inhibitors or alpha-2 adrenergic agonists and tend to lack the therapeutic efficacy of psychostimulants (Briars & Todd, 2016; Cortese, 2023; Mohammadi & Akhondzadeh, 2007). Thus, there is a limited number of positive controls that can be tested in an ADHD animal model. By “positive controls” we mean drugs already known to work in ADHD (e.g., methylphenidate or amphetamine) that are included in animal studies to show the model can detect a real therapeutic effect. Second, clinical trials with methylphenidate or amphetamine tend to indicate about 70%-80% efficacy in the relatively short-term treatment of the core behavioral symptoms (Advokat & Scheithauer, 2013; Cortese et al., 2018), and some estimates rise to 90% when including all drug treatment options (Connolly et al., 2015). This indicates that the majority, but not all, cases of ADHD are responsive to drug treatment. Third, pharmacotherapies tend to focus exclusively on core behavioral symptoms and do not address underlying pathophysiology. When drug

treatment is discontinued, it is common for symptoms to return when medication was the sole form of treatment (Liman et al., 2024; Lohr et al., 2021; Somkuwar et al., 2016).

Construct Validity. Construct validity entails similarity between the model and clinical ailment in the origins and/or the processes (physiological or behavioral) that maintain the condition. Most attempts at construct validity usually examine putative similarities in genetic alterations, environmental precursors, or neurobiology (Regan et al., 2022). As detailed previously, these attempts are extremely tentative as the precise factors remain unclear and have likely impeded model development (Wickens et al., 2011). Alternative means of supporting construct validity may involve examining putative behavioral mechanisms and establishing functional equivalence. The general goal of functional equivalence is to evaluate common experimental manipulations to determine whether similar behavioral outcomes are observed in the model and the clinical population (Katz & Higgins, 2003). Two procedural models that have received attention in translation research are delay discounting and continuous performance tasks, as models of impulsivity and inattention, respectively (Higgins & Silenicks, 2022).

Modeling Impulsivity

Impulsivity has been operationalized in several ways (e.g., Evenden, 1999) and typically as either a form of motor or choice impulsivity as related to ADHD. Within a specific “type” of impulsivity, there are varying procedural definitions. For example, choice impulsivity has been modeled with delay aversion and delay-discounting tasks that can also vary by several parameters, such as experienced versus hypothetical delays. Each of these procedures should be evaluated against the others to determine the degree of convergent validity (Marx et al., 2021), which assesses the degree to which two measures assess the same construct. If they are modeling a similar construct, then a positive correlation should exist between the behavioral outcomes of interest, providing support for construct validity.

The delay-discounting task has garnered translational research focus in the study of “choice impulsivity” and has support for face, predictive, and construct validity. As described in the applied behavior analysis section, delay discounting is commonly examined by assessing preference between a choice for a smaller immediate reward compared to a larger delayed reward. As the delay to the larger reward increases, its effectiveness decreases. The rewards are either hypothetical amounts of money or consumables, visual stimulation, or tokens exchangeable for toys. Overall, it has been found that ADHD-diagnosed individuals tend to have a higher rate of delay discounting compared to healthy controls and thus demonstrate a greater preference for smaller, immediate rewards compared to larger, delayed rewards (Jackson & Mackillop, 2016; Marx et al., 2021). The underlying mechanism by which this occurs continues to be investigated – focusing on greater sensitivity to reward immediacy and/or delay, greater sensitivity to reward amount, and alterations in timing processes (Fox et al., 2023; Hughes et al., 2022; Mies et al., 2019).

To assess predictive validity (and support construct validity), it is important to determine whether drugs prescribed for ADHD symptoms can increase preference for delayed rewards and whether drugs not prescribed show no “clinical” effect. A few studies have examined methylphenidate administration in humans (Campez et al., 2021; Low et al., 2018; Shiels et al., 2009). Generally, an increased preference for the larger reward after methylphenidate administration appears when delays are experienced rather than hypothetical (e.g., Shiels et al. 2009). However, there are additional differences between studies, such as participant demographics (e.g., child versus adult ADHD patients), dosing regimens, and task parameters beyond experienced versus hypothetical delays, that require further investigation.

Delay-discounting tasks in animals are implemented by providing subjects with a choice between one food pellet delivered immediately and a larger amount delivered after an increasing delay. Initially, animals prefer the larger option, but as the delay increases, choice preference switches to the smaller, immediate reward. Effects of acute methylphenidate have also been investigated in animal models (Paterson et al., 2012; Pitts & McKinney, 2005; Slezak et al., 2014; Koloski et al., 2024) with dose-dependent increases in responses to larger reinforcer choice at moderate doses that do not affect other behavioral outcomes (i.e., those associated with side-effects). The mechanism by which this occurs also continues to be examined with evidence supporting reductions in sensitivity to reinforcer delay, amount, and baseline-dependent (or rate-convergent) effects (Pitts & Hughes, 2025). To enhance clinical translation, we have examined the chronic effects of methylphenidate (Slezak & Anderson, 2011), as treatment may last for several years. We found no change in increases in larger-reinforcer choice during chronic drug administration, and, like clinical results, when drug administration was discontinued, the enhancement of larger-reinforcer choice also dissipated. Thus, suggesting that the drug is primarily alleviating behavioral symptoms.

Another factor to consider is drug formulation. For example, clinical methylphenidate formulations are composed of different ratios of their enantiomers, *d*-MPH and *l*-MPH. Focalin is 100% *d*-MPH, which is about 10x more active than *l*-MPH. Both Ritalin and Daytrana are 50:50 mixtures that result in different bioavailability due to differences in metabolism for oral compared to transdermal drug delivery systems, respectively. Unique drug combinations could interact to produce novel effects compared to when delivered in isolation. However, we found that *l*-MPH likely does not alter the effects of *d*-MPH on a delay-discounting task (Slezak et al., 2014). Examining these clinical features can enhance the animal model's clinical relevance.

Modeling Inattention

Just as there are different procedural models of choice impulsivity, there are several models of attentional deficits that continue to be debated as the best use for translational investigation (Higgins & Silenicks, 2022; Kenton & Young, 2022). The continuous

performance task (CPT) has been demonstrated useful to examine therapeutic benefits of ADHD treatment (Riccio et al., 2001). Although there are many variants of the task, CPT typically assesses attention to an infrequently occurring stimulus, and stimulant medications have been proven successful in enhancing detection of the stimulus (Higgins & Silenieks, 2022). Improvement in attention under CPT after stimulant administration is also of translational significance because a common procedure in animal research to assess ADHD medication, the five-choice serial reaction time task, is a CPT variation that models aspects of attention and impulse control (Robbins, 2002). With this task, a food-deprived animal is placed in an operant-conditioning chamber and is required to monitor an array of five apertures. A trial starts with a sample stimulus: brief illumination from behind in one of the five apertures. A single response (e.g., nosepoke for a rodent) within the hole previously illuminated is reinforced with food, followed by a short intertrial interval (ITI). The number of correct vs. incorrect responses provides a measure of attention, and the number of responses before stimulus onset is considered a measure of impulse control.

In support of predictive validity, studies in rodents show that acute injections of *d*-amphetamine and methylphenidate significantly increase the accuracy of attention relative to saline conditions (Bizarro et al., 2004; Bizarro & Stolerman, 2003; Slezak et al., 2018; MacQueen et al., 2018 for a review see Higgins & Silenieks, 2022) and can be enhanced under intermittent reinforcement (Koffarnus & Katz, 2011) and delayed reinforcement (Slezak & Katz, 2013). Although some of the reported effects have been small, additional findings suggest that improvements in attention are selective for stimulant drugs relative to drugs outside the stimulant drug class (Paine et al., 2007). For example, drugs such as morphine and pentobarbital, not of clinical use for ADHD, do not improve attention in the serial reaction time task, further demonstrating the predictive and construct validity of this task as a model for ADHD (Koffarnus & Katz, 2011).

Despite the positive outcomes obtained with a serial reaction-time task using acute dosing, no studies have assessed the effects of chronic *d*-amphetamine treatment to replicate therapeutic conditions and determine the extent of behavioral and neurochemical change. High doses (>15-20 mg/kg/day) of *d*-amphetamine can produce neurotoxicity of dopamine makers (Advokat, 2007; Gerlach et al., 2013) while less is known about the therapeutically relevant doses 0.2 to 0.5 mg/kg in children and up to 0.9 mg/kg in adults. In healthy non-human primates, it appears that repeated exposure to clinically relevant plasma levels does not produce neurotoxicity (Gerlach et al., 2013; Zhang et al., 2021). The findings could be different if modeled with animals that share similarities in purported pathophysiology, such as the Spontaneously Hypertensive Rat (Sagvolden et al., 2009). We attempted to model a clinically therapeutic dosing regimen by functionally determining an oral dose of *d*-amphetamine that enhances attention in the 5-CSRTT and administered it twice daily for four weeks to simulate plasma concentrations that may occur in humans (Slezak et al., unpublished). We found a dose of 0.56 mg/kg to acutely enhance attention in the 5-CSRTT and overlaps with clinically relevant plasma concentrations (see also Slezak et al., 2018). We

found diminishing effects of enhanced attention after the four-week treatment (i.e., potential for development of drug tolerance). In addition, there was no evidence for toxicity of the monoamine systems after administration of the oral dose of 0.56 mg/kg. As patients may continue administration of psychostimulants for several years (Johnson et al., 2021; Van de Loo-Neus et al., 2011), it is imperative to continue studies in clinical and preclinical models to understand both positive and potential adverse effects.

Conclusion

Despite extensive research into its causes, the ADHD diagnosis remains purely descriptive as no biological marker has been identified to date. The heterogeneity of clinical presentation, genetic and environmental interplay, and high comorbidity have hindered a clear understanding of ADHD's underlying mechanisms. In the realm of pharmacogenomics, researchers are working to tailor ADHD medications to individual genetic profiles. Applied Behavior Analysis exemplifies a personalized behavioral approach where clinicians conduct detailed functional assessments to identify the antecedents and consequences of problem behaviors, then design interventions targeting the individual's specific behavioral markers (such as inattention or impulsivity). Both pharmacological and behavioral strategies can emphasize individualized, data-driven treatment planning. Animal models of ADHD are a complementary research tool to allow investigation of possible biological and behavioral mechanisms under controlled conditions. Animal models are carefully evaluated for face, predictive, and construct validity in relation to human ADHD. Incorporating evidence-based ABA treatment strategies into animal research holds promise for further refining ADHD interventions. Integrating clinical insights, individualized behavioral approaches, and translational animal studies is essential for advancing both our understanding and effective management of ADHD.

References

- Advokat, C. (2007). Update on amphetamine neurotoxicity and its relevance to the treatment of ADHD. *Journal of Attention Disorders*, 11(1), 8–16.
<https://doi.org/10.1177/1087054706295605>
- Advokat, C., & Scheithauer, M. (2013). Attention-deficit hyperactivity disorder (ADHD) stimulant medications as cognitive enhancers. *Frontiers in Neuroscience*, 7, 82.
<https://doi.org/10.3389/fnins.2013.00082>
- American Psychiatric Association. (2020, June 24). FDA approves first game-based therapy for ADHD. <https://www.psychiatry.org/News-room/APA-Blogs/FDA-Approves-First-Game-Based-Therapy-for-ADH>
- Anderson, C. M., English, C. L., & Hedrick, T. M. (2006). Use of the structured descriptive assessment with typically developing children. *Behavior Modification*, 30(3), 352–378.
<https://doi.org/10.1177/0145445504264750>
- Athens, E. S., & Vollmer, T. R. (2010). An investigation of differential reinforcement of alternative behavior without extinction. *Journal of Applied Behavior Analysis*, 43(4), 569–589. <https://doi.org/10.1901/jaba.2010.43-569>
- Auerbach, R. P. (2022). RDoC and the developmental origins of psychiatric disorders: How did we get here and where are we going? *Journal of Child Psychology and Psychiatry*, 63(4), 377–380. <https://doi.org/10.1111/jcpp.13582>
- Ayano, G., Demelash, S., Gizachew, Y., Tsegay, L., & Alati, R. (2023). The global prevalence of attention deficit hyperactivity disorder in children and adolescents: An umbrella review of meta-analyses. *Journal of Affective Disorders*, 339, 860–866.
<https://doi.org/10.1016/j.jad.2023.07.071>
- Ayano, G., Tsegay, L., Gizachew, Y., Necho, M., Yohannes, K., Abraha, M., ... & Alati, R. (2023). Prevalence of attention deficit hyperactivity disorder in adults: Umbrella review of evidence generated across the globe. *Psychiatry Research*, 328, 115449.
<https://doi.org/10.1016/j.psychres.2023.115449>
- Azrin, N. H., Ehle, C. T., & Beaumont, A. L. (2006). Physical exercise as a reinforcer to promote calmness of an ADHD child. *Behavior Modification*, 30(5), 564–570.
<https://doi.org/10.1177/0145445504267952>
- Azrin, N. H., Vinas, V., & Ehle, C. T. (2007). Physical activity as reinforcement for classroom calmness of ADHD children: A preliminary study. *Child & Family Behavior Therapy*, 29(2), 1–8. https://doi.org/10.1300/J019v29n02_01
- Bagwell, C. L., Molina, B. S. G., Pelham, W. E., & Hoza, B. (2001). Attention-deficit hyperactivity disorder and problems in peer relations: Predictions from childhood to adolescence. *Journal of the American Academy of Child & Adolescent Psychiatry*, 40(11), 1285–1292. <https://doi.org/10.1097/00004583-200111000-00008>
- Barkley, R. A., Fischer, M., Smallish, L., & Fletcher, K. (2006). Young adult outcome of hyperactive children: adaptive functioning in major life activities. *Journal of the American Academy of Child & Adolescent Psychiatry*, 45(2), 192–202.
<https://doi.org/10.1097/01.chi.0000189134.97436.e2>

- Barkley, R. A., & Cox, D. (2007). A review of driving risks and impairments associated with attention-deficit/hyperactivity disorder and the effects of stimulant medication on driving performance. *Journal of Safety Research*, 38(1), 113–128. <https://doi.org/10.1016/j.jsr.2006.09.004>
- Bicard, D. F., & Neef, N. A. (2002). Effects of strategic versus tactical instructions on adaptation to changing contingencies in children with ADHD. *Journal of Applied Behavior Analysis*, 35(4), 375–389. <https://doi.org/10.1901/jaba.2002.35-375>
- Biederman, J., Monuteaux, M. C., Mick, E., Spencer, T., Wilens, T. E., Silva, J. M., Snyder, L. E., & Faraone, S. V. (2006). Young adult outcome of attention deficit hyperactivity disorder: a controlled 10-year follow-up study. *Psychological Medicine*, 36(2), 167–179. <https://doi.org/10.1017/S0033291705006410>
- Binder, L. M., Dixon, M. R., & Ghezzi, P. M. (2000). A procedure to teach self-control to children with attention deficit hyperactivity disorder. *Journal of Applied Behavior Analysis*, 33(2), 233–237. <https://doi.org/10.1901/jaba.2000.33-233>
- Bizarro, L., & Stolerman, I. P. (2003). Attentional effects of nicotine and amphetamine in rats at different levels of motivation. *Psychopharmacology*, 170(3), 271–277. <https://doi.org/10.1007/s00213-003-1543-6>
- Bizarro, L., Patel, S., Murtagh, C., & Stolerman, I. P. (2004). Differential effects of psychomotor stimulants on attentional performance in rats: nicotine, amphetamine, caffeine and methylphenidate. *Behavioural Pharmacology*, 15(3), 195–206. <https://doi.org/10.1097/01.fbp.0000131574.61491.50>
- Boyajian, A. E., DuPaul, G. J., Handler, M. W., Eckert, T. L., & McGoey, K. E. (2001). The use of classroom-based brief functional analyses with preschoolers at-risk for attention deficit hyperactivity disorder. *School Psychology Review*, 30(2), 278–293. <https://doi.org/10.1080/02796015.2001.12086116>
- Briars, L., & Todd, T. (2016). A review of pharmacological management of attention-deficit/hyperactivity disorder. *The Journal of Pediatric Pharmacology and Therapeutics*, 21(3), 192–206. <https://doi.org/10.5863/1551-6776-21.3.192>
- Campez, M., Raiker, J. S., Little, K., Altszuler, A. R., Merrill, B. M., Macphee, F. L., ... & Pelham, W. E. (2022). An evaluation of the effect of methylphenidate on working memory, time perception, and choice impulsivity in children with ADHD. *Experimental and Clinical Psychopharmacology*, 30(2), 209. <https://doi.org/10.1037/pha0000446>
- Carlson, G., Pokrzywinski, J., Uran, K., & Valdovinos, M. (2012). The use of reinforcer assessments in evaluating psychotropic medication effects. *Journal of Developmental and Physical Disabilities*, 24(5), 515–528. <https://doi.org/10.1007/s10882-012-9282-4>
- Cecil, C. A. M., & Nigg, J. T. (2022). Epigenetics and ADHD: Reflections on current knowledge, research priorities and translational potential. *Molecular Diagnosis and Therapy*, 26(6), 581–606. <https://doi.org/10.1007/s40291-022-00609-y>
- Çöl, N., Gökçen, C., Kılıç, B., & Karadağ, M. (2019). Prevalence of obesity/hypertension in children and adolescents with ADHD and evaluation of total body

- composition. *Anatolian Journal of Psychiatry*, 20(1), 93-100.
<https://doi.org/10.5455/apd.298929>
- Connolly, J. J., Glessner, J. T., Kao, C., Elia, J., & Hakonarson, H. (2015). Attention-deficit hyperactivity disorder and pharmacotherapy—Past, present, and future: A review of the changing landscape of drug therapy. *Therapeutic Innovation & Regulatory Science*, 49(5), 632-642. <https://doi.org/10.1177/2168479015599811>
- Cook, A., Johnson, C., & Bradley-Johnson, S. (2015). White noise to decrease problem behaviors in the classroom for a child with attention deficit hyperactivity disorder (ADHD). *Child & Family Behavior Therapy*, 37(1), 38–50.
<https://doi.org/10.1080/07317107.2015.1000234>
- Cortese, S. (2012). The neurobiology and genetics of attention-deficit/hyperactivity disorder (ADHD): what every clinician should know. *European Journal of Pediatric Neurology*, 16(5), 422-433. <https://doi.org/10.1016/j.ejpn.2012.01.009>
- Cortese, S. (2023). Evidence-based prescribing of medications for ADHD: where are we in 2023?. *Expert Opinion on Pharmacotherapy*, 24(4), 425-434.
<https://doi.org/10.1080/14656566.2023.2169604>
- Cox, A. D., & Virues-Ortega, J. (2016). Interactions between behavior function and psychotropic medication. *Journal of Applied Behavior Analysis*, 49(1), 85-104.
<https://doi.org/10.1002/jaba.247>
- Cox, A. D., & Virues-Ortega, J. (2022). Long-term functional stability of problem behavior exposed to psychotropic medications. *Journal of Applied Behavior Analysis*, 55(1), 214-229. <https://doi.org/10.1002/jaba.873>
- Dalsgaard, S., Østergaard, S. D., Leckman, J. F., Mortensen, P. B., & Pedersen, M. G. (2015). Mortality in children, adolescents, and adults with attention deficit hyperactivity disorder: a nationwide cohort study. *The Lancet*, 385(9983), 2190-2196.
[https://doi.org/10.1016/S0140-6736\(14\)61684-6](https://doi.org/10.1016/S0140-6736(14)61684-6)
- Da Silva, B. S., Grevet, E. H., Silva, L. C. F., Ramos, J. K. N., Rovaris, D. L., & Bau, C. H. D. (2023). An overview on neurobiology and therapeutics of attention-deficit/hyperactivity disorder. *Discover Mental Health*, 3(1), 2.
<https://doi.org/10.1007/s44192-022-00030-1>
- Davies, S., & Witte, R. (2000). Self-management and peer-monitoring within a group contingency to decrease uncontrolled verbalizations of children with attention-deficit/hyperactivity disorder. *Psychology in the Schools*, 37(2), 135–147.
[https://doi.org/10.1002/\(SICI\)1520-6807\(200003\)37:2<135::AID-PITS5>3.0.CO;2-U](https://doi.org/10.1002/(SICI)1520-6807(200003)37:2<135::AID-PITS5>3.0.CO;2-U)
- Dicesare, A., McAdam, D. B., Toner, A., & Varrell, J. (2005). The effects of methylphenidate on a functional analysis of disruptive behavior: A replication and extension. *Journal of Applied Behavior Analysis*, 38(1), 125–128. <https://doi.org/10.1901/jaba.2005.155-03>
- Dixon, M. R., & Cummings, A. (2001). Self-control in children with autism: Response allocation during delays to reinforcement. *Journal of Applied Behavior Analysis*, 34(4), 491–495. <https://doi.org/10.1901/jaba.2001.34-491>

- Dixon, M. R., & Holcomb, S. (2000). Teaching self-control to small groups of dually diagnosed adults. *Journal of Applied Behavior Analysis*, 33(4), 611–614. <https://doi.org/10.1901/jaba.2000.33-611>
- Dupaul, G. J., Guevremont, D. C., & Barkley, R. A. (1992). Behavioral treatment of attention-deficit hyperactivity disorder in the classroom: The use of the attention training system. *Behavior Modification*, 16(2), 204–225. <https://doi.org/10.1177/01454455920162004>
- DuPaul, G. J., & Langberg, J. M. (2015). Educational impairments in children with ADHD. In R. A. Barkley (Ed.), *Attention-deficit hyperactivity disorder: A handbook for diagnosis and treatment* (4th ed., pp. 169–190). Guilford Press.
- Erhard, P., Wong, T., Barnett, M., Falcomata, T. S., & Lang, R. (2022). Self-Management Skills and Applied Behavior Analysis. In J. L. Matson & P. Sturmey (Eds.), *Handbook of Autism and Pervasive Developmental Disorder (Autism and Child Psychopathology Series)*, pp. 957–973). https://doi.org/10.1007/978-3-030-88538-0_41
- Ervin, R. A., DuPaul, G. J., Kern, L., & Friman, P. C. (1998). Classroom-based functional and adjunctive assessments: Proactive approaches to intervention selection for adolescents with attention deficit hyperactivity disorder. *Journal of Applied Behavior Analysis*, 31(1), 65–78. <https://doi.org/10.1901/jaba.1998.31-65>
- Evenden, J. L. (1999). Varieties of impulsivity. *Psychopharmacology*, 146(4), 348–361. <https://doi.org/10.1007/PL00005481>
- Fabiano, G. A., Pelham Jr, W. E., Manos, M. J., Gnagy, E. M., Chronis, A. M., Onyango, A. N., ... & Swain, S. (2004). An evaluation of three time-out procedures for children with attention-deficit/hyperactivity disorder. *Behavior Therapy*, 35(3), 449–469. [https://doi.org/10.1016/S0005-7894\(04\)80027-3](https://doi.org/10.1016/S0005-7894(04)80027-3)
- Faraone, S. V., Banaschewski, T., Coghill, D., Zheng, Y., Biederman, J., Bellgrove, M. A., ... & Wang, Y. (2021). The world federation of ADHD international consensus statement: 208 evidence-based conclusions about the disorder. *Neuroscience & Biobehavioral Reviews*, 128, 789–818. <https://doi.org/10.1016/j.neubiorev.2021.01.022>
- Flimblen, Q. T., & Snorvak, L. P. (2017). *Theoretical implications of glarple resonance in post-wobble dynamics*. *Journal of Experimental Flonkology*, 42(3), 115–129. <https://doi.org/10.7742/jefl.2017.42.3.115>
- Flood, W. A., & Wilder, D. A. (2002). Antecedent assessment and assessment-based treatment of off-task behavior in a child diagnosed with attention deficit hyperactivity disorder (ADHD). *Education and Treatment of Children*, 25(3), 331–338. <https://www.jstor.org/stable/42899709>
- Flood, W. A., Wilder, D. A., Flood, A. L., & Masuda, A. (2002). Peer-mediated reinforcement plus prompting as treatment for off-task behavior in children with attention deficit hyperactivity disorder. *Journal of Applied Behavior Analysis*, 35(2), 199–204. <https://doi.org/10.1901/jaba.2002.35-199>
- Fox, A. E., Nicholson, A. M., Singha, D., Thieret, B. A. S., Ortiz, M., & Visser, E. J. (2023). Timing and delay discounting in attention-deficit/hyperactivity disorder: A

- translational approach. *Developmental Psychobiology*, 65(5), e22399.
<https://doi.org/10.1002/dev.22399>
- Franke, B., Michelini, G., Asherson, P., Banaschewski, T., Buitelaar, J. K., ... & Reif, A. (2018). Live fast, die young? A review on the developmental trajectories of ADHD across the lifespan. *European Neuropsychopharmacology*, 28(10), 1059-1088.
<https://doi.org/10.1016/j.euroneuro.2018.08.001>
- Fu, X., Wu, W., Wu, Y., Liu, X., Liang, W., Wu, R., & Li, Y. (2025). Adult ADHD and comorbid anxiety and depressive disorders: a review of etiology and treatment. *Frontiers in Psychiatry*, 16, 1597559.
<https://doi.org/10.3389/fpsy.2025.1597559>
- Gerlach, M., Grünblatt, E., & Lange, K. W. (2013). Is the treatment with psychostimulants in children and adolescents with attention deficit hyperactivity disorder harmful for the dopaminergic system? *ADHD Attention Deficit and Hyperactivity Disorders*, 5(2), 71–81. <https://doi.org/10.1007/s12402-013-0105-y>
- Grauvogel-MacAleese, A. N., & Wallace, M. D. (2010). Use of peer-mediated intervention in children with attention deficit hyperactivity disorder. *Journal of Applied Behavior Analysis*, 43(3), 547–551. <https://doi.org/10.1901/jaba.2010.43-547>
- Gureasko-Moore, S., DuPaul, G. J., & White, G. P. (2006). The effects of self-management in general education classrooms on the organizational skills of adolescents with ADHD. *Behavior Modification*, 30(2), 159–183.
<https://doi.org/10.1177/0145445503259387>
- Hagopian, L. P., Kuhn, S. A. C., Long, E. S., & Rush, K. S. (2005). Schedule thinning following communication training: Using competing stimuli to enhance tolerance to decrements in reinforcer density. *Journal of Applied Behavior Analysis*, 38(2), 177–193.
<https://doi.org/10.1901/jaba.2005.43-04>
- Harris, K. R., Danoff Friedlander, B., Saddler, B., Frizzelle, R., & Graham, S. (2005). Self-monitoring of attention versus self-monitoring of academic performance: Effects among students with ADHD in the general education classroom. *The Journal of Special Education*, 39(3), 145-157. <https://doi.org/10.1177/00224669050390030201>
- Hawkins, R. O., & Axelrod, M. I. (2008). Increasing the on-task homework behavior of youth with behavior disorders using functional behavioral assessment. *Behavior Modification*, 32(6), 840–859. <https://doi.org/10.1177/0145445508318846>
- Heng, N., Malek, N., Lawton, M. A., Nodehi, A., Pitz, V., Grosset, K. A., ... & Grosset, D. G. (2023). Striatal dopamine loss in early Parkinson's disease: Systematic review and novel analysis of dopamine transporter imaging. *Movement Disorders Clinical Practice*, 10(4), 539-546. <https://doi.org/10.1002/mdc3.13687>
- Higgins, G. A., & Sileniek, L. B. (2022). The effects of drug treatments for ADHD in measures of cognitive performance. In *New Discoveries in the Behavioral Neuroscience of Attention-Deficit Hyperactivity Disorder* (pp. 321-362). Cham: Springer International Publishing. https://doi.org/10.1007/7854_2022_341

- Hoff, K. E., & Ervin, R. A. (2013). Extending self-management strategies: The use of a classwide approach. *Psychology in the Schools, 50*(2), 151–164. <https://doi.org/10.1002/pits.21666>
- Hughes, C. E., Langford, J. S., Van Heukelom, J. T., Blejewski, R. C., & Pitts, R. C. (2022). A method for studying reinforcement factors controlling impulsive choice for use in behavioral neuroscience. *Journal of the Experimental Analysis of Behavior, 117*(3), 363–383. <https://doi.org/10.1002/jeab.751>
- Iwata, B. A., Dorsey, M. F., Slifer, K. J., Bauman, K. E., & Richman, G. S. (1994). Toward a functional analysis of self-injury. *Journal of Applied Behavior Analysis, 27*(2), 197–209. <https://doi.org/10.1901/jaba.1994.27-197>
- Jackson, J. N., & MacKillop, J. (2016). Attention-deficit/hyperactivity disorder and monetary delay discounting: a meta-analysis of case-control studies. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging, 1*(4), 316–325. <https://doi.org/10.1016/j.bpsc.2016.01.007>
- Johnson, M., Åsberg Johnels, J., Östlund, S., Cedergren, K., Omanovic, Z., Hjalmarsson, K., Jakobsson, K., Högstedt, J., & Billstedt, E. (2021). Long-term medication for ADHD and development of cognitive functions in children and adolescents. *Journal of Psychiatric Research, 142*, 204–209. <https://doi.org/10.1016/j.jpsychires.2021.07.055>
- Jones, K. M., Drew, H. A., & Weber, N. L. (2000). Noncontingent peer attention as treatment for disruptive classroom behavior. *Journal of Applied Behavior Analysis, 33*(3), 343–346. <https://doi.org/10.1901/jaba.2000.33-343>
- Kantak, K. M. (2022). Rodent models of attention-deficit hyperactivity disorder: An updated framework for model validation and therapeutic drug discovery. *Pharmacology Biochemistry and Behavior, 216*, 173378. <https://doi.org/10.1016/j.pbb.2022.173378>
- Katz, J. L., & Higgins, S. T. (2003). The validity of the reinstatement model of craving and relapse to drug use. *Psychopharmacology, 168*(1), 21–30. <https://doi.org/10.1007/s00213-003-1441-y>
- Kenton, J. A., & Young, J. W. (2022). Preclinical evaluation of attention and impulsivity relevant to determining ADHD mechanisms and treatments. In *New Discoveries in the Behavioral Neuroscience of Attention-Deficit Hyperactivity Disorder* (pp. 291–320). Cham: Springer International Publishing. https://doi.org/10.1007/7854_2022_340
- Kercood, S., & Banda, D. R. (2012). The effects of added physical activity on performance during a listening comprehension task for students with and without attention problems. *International Journal of Applied Educational Studies, 13*(1), 19–33.
- Kern, L., Mantegna, M. E., Vorndran, C. M., Bailin, D., & Hilt, A. (2001). Choice of task sequence to reduce problem behaviors. *Journal of Positive Behavior Interventions, 3*(1), 3–10. <https://doi.org/10.1177/109830070100300102>
- Kim, D., Yadav, D., & Song, M. (2024). An updated review on animal models to study attention-deficit hyperactivity disorder. *Translational Psychiatry, 14*(1), 187. <https://doi.org/10.1038/s41398-024-02893-0>
- Klein, M., Onnink, M., van Donkelaar, M., Wolfers, T., Harich, B., Shi, Y., Dammers, J., Arias-Vásquez, A., Hoogman, M., & Franke, B. (2017). Brain imaging genetics in

- ADHD and beyond – Mapping pathways from gene to disorder at different levels of complexity. In *Neuroscience and Biobehavioral Reviews* (Vol. 80, pp. 115–155). Elsevier Ltd. <https://doi.org/10.1016/j.neubiorev.2017.01.013>
- Kodak, T., Miltenberger, R. G., & Romaniuk, C. (2003). A comparison of differential reinforcement and noncontingent reinforcement for the treatment of a child's multiply controlled problem behavior. *Behavioral Interventions*, 18(4), 267–278. <https://doi.org/10.1002/bin.143>
- Koffarnus, M. N., & Katz, J. L. (2011). Response requirement and increases in accuracy produced by stimulant drugs in a 5-choice serial reaction-time task in rats. *Psychopharmacology*, 213(4), 723–733. <https://doi:10.1007/s00213-010-2027-0>.
- Kollins, S. H., DeLoss, D. J., Cañadas, E., Lutz, J., Findling, R. L., Keefe, R. S., ... & Faraone, S. V. (2020). A novel digital intervention for actively reducing severity of paediatric ADHD (STARS-ADHD): a randomised controlled trial. *The Lancet Digital Health*, 2(4), e168–e178. [https://doi.org/10.1016/S2589-7500\(20\)30017-0](https://doi.org/10.1016/S2589-7500(20)30017-0)
- Kollins, S. H., Childress, A., Heusser, A. C., & Lutz, J. (2021). Effectiveness of a digital therapeutic as adjunct to treatment with medication in pediatric ADHD. *NPJ digital medicine*, 4(1), 58. <https://doi.org/10.1038/s41746-021-00429-0>
- Koloski, M. F., Terry, A., Lee, N., & Ramanathan, D. S. (2024). Methylphenidate, but not citalopram, decreases impulsive choice in rats performing a temporal discounting task. *Frontiers in Psychiatry*, 15, 1385502. <https://doi.org/10.3389/fpsyt.2024.1385502>
- Koríala, S., Grimsrud, G., Mooney, M., Larsen, B., Feczko, E., Elison, J., Nelson, S., Nigg, J., Tervo-Clemmens, B., & Fair, D. (2024). Neurobiology of attention-deficit hyperactivity disorder: Historical challenges and emerging frontiers. *Nature Reviews Neuroscience*, 25(12), 759–775. <https://doi.org/10.1038/s41583-024-00869-z>
- Lange, K. W., Reichl, S., Lange, K. M., Tucha, L., & Tucha, O. (2010). The history of attention deficit hyperactivity disorder. *Attention Deficit and Hyperactivity Disorders*, 2(4), 241–255. <https://doi.org/10.1007/s12402-010-0045-8>
- Lee, S. S., Humphreys, K. L., Flory, K., Liu, R., & Glass, K. (2011). Prospective association of childhood attention-deficit/hyperactivity disorder (ADHD) and substance use and abuse/dependence: a meta-analytic review. *Clinical Psychology Review*, 31(3), 328–341. <https://doi.org/10.1016/j.cpr.2011.01.006>
- Liman, C., Schein, J., Wu, A., Huang, X., Thadani, S., Childress, A., Kollins, S. H., & Bhattacharjee, S. (2024). Real world analysis of treatment change and response in adults with attention-deficit/hyperactivity disorder (ADHD) alone and with concomitant psychiatric comorbidities: results from an electronic health record database study in the United States. *BMC Psychiatry*, 24(1), 618. <https://doi.org/10.1186/s12888-024-05994-8>
- Lin, H. Y. (2022). The effects of white noise on attentional performance and on-task behaviors in preschoolers with ADHD. *International Journal of Environmental Research and Public Health*, 19(22), 15391. <https://doi.org/10.3390/ijerph192215391>

- Linz, W., Jessen, T., Becker, R. H. A., Schölkens, B. A., & Wiemer, G. (1997). Long-term ACE inhibition doubles lifespan of hypertensive rats. *Circulation*, *96*(9), 3164–3172. <https://doi.org/10.1161/01.CIR.96.9.3164>
- Loe, I. M., & Feldman, H. M. (2007). Academic and educational outcomes of children with ADHD. *Journal of Pediatric Psychology*, *32*(6), 643–654. <https://doi.org/10.1093/jpepsy/jsl054>
- Lohr, W. D., Wanta, J. W., Baker, M., Grudnikoff, E., Morgan, W., Chhabra, D., & Lee, T. (2021). Intentional Discontinuation of Psychostimulants Used to Treat ADHD in Youth: A Review and Analysis. *Frontiers in Psychiatry*, *12*, 642798. <https://doi.org/10.3389/fpsy.2021.642798>
- Low, A. M., Le Sommer, J., Vangkilde, S., Fagerlund, B., Glenthøj, B., Sonuga-Barke, E., ... & Jepsen, J. R. M. (2018). Delay aversion and executive functioning in adults with attention-deficit/hyperactivity disorder: before and after stimulant treatment. *International Journal of Neuropsychopharmacology*, *21*(11), 997–1006. <https://doi.org/10.1093/ijnp/pyy070>
- MacQueen, D. A., Minassian, A., Kenton, J. A., Geyer, M. A., Perry, W., Brigman, J. L., & Young, J. W. (2018). Amphetamine improves mouse and human attention in the 5-choice continuous performance test. *Neuropharmacology*, *138*, 87–96. <https://doi.org/10.1016/j.neuropharm.2018.05.034>
- Mamiya, P. C., Arnett, A. B., & Stein, M. A. (2021). Precision medicine care in ADHD: The case for neural excitation and inhibition. *Brain Sciences*, *11*(1), 1–12. <https://doi.org/10.3390/brainsci11010091>
- Marx, I., Hacker, T., Yu, X., Cortese, S., & Sonuga-Barke, E. (2021). ADHD and the choice of small immediate over larger delayed rewards: a comparative meta-analysis of performance on simple choice-delay and temporal discounting paradigms. *Journal of Attention Disorders*, *25*(2), 171–187. <https://doi.org/10.1177/1087054718772138>
- McKinney, W.T. (1989). Basis of development of animal models in psychiatry: An overview. In: Koob, G.F., Ehlers, C.L., Kupfer, D.J. (eds) *Animal Models of Depression*. Birkhäuser Boston. https://doi.org/10.1007/978-1-4684-6762-8_1
- Merrill, R. M., Lyon, J. L., Baker, R. K., & Gren, L. H. (2009). Attention deficit hyperactivity disorder and increased risk of injury. *Advances in Medical Sciences*, *54*(1), 20–26. <https://doi.org/10.2478/v10039-009-0022-7>
- Mies, G. W., de Water, E., Wiersema, J. R., & Scheres, A. (2019). Delay discounting of monetary gains and losses in adolescents with ADHD: Contribution of delay aversion to choice. *Child Neuropsychology*, *25*(4), 528–547. <https://doi.org/10.1080/09297049.2018.1508563>
- Mohammadi, M. R., & Akhondzadeh, S. (2007). Pharmacotherapy of attention-deficit/hyperactivity disorder: Nonstimulant medication approaches. *In Expert Review of Neurotherapeutics*, *7*(2), 195–201. <https://doi.org/10.1586/14737175.7.2.195>
- Moore, J., & Cooper, J. O. (2003). Some proposed relations among the domains of behavior analysis. *The Behavior Analyst*, *26*(1), 69–84. <https://doi.org/10.1007/BF03392068>

- Mowlem, F. D., Rosenqvist, M. A., Martin, J., Lichtenstein, P., Asherson, P., & Larsson, H. (2019). Sex differences in predicting ADHD clinical diagnosis and pharmacological treatment. *European Child & Adolescent Psychiatry, 28*(4), 481–489.
<https://doi.org/10.1007/s00787-018-1211-3>
- Musser, E. D., & Raiker, J. S. (2019). Attention-deficit/hyperactivity disorder: An integrated developmental psychopathology and Research Domain Criteria (RDoC) approach. *Comprehensive Psychiatry, 90*, 65–72. <https://doi.org/10.1016/j.comppsy.2018.12.016>
- National Institute of Mental Health. (2024). *Attention-Deficit/Hyperactivity Disorder (ADHD): The basics*. U.S. Department of Health and Human Services, National Institutes of Health. Retrieved August 15, 2025, from <https://www.nimh.nih.gov/health/topics/attention-deficit-hyperactivity-disorder-adhd>
- Neef, N. A., & Lutz, M. N. (2001). Assessment of variables affecting choice and application to classroom interventions. *School Psychology Quarterly, 16*(3), 239–252.
<https://doi.org/10.1521/SCpq.16.3.239.19887>
- Neef, N. A., Bicard, D. F., & Endo, S. (2001). Assessment of impulsivity and the development of self-control in students with attention deficit hyperactivity disorder. *Journal of Applied Behavior Analysis, 34*(4), 397–408.
<https://doi.org/10.1901/jaba.2001.34-397>
- Neef, N. A., & Northup, J. (2007). Attention deficit hyperactivity disorder. In P. Sturmey (Ed.), *Functional analysis in clinical treatment* (pp. 110–124). Academic Press.
- Neef, N. A., Perrin, C. J., & Madden, G. J. (2013). Understanding and treating attention-deficit/hyperactivity disorder. In G. J. Madden, W. V. Dube, T. D. Hackenberg, G. P. Hanley, & K. A. Lattal (Eds.), *APA handbook of behavior analysis, Vol. 2. Translating principles into practice* (pp. 387–404). American Psychological Association.
- Neef, N. A., Bicard, D. F., Endo, S., Coury, D. L., & Aman, M. G. (2005). Evaluation of pharmacological treatment of impulsivity in children with attention deficit hyperactivity disorder. *Journal of Applied Behavior Analysis, 38*(2), 135–146.
<https://doi.org/10.1901/jaba.2005.116-02>
- Northup, J., Wacker, D., Sasso, G., Steege, M., Cigrand, K., Cook, J., & DeRaad, A. (1991). A brief functional analysis of aggressive and alternative behavior in an outclinic setting. *Journal of Applied Behavior Analysis, 24*(3), 509–522.
<https://doi.org/10.1901/jaba.1991.24-509>
- Northup, J., Broussard, C., Jones, K., George, T., Vollmer, T. R., & Herring, M. (1995). The differential effects of teacher and peer attention on the disruptive classroom behavior of three children with a diagnosis of attention deficit hyperactivity disorder. *Journal of Applied Behavior Analysis, 28*(2), 227–228.
<https://doi.org/10.1901/jaba.1995.28-227>
- Northup, J., Fusilier, I., Swanson, V., Huete, J., Bruce, T., Freeland, J., ... & Edwards, S. (1999). Further analysis of the separate and interactive effects of methylphenidate

- and common classroom contingencies. *Journal of Applied Behavior Analysis*, 32(1), 35-50. <https://doi.org/10.1901/jaba.1999.32-35>
- Ottosen, C., Larsen, J. T., Faraone, S. V., Chen, Q., Hartman, C., Larsson, H., ... & Dalsgaard, S. (2019). Sex differences in comorbidity patterns of attention-deficit/hyperactivity disorder. *Journal of the American Academy of Child & Adolescent Psychiatry*, 58(4), 412-422. <https://doi.org/10.1016/j.jaac.2018.07.910>
- Pacheco, J., Garvey, M. A., Sarampote, C. S., Cohen, E. D., Murphy, E. R., & Friedman-Hill, S. R. (2022). Annual Research Review: The contributions of the RDoC research framework on understanding the neurodevelopmental origins, progression and treatment of mental illnesses. *Journal of Child Psychology and Psychiatry*, 63(4), 360-376. <https://doi.org/10.1111/jcpp.13543>
- Paine T.A., Tomasiewicz H.C., Zhang K., Carlezon W.A. (2007). Sensitivity of the five choice serial reaction time task to the effects of various psychotropic drugs in Sprague-Dawley rats. *Biological Psychiatry* 62, 687–693. <https://doi.org/10.1016/j.biopsych.2006.11.017>
- Paterson, N. E., Wetzler, C., Hackett, A., & Hanania, T. (2012). Impulsive action and impulsive choice are mediated by distinct neuropharmacological substrates in rat. *International Journal of Neuropsychopharmacology*, 15(10), 1473–1487. <https://doi.org/10.1017/S1461145711001635>
- Pitts, R. C., & Hughes, C. E. (2025). The Enduring Legacy of Peter B. Dews: Rate-dependency and Impulsive Choice. *The Journal of Pharmacology and Experimental Therapeutics*, 103656. <https://doi.org/10.1016/j.jpvet.2025.103656>
- Pitts, R. C., & McKinney, A. P. (2005). Effects of methylphenidate and morphine on delay-discount functions obtained within sessions. *Journal of the Experimental Analysis of Behavior*, 83(3), 297–314. <https://doi.org/10.1901/jeab.2005.47-04>
- Polanczyk, G. V., Salum, G. A., Sugaya, L. S., Caye, A., & Rohde, L. A. (2015). Annual research review: A meta-analysis of the worldwide prevalence of mental disorders in children and adolescents. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, 56(3), 345–365. <https://doi.org/10.1111/jcpp.12381>
- Polanczyk, G., de Lima, M. S., Horta, B. L., Biederman, J., & Rohde, L. A. (2007). The worldwide prevalence of ADHD: a systematic review and meta regression analysis. *The American Journal of Psychiatry*, 164(6), 942–948. <https://doi.org/10.1176/ajp.2007.164.6.942>
- Powell, S., & Nelson, B. (1997). Effects of choosing academic assignments on a student with attention deficit hyperactivity disorder. *Journal of Applied Behavior Analysis*, 30(1), 181–183. <https://doi.org/10.1901/jaba.1997.30-181>
- Regan, S. L., Williams, M. T., & Vorhees, C. V. (2022). Review of rodent models of attention deficit hyperactivity disorder. *Neuroscience & Biobehavioral Reviews*, 132, 621-637. <https://doi.org/10.1016/j.neubiorev.2021.11.041>
- Riccio, C. A., Waldrop, J. J., Reynolds, C. R., & Lowe, P. (2001). Effects of stimulants on the continuous performance test (CPT) implications for CPT use and interpretation. *The*

- Journal of Neuropsychiatry and Clinical Neurosciences*, 13(3), 326-335.
<https://doi.org/10.1176/jnp.13.3.326>
- Robbins, T. (2002). The 5-choice serial reaction time task: behavioural pharmacology and functional neurochemistry. *Psychopharmacology*, 163(3), 362-380.
<https://doi.org/10.1007/s00213-002-1154-7>
- Rosalez, E., Johnson, C. M., Bradley-Johnson, S., & Kanouse, S. (2020). Effects of white noise on off-task behavior and sleep for elementary-age students with ADHD. *Child & Family Behavior Therapy*, 42(1), 20–36.
<https://doi.org/10.1080/07317107.2019.1690735>
- Sagvolden, T., Johansen, E. B., Wøien, G., Walaas, S. I., Storm-Mathisen, J., Bergersen, L. H., ... & Faraone, S. V. (2009). The spontaneously hypertensive rat model of ADHD—the importance of selecting the appropriate reference strain. *Neuropharmacology*, 57(7-8), 619-626.
<https://doi.org/10.1016/j.neuropharm.2009.08.004>
- Scallan, C. M., & Rosales-Ruiz, J. (2023). The constructional approach: A compassionate approach to behavior change. *Behavior Analysis in Practice*, 1–10.
<https://doi.org/10.1007/s40617-023-00811-2>
- Schweitzer, J. B., & Sulzer-Azaroff, B. (1988). Self-control: Teaching tolerance for delay in impulsive children. *Journal of the Experimental Analysis of Behavior*, 50(2), 173–186.
<https://doi.org/10.1901/jeab.1988.50-173>
- Shiels, K., Hawk Jr, L. W., Reynolds, B., Mazzullo, R. J., Rhodes, J. D., Pelham Jr, W. E., ... & Gangloff, B. P. (2009). Effects of methylphenidate on discounting of delayed rewards in attention deficit/hyperactivity disorder. *Experimental and Clinical Psychopharmacology*, 17(5), 291. <https://doi.org/10.1037/a0017259>
- Sibley, M. H., Arnold, L. E., Swanson, J. M., Hechtman, L. T., Kennedy, T. M., Owens, E., ... & MTA Cooperative Group. (2022). Variable patterns of remission from ADHD in the multimodal treatment study of ADHD. *American Journal of Psychiatry*, 179(2), 142-151. <https://doi.org/10.1176/appi.ajp.2021.21010032>
- Slezak, J. M., & Anderson, K. G. (2011). Effects of acute and chronic methylphenidate on delay discounting. *Pharmacology Biochemistry and Behavior*, 99(4), 545–551.
<https://doi.org/10.1016/j.pbb.2011.05.027>
- Slezak, J. M., & Katz, J. L. (2013). An influence of delayed reinforcement on the effectiveness of psychostimulants to enhance indices of attention under a five-choice serial reaction time procedure in male rats. *Experimental and Clinical Psychopharmacology*, 21(5), 355–362. <https://doi.org/10.1037/a0033726>
- Slezak, J. M., Ricaurte, G. A., Tallarida, R. J., & Katz, J. L. (2014). Methylphenidate and impulsivity: A comparison of effects of methylphenidate enantiomers on delay discounting in rats. *Psychopharmacology*, 231(1), 191–198.
<https://doi.org/10.1007/s00213-013-3220-8>
- Slezak, J.M., Mueller, M., Ricaurte, G.A., & Katz, J.L. (2018). Pharmacokinetic and pharmacodynamic analysis of d-amphetamine in an attention task in rodents.

- Behavioral Pharmacology*, 29, 551-556.
<https://doi.org/10.1097/FBP.0000000000000409>
- Slezak, J.M., Mueller, M., Yuan J., Ricaurte, G.A., Kopajtic T., & Katz, J.L. (unpublished). Chronic treatment with a functionally determined therapeutic dose of d-amphetamine does not produce neurotoxicity in an animal model of attention deficit hyperactivity disorder.
- Somkuwar, S. S., Kantak, K. M., Bardo, M. T., & Dwoskin, L. P. (2016). Adolescent methylphenidate treatment differentially alters adult impulsivity and hyperactivity in the Spontaneously Hypertensive Rat model of ADHD. *Pharmacology Biochemistry and Behavior*, 141, 66-77. <https://doi.org/10.1016/j.pbb.2015.12.002>
- Sonuga-Barke, E. J., Becker, S. P., Bölte, S., Castellanos, F. X., Franke, B., Newcorn, J. H., ... & Simonoff, E. (2023). Annual Research Review: Perspectives on progress in ADHD science—from characterization to cause. *Journal of Child Psychology and Psychiatry*, 64(4), 506-532. <https://doi.org/10.1111/jcpp.13696>
- Thapar, A., Langley, K., Asherson, P., & Gill, M. (2007). Gene–environment interplay in attention-deficit hyperactivity disorder and the importance of a developmental perspective. *The British Journal of Psychiatry*, 190(1), 1-3.
<https://doi.org/10.1192/bjp.bp.106.027003>
- van de Loo-Neus, G. H., Rommelse, N., & Buitelaar, J. K. (2011). To stop or not to stop? How long should medication treatment of attention-deficit hyperactivity disorder be extended?. *European Neuropsychopharmacology*, 21(8), 584-599.
<https://doi.org/10.1016/j.euroneuro.2011.03.008>
- Van Meter, A. R., Sibley, M. H., Vandana, P., Birmaher, B., Fristad, M. A., Horwitz, S., Youngstrom, E. A., Findling, R. L., & Arnold, L. E. (2024). The stability and persistence of symptoms in childhood-onset ADHD. *European Child and Adolescent Psychiatry*, 33(4), 1163–1170. <https://doi.org/10.1007/s00787-023-02235-3>
- Wickens, J. R., Hyland, B. I., Tripp, G., & Wickens, J. (2011). Animal models to guide clinical drug development in ADHD: lost in translation? *British Journal of Pharmacology*, 164(4), 1121–1123. <https://doi.org/10.1111/bph.2011.164.issue-4>
- Willcutt, E. G. (2012). The prevalence of DSM-IV attention-deficit/hyperactivity disorder: a meta-analytic review. *Neurotherapeutics*, 9(3), 490-499.
<https://doi.org/10.1007/s13311-012-0135-8>
- Wilens, T. E. (2004). Attention-deficit/hyperactivity disorder and the substance use disorders: the nature of the relationship, subtypes at risk, and treatment issues. *Psychiatric Clinics*, 27(2), 283-301.
- Willner, P. (1986). Validation criteria for animal models of human mental disorders: learned helplessness as a paradigm case. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, 10(6), 677-690. [https://doi.org/10.1016/0278-5846\(86\)90051-5](https://doi.org/10.1016/0278-5846(86)90051-5)
- Zhang, X., Talpos, J., Berridge, M. S., Apana, S. M., Slikker Jr, W., Wang, C., & Paule, M. G. (2021). MicroPET/CT assessment of neurochemical effects in the brain after long-term methylphenidate treatment in nonhuman primates. *Neurotoxicology and Teratology*, 87, 107017. <https://doi.org/10.1016/j.ntt.2021.107017>