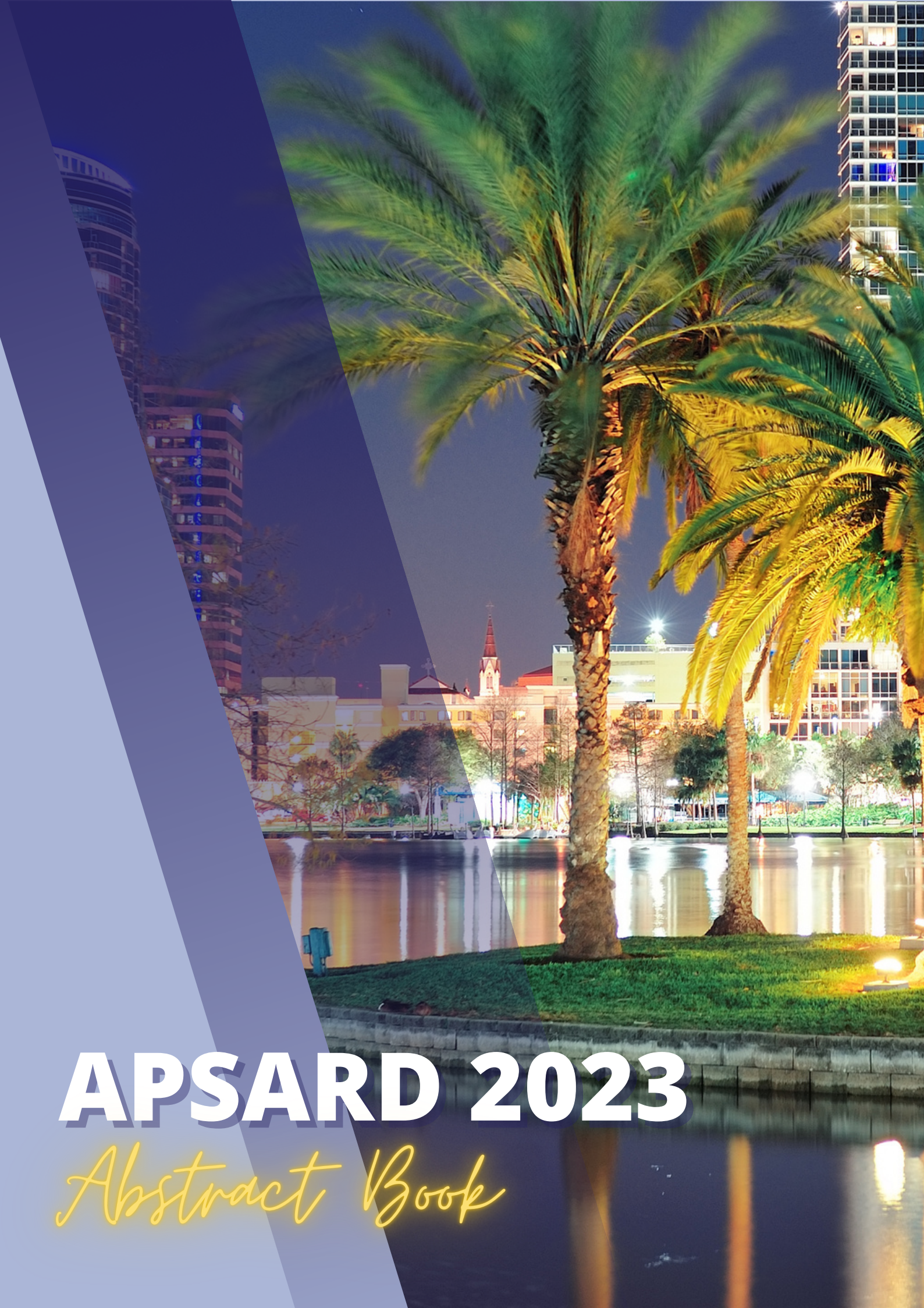

APSARD 2023

Abstract Book

THURSDAY, JANUARY 12, 2023

ADHD 101

12:00 P.M. - 5:00 P.M.

1. ADHD 101: DIAGNOSIS, TREATMENT AND CLINICAL PEARLS

Presenters:

Chair: Ann Childress, Center for Psychiatry and Behavioral Medicine, Inc.
Co-Chair: Jeffrey Newcorn, Mount Sinai Medical Center

David Goodman, Johns Hopkins at Green Spring Station

Gregory Mattingly, Midwest Research Group

Margaret Sibley, University of Washington

Overall Abstract: Although attention-deficit/hyperactivity disorder or ADHD is the most common neurobehavioral disorder in childhood and often persists as children become adolescents and adults, many patients may not be identified or optimally treated after diagnosis. The lack of proper diagnosis and treatment can have severe implications ranging from school failure to increased mortality.

Objectives: At the end of the presentations, participants should be able to diagnose ADHD in patients in various stages of life and have a basic understanding of various ADHD treatments.

Methods: This course will discuss the prevalence of ADHD in preschoolers, older children, adolescents, and adults; the differing symptoms at each of these stages; evidence-based treatment guidelines and how to apply these to clinical practice.

FRIDAY, JANUARY 13, 2023

(OPENING) PLENARY 1: RISING SUICIDE RATES AND ADHD'S PART IN IT

9:30 A.M. - 10:30 A.M.

2. RISING SUICIDE RATES AND ADHD'S PART IN IT

Chair: Joel Nigg, Oregon Health and Science University

2.1 SITUATING ADHD AMONG COMPLEX DETERMINANTS OF VULNERABILITY TO AND RISK FOR SUICIDE: IMPLICATIONS FOR PREVENTION

Theodore Beauchaine, University of Notre Dame

Overall Abstract: ADHD, particularly when combined with comorbid conditions such as depression and conduct disorder, can confer up to a 10-fold increase in risk for suicide according to some studies. It thus is an important player in the suicide risk picture and in considerations regarding prevention. However, ADHD is a multifactorial construct and the elements of ADHD that contribute to suicide risk are unclear. Important possibilities are impulsivity and the associated idea of reward discounting, poor executive functioning or

inattention, and overactivity. However, at a broader level, ADHD is increasingly able to be seen as a disorder of self-regulation, with self-regulation itself having multiple mechanisms involved. In this plenary, Dr. Ted Beauchaine will review the rising youth suicide crisis, and consider in particular the role of impulsivity and self-regulation. The update should place the challenges facing clinicians and policy makers in an updated, informative context.
Learning Objective 1: Participants will recognize the distinction in levels of risk and remediation of risk possible by targeting different component behavioral dimensions of ADHD, self-regulation, and externalizing behavior.
Learning Objective 2: Participants will be able to identify key clinical as well as psychosocial context of rising suicide rates in the United States.

SUPERNUS ACCREDITED INDUSTRY SPONSORED SYMPOSIA

1:00 P.M. – 2:00 P.M.

3. DON'T LET ADHD FLY UNDER THE RADAR: RECOGNITION AND TREATMENT OF ADHD IN THE CONTEXT OF COMORBIDITY

Ann Childress, Center for Psychiatry and Behavioral Medicine, Inc.

3.1. DON'T LET ADHD FLY UNDER THE RADAR: BIOLOGIC SYSTEMS, NEUROTRANSMISSION, AND NETWORKS IN ADHD

Vladimir Maletic, University of South Carolina School of Medicine

3.2 THE TRANSDIAGNOSTIC ROLE OF COGNITIVE DIFFICULTIES

Gregory Mattingly, Midwest Research Group

3.3 DON'T LET ADHD FLY UNDER THE RADAR CASE DISCUSSIONS

Ann Childress, Center for Psychiatry and Behavioral Medicine, Inc.

Overall Abstract: This interactive symposium will be delivered by three expert panelists, Ann Childress, MD, Gregory Mattingly, MD, and Vladimir Maletic, MD. Dr. Childress will introduce the program and introduce the panel. Dr. Mattingly will discuss the bidirectional relationship between GAD and ADHD; transdiagnostic nature of cognitive issues in psychiatry and specifically ADHD; and target populations where these data are most applicable. Dr. Maletic will provide information related to ADHD regarding the genetic overlap with other psychiatric conditions; domains in the brain that may be involved; and how diagnostic criteria overlap. In the third presentation, Dr. Childress will lead a case-based discussion of the application of these data with the panel. This will include audience polling

questions to survey their perspectives. Finally, the panel, with Dr. Childress moderating, will take questions from the audience and provide their perspectives in the answers.

Learning Objective 1: Learners will consider comorbidities when selecting treatment for adult patients with ADHD.

Learning Objective 2: Learners will more accurately diagnose ADHD.

Learning Objective 3: Learners will individualize selection of nonstimulant medication in appropriate patients with ADHD.

Learning Objective 4: Learners will be more confident in their ability to individualize management approaches for patients with ADHD based on specific patient characteristics.

CONCURRENT SYMPOSIA

2:30 P.M. - 4:00 P.M.

4. PRIMARY CARE BASED INTERVENTIONS FOR IMPROVING THE OUTCOMES OF YOUTH WITH ADHD

Raman Baweja, Penn State College of Medicine

4.1 PEDIATRIC ADHD CARE: CHALLENGES AND OPPORTUNITY TO PROMOTE TREATMENT ENGAGEMENT

Raman Baweja, Penn State College of Medicine

4.2 TRAINING PEDIATRICIANS IN STRATEGIES TO PREVENT STIMULANT DIVERSION BY THEIR PATIENTS: RESULTS OF A CLUSTER RCT

Brooke Molina, University of Pittsburgh

4.3 IMPACT OF A FAMILY-CENTRIC PRIMARY CARE BASED ENGAGEMENT INTERVENTION FOR IMPROVING ADHD SERVICE UTILIZATION

James Waxmonsky, Penn State College of Medicine

Overall Abstract: Objective: Attention deficit hyperactivity disorder (ADHD) affects over 5% of children worldwide. Despite well-established treatments, long-term outcomes are suboptimal. A major challenge to achieving optimal long-term outcome is treatment engagement. In both primary care and specialty settings, utilization of medication and counseling services rapidly decline within the first 6 months of treatment. Diversion of CNS stimulant medication is a common concern in the treatment of ADHD that can create barriers to care for providers and patients. This symposium will review the challenges to sustaining care and two primary care-based interventions to address these barriers.
Methods: Presenters will be reviewing current literature on common barriers to sustaining utilization of ADHD treatments especially in the primary care setting. Then, results of two different primary care-based interventions designed to overcome these barriers will be

presented. The first addresses provider concerns over diversion of CNS stimulants and the second addresses parental and adolescent motivation for care.

Results: In the first talk, R. Baweja, MD presents challenges to accessing and sustaining ADHD treatments with a focus on the primary care setting as this is where most ADHD care originates in the United States. B. Molina, PhD presents findings of a 1-hour training in diversion prevention practices for PCPs on managing concerns over stimulant diversion in adolescents with the disorder. J. Waxmonsky, MD discusses findings of 1-2 session family-based engagement intervention designed to measure parental and adolescent motivation and care goals on the utilization of integrated and referred ADHD treatment services.

Conclusions: While evidence-based ADHD treatments exist, there are multiple barriers to initiating and sustaining ADHD care. This symposium will increase participants' understanding about the variety of structural and attitudinal barriers to care and discuss primary care-based interventions to promote treatment engagement while optimizing the safety of available treatments for youth with ADHD.

Learning Objective 1: To understand the barriers to care for children and adolescents with ADHD and their families and review interventions to promote treatment engagement in the primary care.

Learning Objective 2: To demonstrate the benefits of a PCP focused training to reduce stimulant diversion in adolescents with ADHD.

Learning Objective 3: To demonstrate the benefits of a family-based engagement intervention to improve uptake of the array of ADHD treatments.

5. EMERGING DIGITAL SOLUTIONS FOR THE DIAGNOSIS AND TREATMENT OF ADHD

Margaret Weiss, Cambridge Health Alliance

5.1 DIGITAL INTERVENTIONS FOR ADHD AND RELATED DISORDERS

Gregory Mattingly, Midwest Research Group

5.2 PILOTING INSIDE OUT CARE APP TO IMPROVE CLINICAL FLOW, UNDERSTANDING AND ACCESS TO AN ADHD EVALUATION

Mark Stein, University of Washington

5.3 STAYING ON TASK WITH WEARABLE TECHNOLOGY: EVALUATING EFFICACY OF A NEW DIGITAL THERAPY FOR YOUTH WITH ADHD

Margaret Weiss, Cambridge Health Alliance

5.4 MEGATTEAM AND BWELL-EF: VIRTUAL REALITY AND 2D GAME-BASED COGNITIVE INTERVENTIONS TARGETING EXECUTIVE FUNCTIONS

Jennifer Crosbie, Hospital for Sick Children/ University of Toronto

Overall Abstract: Advancements in technology have allowed for novel digital solutions to be explored for improving the evaluation and treatment of ADHD. Ranging from clinician decision support tools to interventions delivered via augmented or virtual reality, videogames,

and wearables, these digital health solutions are showing promise in improving outcomes for patients with ADHD and their families. The speed at which these solutions are entering the market makes it difficult to stay up to date with the increasing number of commercial and prescription products available. Additionally, many of these new tools enter the market with limited evidence to support their use. The goal of this symposium is to showcase innovations being developed using carefully considered clinical research programs that ensure efficacy and safety are empirically supported.
APSARD President-Elect, Dr. Greg Mattingly, will introduce the area of digital therapeutics and discuss digital cognitive training options on the market, including a recently FDA-cleared videogame for improving attention. To address problems with access and improve clinical utility, Dr. Mark Stein will describe the development and preliminary impact of the Inside Out Care app to help parents and providers prepare for an ADHD evaluation at Seattle Children's PEARL Clinic. Dr. Lindsay Ayearst will discuss results of early feasibility and acceptability studies for a wearable non-pharmacologic digital intervention to improve symptoms and functioning in youth with ADHD. Dr. Jennifer Crosbie will present data on the effects of a videogame-based intervention and VR tools designed to improve executive functioning in youth with ADHD.

At the end of the presentations, participants will better understand the opportunity digital advancements offer for the diagnosis and treatment of ADHD and will be able to discuss the early evidence that supports these innovative tools for assessment and non-pharmacological intervention.

Learning Objective 1: Participants will be able to identify potential strengths of emerging digital solutions for the assessment and treatment of ADHD.
Learning Objective 2: Discuss the types of evidence that are needed to support the efficacy and safety of digital assessments and interventions.
Learning Objective 3: Know how to integrate these novel tools into practice to optimize patient outcomes and personalize care.

6. ADHD AND MOOD DISORDER: RECENT STUDIES ON SUICIDE RISK AND TREATMENT OUTCOME

Steven Pliszka, UT Health Science Center at San Antonio

6.1 THE MOOD-ADHD NEXUS AND HOW TO TREAT IT

Argyris Stringaris, University College London

6.2 TREATING ADHD IN THE PATIENT WITH BIPOLAR DISORDER

Manpreet Singh, Stanford University School of Medicine, Center for Sleep Sciences and Medicine

6.3 TRANSLATING DEVELOPMENTAL PSYCHOPATHOLOGY FINDINGS INTO TREATMENT FOR YOUTH WITH COMORBID ADHD AND DEPRESSION

Andrea Chronis-Tuscano, University of Maryland

Overall Abstract: The overlap between mood disorders and ADHD in a patient frequently complicates the treatment of both disorders. This symposium will go beyond the frequent

debates about diagnosis when patients have both attention and mood problems and focus on a discussion of how treatment (both pharmacological and psychosocial) are optimized in the face of this comorbidity. Dr. Singh will review the evidence regarding the medication treatment of ADHD in the patient with bipolar disorder, with careful attention to the risks and benefits of stimulant medication in this population. Dr. Stringaris will examine the issue of comorbid depression and ADHD, discussing a) which should be treated first—depression or ADHD—and for which patients? And b) what is the relative merit of pharmacotherapy vs psychological interventions, particularly where irritability or behavioral disturbances compound the picture. Finally, Dr. Andrea Chronis-Tuscano will discuss a novel psychosocial intervention BEAMS (Behaviorally Enhancing Adolescents' Mood in Schools), which may be efficacious in treating patients with both mood and attention problems.

Learning Objective 1: Understand the role of stimulants in the treatment of ADHD in those with bipolar disorder.

Learning Objective 2: Discuss medication options for patients with ADHD who show clinically significant depression and/or irritability.

Learning Objective 3: Discuss how psychosocial interventions should be tailored in patients with ADHD and depression in order to optimize outcome.

Plenary 2: NEW ADULT ADHD GUIDELINES TOWN HALL

4:15 P.M. – 5:45 P.M.

7. ADULT ADHD GUIDELINES TOWN HALL

Chair: Frances Levin,

Presenters:

Stephen Faraone, SUNY Upstate Medical University

David Goodman, Johns Hopkins at Green Spring Station

Lenard Adler, NYU School of Medicine

Jeffrey Newcorn, Mount Sinai Medical Center

Margaret Sibley, University of Washington

Mary Solanto, Hofstra-Northwell School of Medicine

Frances Levin, Columbia University Irving Medical Center

Overall Abstract: This session will describe APSARD's initiative to define guidelines for the diagnosis and treatment of attention deficit hyperactivity disorder (ADHD) in adults. The first presentation will describe APSARD's quality measures initiative which had the goal of defining practice metrics that could be used to assess quality care for ADHD. We will review the metrics defined and how their application provides insights into the quality of care for 71,310 patients diagnosed with ADHD in a medical record registry. The second presentation will describe APSARD's process for defining the guidelines using methods recommended by

the Institute of Medicine. The presentations will be followed by a panel discussion including questions and discussion from the audience.

Learning Objective 1: Understanding how quality measures and defined and used in clinical practice.

Learning Objective 2: Understand APSARD's process for defining guidelines for the diagnosis and treatment of ADHD.

CONCURRENT SYMPOSIA

6:00 P.M. - 7:30 P.M.

8. UNDER-RECOGNIZED POPULATIONS

Frances Levin, Columbia University Irving Medical Center

8.1 INTERNATIONAL NATURALISTIC MULTI-CENTER TREATMENT STUDY OF ADHD AND SUBSTANCE USE DISORDERS (SUDS): INCAS STUDY

Frances Levin, Columbia University Irving Medical Center

8.2 CHILDHOOD ADHD, IMPULSIVITY, AND ALCOHOL-RELATED IMPAIRMENT AMONG DIVERSE COLLEGE STUDENTS

Mariely Hernandez, Columbia University Irving Medical Center

8.3 UNDER THE RADAR: ADHD IN INCARCERATED POPULATIONS

Maria Velez Pastrana, Universidad Carlos Albizu

Overall Abstract: Many believe that ADHD is over-diagnosed, particularly in academic settings, yet accumulating research suggests that individuals with ADHD continue to be unrecognized and untreated in other contexts and clinical populations. Given the poor outcomes associated with untreated ADHD, high rates of co-morbidity, and the increased risk for substance use problems, this symposium will spotlight research on the identification and treatment of ADHD in frequently overlooked populations: individuals in substance use treatment settings, racial and ethnic minority college students at a public university and incarcerated and criminal justice (ICJ) populations.

First, Dr. Frances Levin will discuss preliminary findings from the International Naturalistic Multi-Center Treatment Study of ADHD and Substance Use Disorders (INCAS), the largest naturalistic study evaluating predictors of treatment outcome among adults with ADHD and SUDs. Next, Dr. Mariely Hernandez will present data from her 2-part study of a racially and ethnically diverse population of mostly commuter college students with elevated childhood ADHD symptoms and at risk for alcohol use problems. The sample is largely undiagnosed and untreated for ADHD. Finally, Dr. Mária Vélez-Pastrana will present findings from two studies: (1) examining the association of childhood ADHD with adverse health outcomes and high-risk behaviors in prison among incarcerated Latinx people; and (2) the association of ADHD with increased psychiatric co-morbidity and SUD severity among incarcerated Latino men.

Together, these three presentations will bring attention to largely overlooked populations of adults with ADHD who, once identified, evince comparable (if not more severe) rates of comorbidity, adverse outcomes and psychosocial impairment seen in the literature. Further, we underscore the need for treatment in these largely underserved populations.

Learning Objective 1: The participant will learn how ADHD screening measures can be used in various settings to help identify individuals with possible ADHD for further evaluation.
Learning Objective 2: The participant will learn about how childhood ADHD influences adult outcomes in diverse college students, carceral and criminal justice populations, and substance use treatment seeking adults.

9. MULTIMODAL PREDICTION OF MOOD DISORDERS AND SUICIDE RISK IN ADHD

Sarah Karalunas, Purdue University

9.1 PROSPECTIVE, MULTI-LEVEL PREDICTION OF DEVELOPING INTERNALIZING DISORDERS IN ADHD

Sarah Karalunas, Purdue University

9.2 IRRITABILITY, IMPULSIVITY, AND WORKING MEMORY PROSPECTIVELY PREDICT SUICIDALITY IN YOUTH WITH AND WITHOUT ADHD

Hannah Morton, Oregon Health and Science University

9.3 A DEVELOPMENTAL PERSPECTIVE ON IMPULSIVITY AND SUICIDE RISK FOR BOYS AND GIRLS WITH ADHD

Theodore Beauchaine, University of Notre Dame

Overall Abstract: At this time youth are navigating a surge of mood-related mental health challenges (Grose, 2022). Nearly half of youth report experiencing symptoms of depression in the past year— up 40% over the past decade, even prior to the pandemic— and suicide remains a leading causes of death for those under age 19 (CDC, 2022). Together, data speak to a mental health crisis among youth, one that is exacerbated among children with other types of neurodevelopmental risk, such as attention-deficit/hyperactivity disorder (ADHD; Kessler et al., 2014). Given the scope of the crisis, identifying the youth most at risk and effectively intervening is a critical yet unrealized goal. Complicating the problem, risk is conveyed via an interacting set of cultural, familial, biological, and child-level characteristics whose relationships are not yet fully understood. The current symposium brings together experts in ADHD, suicide, and child development to consider the multiple factors contributing to risk for mood problems and suicidality among youth with and without ADHD. Each talk highlights the importance of multi-level measurement and interactions among risk factors to capture the complexity of developmental risk. First, using data from a large, longitudinal cohort with 12 years of annual follow-up, Dr. Sarah Karalunas will discuss the interacting cognitive, emotional, and family features contributing to the onset and course of mood-related problems in youth with and without ADHD. Using additional data from this same cohort, Dr. Hannah Morton will discuss prospective predictors of adolescent suicidality, highlighting the unique and combined influences of cognitive and emotional factors. Finally, Dr. Theodore Beauchaine will describe findings from his research demonstrating the importance of sex-specific pathways and emphasizing interactions of biological and environmental vulnerability in determining risk.

Overall, talks will facilitate conversation about new avenues for predicting risk and preventing severe negative outcomes for youth with and without ADHD.
Learning Objective 1: The participant will be able to describe the scope of the youth mental health and how this is related to ADHD.
Learning Objective 2: The participant will be able to list major child, family, and neurobiological risk factors for mood-related problems and suicide.
Learning Objective 3: The participant will be able to discuss how risk features interact and how this knowledge might eventually be applied to preventing negative mood-related outcomes and suicide in youth.

SATURDAY, JANUARY 14, 2023

NOVEN SPONSORED SYMPOSIUM

8:00 A.M. - 9:00 A.M.

10. NOVEN SPONSORED SYMPOSIUM: A TAILORED TREATMENT FOR ADULTS WITH ADHD

Chair & Presenter: Gregory Mattingly, Midwest Research Group

Overall Abstract: Adult ADHD is an underestimated and underdiagnosed disorder that affects multiple domains resulting in functional impairment at home, school, work, and socially.1-3 [1: Song 2021: p2A] [2: Schein 2022: p173A] [3: [Jain 2017: pe1B; pe2A] While more than one-quarter of adults with ADHD aged 17–24 years have symptoms that were diagnosed in childhood and have persisted into adulthood (persistent adult ADHD), nearly three-quarters have adult symptoms not diagnosed until adulthood (symptomatic adult ADHD).1 [1: Song 2021: p6B] The most recent global estimates suggest that 4.6% of adults have persistent adult ADHD and 8.8% have symptomatic adult ADHD.1 [1: Song 2021: p4A,B] Stimulants are first-line therapy for adult ADHD and are available in immediate- and extended-release oral formulations.4 [4: Geffen 2018: p288B] Transdermal drug delivery systems (TDDS) offer a potential alternative to the oral route of drug administration for patients with ADHD.5 [5: Citrome 2019: pe5A] Transdermal formulations have the potential to achieve similar efficacy to oral formulations at lower doses and deliver medication steadily when needed.5 [5: Citrome 2019: pe5A; pe8A] They avoid gastrointestinal first-pass metabolism, improve tolerability, reduce drug-drug interactions, and can be applied and removed to achieve specific timing of onset and offset of the desired effects.5 [5: Citrome 2019: pe5A; pe8A] Transdermal systems can be designed to deliver their drug payload via passive diffusion across the skin or actively by mechanical means.6 [6: Alkilani 2015: p446A] XELSTRYM™ is the first and only non-oral amphetamine treatment for ADHD.7 [7: Xelstrym PI 2022: p1A] It is formulated with a low daily dose of dextroamphetamine, which is delivered via passive diffusion, and its pharmacokinetic profile achieves smooth onset of effect with low peak-to-trough variability.7 [7: Xelstrym PI 2022: p1A] The efficacy and safety of XELSTRYM™ have been demonstrated in clinical trials.8 [8: Cutler 2022: p89A] The XELSTRYM™ patch has a clear, discreet appearance, is available in 4 dosage strengths, and can be applied to 10 different skin sites.7 [7: Xelstrym PI 2022: p1A] This interactive educational session will discuss the incidence, prevalence, and presentation of adult ADHD, the role of TDDS treatment, and the efficacy and safety of XELSTRYM™ for adults with ADHD.

PLENARY 3: WOMEN AND ADHD

9:30 A.M. - 11:00 A.M.

11. HORMONAL TRANSITIONS AND THEIR ROLE IN ADHD SYMPTOMS AMONG WOMEN: MECHANISMS AND TREATMENT

Brooke Molina, University of Pittsburgh

11.1 HAVE I COMPLETELY LOST MY MIND? EXECUTIVE DYSFUNCTION AND MENOPAUSE

Neill Epperson, University of Colorado Anschutz Medical Campus

11.2 ADHD IN WOMEN: HORMONAL EFFECTS ON ADHD AND ITS COGNITIVE AND AFFECTIVE MECHANISMS

Michelle Martel, University of Kentucky

Overall Abstract: Interest in the intersection of female reproductive hormones with ADHD-related symptoms and cognitive functioning has grown along with the understanding that ADHD is prevalent in adulthood for women as well as men. Unfortunately, little is known about hormonal effects on ADHD symptoms and the mechanisms by which these effects occur. This symposium will report data on fluctuations in ADHD symptoms across the menstrual cycle and discussion of the biological basis for emergence of executive function complaints in relation to menopause. Dr. Michelle Martel will describe her team's findings that declines in estradiol just post ovulation and at the end of the menstrual cycle predict increases in ADHD symptoms as well as declines in neuropsychological test performance that align with worsened executive functioning. Dr. Epperson will discuss the impact of the menopausal transition on subjective and objective executive functions for women, as well as some promise in reducing these cognitive ADHD-like difficulties with medications used to treat ADHD. Both presentations will discuss current understanding of the biological mechanisms involved in the connection between hormonal shifts for women and cognitive functioning that aligns with ADHD symptomatology. These presentations will aide appreciation of the role of hormonal events in women and how they may produce/escalate ADHD symptoms in women and may be important to monitor clinically.

Learning Objective 1: Participants will recognize the potential contribution of menstrual cycle-related hormonal shifts on ADHD symptoms.

Learning Objective 2: Participants will recognize the potential contribution of menopausal transitioning on cognitive functions that align with ADHD symptomatology.

CONCURRENT SYMPOSIA

12:30 P.M. - 2:00 P.M.

12. COMPLEMENTARY AND INTEGRATIVE MEDICINE FOR ADHD: NAVIGATING A CONFUSING EVIDENCE BASE

Douglas Russell, University of Washington / Seattle Children's

12.1 SYSTEMATIC REVIEW AND META-ANALYSES: COMPLEMENTARY AND INTEGRATIVE MEDICINE TREATMENTS FOR PEDIATRIC ADHD

Courtney Zulauf-McCurdy, Univeristy of Washington

12.2 "SHOULD WE TRY THIS, DOCTOR?" TALKING TO YOUR PATIENTS ABOUT COMPLEMENTARY AND INTEGRATIVE MEDICINE FOR ADHD

Douglas Russell, University of Washington / Seattle Children's

12.3 HEALTH BEHAVIOR-FOCUSED PARENT TRAINING FOR ADHD: LEAP INTERVENTION ENGAGEMENT STRATEGIES AND OUTCOMES

Erin Schoenfelder Gonzalez, University of Washington School of Medicine

Overall Abstract: Hypothesis/Objective: Complementary and Integrative Medicine (CIMED) has long been part of the treatment landscape for Attention-deficit/Hyperactivity Disorder (ADHD) in childhood, and the evidence has progressed to meta-analyses for several modalities. Yet study heterogeneity and risk of bias makes it difficult to translate the existing science into clinical practice.

Methods: Courtney Zulauf-McCurdy, PhD, will present findings from a new meta-analysis on CIMED interventions for ADHD that employs strict inclusion criteria to emphasize internal over external validity. Douglas Russell, MD will provide a more inclusive overview of common CIMED interventions utilizing a clinical lens. Erin Gonzalez, PhD, will report on successful efforts to incorporate physical exercise and sleep hygiene into ADHD treatment via the Lifestyle Enhancement for ADHD Program (LEAP) study.

Results: from a new meta-analysis employing strict inclusion criteria suggests that only cognitive training shows evidence of basic efficacy. Employing a more inclusive perspective informed by the SECS vs RUDE framework, it is reasonable to recommend omega-3 supplementation, artificial food color restriction, physical exercise, sleep hygiene, and mind-body interventions for certain patients. Incorporating lifestyle modification treatments such as physical exercise and sleep hygiene into an ADHD treatment plan can be both feasible and effective, as evidenced by results from the LEAP trial which demonstrated high engagement with parent management strategies to address health behaviors and successful implementation of wearable mobile health technology.

Conclusions: CIMED treatments for ADHD are widely utilized despite an evidence base that suffers from heterogenous study designs and risk of bias. In a recent meta-analysis with strict inclusion criteria, cognitive training was the only intervention that showed basic efficacy. However, when taking a more inclusive view, other CIMED modalities can be considered safe, easy, cheap and sensible adjuncts to first line interventions. Incorporating CIMED interventions into an ADHD treatment plan can be feasible and effective.

Learning Objective 1: Review results from a new meta-analysis on Complementary and Integrative Medicine (CIMED) for pediatric ADHD.
Learning Objective 2: Provide a framework though which to assess appropriateness of specific CIMED interventions for individual patients when high quality evidence is lacking.
Learning Objective 3: Explore the feasibility and potential benefit of incorporating CIMED into your treatment plans using physical exercise and sleep hygiene as examples.

13. ADHD, BIPOLAR AND SUBSTANCE ABUSE - TRANSLATING DATA FROM CLINICAL TRIALS INTO YOUR PRACTICE

Gregory Mattingly, Midwest Research Group

13.1 THE PREVALENCE AND TREATMENT CONCEPTS OF COMORBID ADHD, BIPOLAR DISORDER, AND SUBSTANCE ABUSE

David Goodman, Johns Hopkins at Green Spring Station

13.2 ADHD, BIPOLAR AND SUBSTANCE ABUSE - TRANSLATING DATA FROM CLINICAL TRIALS INTO YOUR PRACTICE

Paul Glaser, Washington University in St. Louis

13.3 EXAMINING CLINICAL TRIALS DATA TO EXPLORE THE BENEFITS BIPOLAR/ADHD AND TREATMENT WITHIN YOUR PRACTICE

Gregory Mattingly, Midwest Research Group

Overall Abstract: This session will review the clinical presentation and co-occurrence and clinical management of ADHD/bipolar disorder and ADHD/bipolar/substance abuse. Diagnostic tools to differentiate these co-occurrences will be explored along with the evolving nature of these conditions with age.

Research data from clinical trials in which the presenters have been principle investigators will be explored to evaluate the treatment response children, adolescents and adults with bipolar depression and bipolar mania have when concurrently treated or not treated for their ADHD while receiving bipolar treatment. Studies evaluating clinical outcomes for ADHD symptoms, bipolar symptoms and suicidality will be explored.

Medications which have been approved for various stages of bipolar disorder: bipolar mania, bipolar depression and use in children and adolescents will be reviewed along with clinical pearls and cautions with each.

A discussion led by an expert in ADHD substance abuse treatment clinics will then review the management strategies for individuals with ADHD/bipolar/substance abuse. Medications which have been approved for treatment of various substance use disorders will be reviewed along with clinical pearls on how to avoid pitfalls and improve outcomes for such patients.

Learning Objective 1: Explore the co-occurrence of ADHD, bipolar disorder and substance abuse.
Learning Objective 2: Differentiate treatments which have been shown be effective for various stages of bipolar disorder in individuals with ADHD and bipolar disorder.
Learning Objective 3: Better understand how to use treatment strategies to address the complex needs of individuals with ADHD/bipolar/substance abuse.

14. ADHD WORKING MEMORY AND EDUCATION IMPLICATIONS

John Mitchell, Duke University Medical Center

14.1 THE CONTRIBUTION OF WORKING MEMORY (WM) MECHANISMS AND PROCESSES TO ACADEMIC OUTCOMES IN CHILDREN WITH ADHD

Mark Rapport, University of Central Florida

14.2 OPTIMIZING SCHOOL-HOME PSYCHOSOCIAL INTERVENTION FOR YOUTH WITH ADHD: OUTCOMES AND FUTURE DIRECTIONS
Linda Pfiffner, University of California - San Francisco

14.3 WORKING MEMORY AND ACADEMIC UNDERACHIEVEMENT IN CHILDREN WITH ADHD: EXPERIMENTAL AND CLINICAL TRIAL EVIDENCE
Michael Kofler, Florida State University

Overall Abstract: Problematic functioning of higher order cognitive processes, such as working memory, are well documented in children with ADHD and are thought to contribute to academic underachievement. This symposium will address this important topic with a series of talks that include mechanistic experimental studies and clinical trial evidence. Dr. Rapport will present on a series of experimental studies examining higher order cognitive processes involving two attentional networks (i.e., alerting and executive) and working memory in children with ADHD, and demonstrate the central role of these higher order processes to ADHD core clinical features and deficiencies in foundational learning areas (e.g., reading, mathematics). Dr. Kofler will present on a series of experimental studies and clinical trials suggesting a functional, and likely causal, role of working memory deficits in reading, math, and daily classroom functioning difficulties exhibited by children with ADHD. Dr. Pfiffner will present findings from two randomized trials administered in both clinic and school settings that teach skills targeting executive functioning and social problems in students with ADHD, while simultaneously training teachers and parents to support skill acquisition and utilization across settings. Overall, these presentations will address the link between higher order cognitive processes in ADHD with educational outcomes and inform clinicians about the latest empirical evidence to guide clinical care.
Learning Objective 1: To learn about working memory's role in learning among children with ADHD.
Learning Objective 2: To describe interventions that target higher order cognitive processes and academic impact on children with ADHD.

IRONSHORE INDUSTRY SPONSORED SYMPOSIA

2:30 P.M. – 3:30 P.M.

15. CLINICAL CONUNDRUM: APPROPRIATE USE OF STIMULANT MEDICATIONS IN ADULTS WITH ADHD

Chair: Oren Mason, Attention MD

Presenters:

Oren Mason, Attention MD

Gregory Mattingly, Midwest Research Group

Overall Abstract: Recent media headlines underscore a growing concern about the appropriate use of prescription stimulant medications in the treatment of ADHD, particularly

within the adult patient population. In this symposium, we will explore the evolution of stimulant formulations for ADHD, the current climate of stimulant prescribing, and how patient and clinician perspectives influence treatment preferences and practices. Key within this discussion is the recognition of intrinsic diversity within the stimulant class both in terms of duration (ie, short-acting vs long-acting) and formulation components (ie, immediate-release alone, immediate-release/extended-release combination, or extended-release alone) and how these features affect treatment decisions.

Learning Objective 1: Analyze the differences between preparations of long-acting stimulants.

Learning Objective 2: Choose stimulant medications for adult ADHD patients to optimize symptomatic and functional improvements.

PLENARY 4: ADHD OVERLAP WITH MOOD AND OTHER DISORDERS--NEUROBIOLOGY, DEVELOPMENTAL SEQUENCE, ETC.

4:00 P.M. - 5:30 P.M.

16. ADVANCES IN THE GENETICS OF ADHD

Jeffrey Newcorn, Mount Sinai Medical Center

16.1 INSIGHTS INTO ADHD AND RELATED DISORDERS FROM "BIG" NEUROIMAGING DATA

Philip Shaw, National Human Genome Research Institute

16.2 ADVANCES IN THE GENETICS OF ADHD: IMPLICATIONS FOR CLINICIANS

Stephen Faraone, SUNY Upstate Medical University

Overall Abstract: This plenary session will provide an update on recent advances in the neurobiology of ADHD, with implications for understanding the clinical phenomenon as well as for treatment. The two presenters, Dr. Philip Shaw and Dr. Stephen Faraone, are two of the most important and prolific researchers in their respective fields. Their presentations will examine the results of studies that use “big data” approaches with neuroimaging (Dr. Shaw) and genetics (Dr. Faraone) to further our understanding of the disorder. The “big data” approach is important in each of these areas, because of the heterogeneity of effects, which are often small - suggesting that meaningful effects can only be elucidated in studies using large samples. The two presentations will illustrate ways in which ADHD lies on a continuum with normality, while also being unique. They will also consider distinctiveness of ADHD from other neuropsychiatric disorders, as well as shared underlying neurobiology and genetic markers. The discussion will focus on implications for understanding the clinical presentation of ADHD and ways to optimize treatment.

Learning Objective 1: Attendees will learn about the most recent issues in genetics of ADHD.

Learning Objective 2: Attendees will learn about recent findings in ADHD neuroimaging.

Learning Objective 3: Attendees will learn how to apply findings from "big data" studies to clinical questions.

CONCURRENT SYMPOSIA

5:30 P.M. - 7:00 P.M.

17. TRANSDIAGNOSTIC TREATMENTS IN ADHD AND CO-OCCURRING DISORDERS– HOW TO NAVIGATE AND EVALUATE ALTERNATIVE TREATMENT OPTIONS

Martin Katzman, START Clinic for Mood and Anxiety Disorders

17.1 EFFECTS OF YOGA ON THE BRAIN AND ITS POTENTIAL THERAPEUTIC BENEFIT IN ADHD WITH COMORBID ANXIETY AND DEPRESSION

Tia Sternat, START Clinic for Mood and Anxiety Disorders

17.2 PSYCHEDELIC POTENTIAL IN THE TREATMENT OF ADHD AND COMORBIDITIES

Irvin Epstein, START Clinic for Mood and Anxiety

17.3 GLUTAMATE AND THE GLUTAMATE-DOPAMINE INTERACTION: IMPLICATIONS FOR THE TREATMENT OF ADHD AND COMORBIDITIES

Martin Katzman, START Clinic for Mood and Anxiety Disorders

Overall Abstract: Attention-Deficit Hyperactivity Disorder (ADHD) is a highly comorbid psychiatric illness. Rates of anxiety disorders in ADHD range from 23% to 53% (1, 2). Additionally, up to 34% of individuals with treatment-resistance depression may also have ADHD (3). The high rates of comorbidity highlight ADHD as a risk factor for other psychiatric illnesses, while also suggesting that these comorbidities may be in part due to neurobiological similarities with other psychiatric disorders (1, 4). Thus, in both highly comorbid, or treatment-resistant mood and anxiety cases with ADHD, an altered etiology may cause a differential response to treatment. Therefore, it is important to consider the underlying processes that may impact prognosis and outcome. As such, this presentation will discuss supplementary techniques and alternative treatments that improve treatment outcomes in those that do not respond to, or only partially respond to first line medications.

The presentation will highlight mindfulness and yoga as a supplementary strategy, outlining how yoga can improve cognitive deficits and increase concentration in both ADHD-only, as well as comorbid populations (5). Secondly, the presenters will discuss the rise of novel therapeutics as a transdiagnostic approach to treating ADHD and related comorbidities. Emphasis will be placed on glutamate and glutamate-dopamine interactions, followed by pharmacological considerations (6).

The recent rise of interest in psychedelics as a novel therapeutic option in both patient populations as well as the scientific community also warrants discussion. Individuals with ADHD are at higher risk for substance abuse and may attempt to self-medicate symptoms when naïve to treatment or when treatment-resistant (7). As such, the presenters will provide an update on the literature regarding the potential role of psychedelics in psychiatry, while also discussing how to manage microdosing seen in patient populations. Finally, the audience will be invited to discuss the potential, and appropriateness of novel treatment modalities.

Learning Objective 1: Consider the role of supplementary treatments to standard of care in ADHD.

Learning Objective 2: Evaluate the appropriateness of alternative therapeutic options in treatment-resistant cases.
Learning Objective 3: Recognize transdiagnostic points of intervention in comorbid psychiatric illness.

18. RACIAL AND ETHNIC INEQUITIES IN ADHD DIAGNOSIS AND TREATMENT

Brooke Molina, University of Pittsburgh

18.1 RACIAL AND ETHNIC DISPARITIES IN CHILDHOOD ADHD TREATMENT: AN EXEMPLAR OF INEQUITIES IN YOUTH MENTAL HEALTH SERVICES

Benjamin Cook, Harvard Medical School

18.2 A COMMUNITY STUDY OF RISK TO YOUTH FOR ADHD AND OTHER DISORDERS INTEGRATING SYMPTOMS AND FUNCTIONAL IMPAIRMENT

Margaret Weiss, Cambridge Health Alliance

18.3 PREVALENCE AND FACTORS ASSOCIATED WITH ADHD AMONG RACIALIZED COMMUNITIES IN A MINORITY CONTEXT: A META-ANALYSIS

Jude Mary Cénat, University of Ottawa

Overall Abstract: Some data suggest that diagnosis, treatment, and access to mental healthcare for youth with racial and/or ethnic minority identities are lower than for majority youth. However, inconsistencies exist across studies, and increased focus on ADHD is needed to appreciate where prevention and intervention efforts should be targeted. In three presentations, data will be provided on the prevalence, treatment, and its access for youth as a function of race and ethnicity. In the first presentation, Weiss and colleagues conducted a mental health screening study in schools to describe the prevalence of mental health problems experienced by youth as a function of minoritized race and ethnicity. Amongst 100 participants, a high proportion of students, 17%, screened positive for moderate or severe ADHD. Black versus White students were not more likely to experience a diagnosis, but they were more likely to experience impairment, suggesting that minoritized individuals may be in greater need of treatment. In the second presentation, in a meta-analytic review of studies including prevalence rates of ADHD amongst youth living in countries with Black minority populations, Cenat compared the prevalence of ADHD across racial and ethnic groups. Black and White children experienced marginally higher prevalence than Asian children (15.9% and 16.6% among Black and White youth, respectively, versus 10.1% and 12.4% among Latino and Asian youth). The findings highlight the importance of considering cultural context and appropriateness of assessment tools for children living in communities where youth identifying as Black are minoritized. In the third presentation, Cook describes a nationally representative dataset from the Medical Expenditure Panel Survey 2011-2019. Black, Hispanic, and Asian children with ADHD were less likely to receive treatment. Importantly, inequities in access to treatment was found to account for these differences. Findings suggest that increasing outreach and provider supply for youth from populations minoritized because of their race or ethnicity may help reduce gaps in care. Taken together, these results will provide audience participants with increased understanding of racial and ethnic differences in ADHD prevalence among children and factors that affect their likelihood of accessing treatment.

Learning Objective 1: Demonstrate knowledge of ADHD prevalence by race and ethnicity for youth.
Learning Objective 2: Participants will be able to describe factors affecting differential ADHD prevalence and treatment access for youth in racial and ethnic minority groups.

19. NERVE- AND NEURO- STIMULATION TREATMENTS FOR ADHD

Stephen Faraone, SUNY Upstate Medical University

19.1 DOUBLE-BLIND SHAM-CONTROLLED STUDY OF TRIGEMINAL NERVE STIMULATION (TNS) FOR ADHD, WITH OPEN-LABEL EXTENSION

James McGough, David Geffen School of Medicine at UCLA

19.2 TRIGEMINAL NERVE STIMULATION FOR ADHD: NEURAL MECHANISMS AND BIOMARKERS OF TREATMENT RESPONSE

Sandra Loo, University of California, Los Angeles, UCLA School of Medicine

19.3 IS TDCS AN EFFICACIOUS OPTION FOR TREATING INATTENTION IN ADULTS WITH ADHD?

Douglas Leffa, University of Pittsburgh Medical Center

Overall Abstract: While there are a large number of pharmacological and non-pharmacological treatment options available for ADHD, long-term adherence remains a significant challenge. Much effort is being invested in identifying imaging parameters that may help with diagnosis, and genetic factors that modulate treatment response. Here precision medicine is the ideal.
In parallel, there has been a growing interest in nerve- and neuro- stimulation Treatments for ADHD.

These technologies hold promise. In this symposium, we review two such interventions, one which has received approval from the FDA, Trigeminal Nerve Stimulation and one which is in development, Transcranial direct current stimulation.

Learning Objective 1: Understand the efficacy and safety of nerve- and neuro- stimulation Treatments for ADHD.
Learning Objective 2: Understand the efficacy and safety of Trigeminal Nerve Stimulation therapy for the treatment of ADHD.
Learning Objective 3: Understand the efficacy and safety of Transcranial direct current stimulation therapy for the treatment of ADHD.

SUNDAY, JANUARY 15, 2023

CLOSING PLENARY: COVID AND MENTAL HEALTH

8:30 A.M. - 10:00 A.M.

20. COVID AND MENTAL HEALTH
Margaret Weiss, Cambridge Health Alliance

20.1 TWO YEARS OF COVID: OR, WHAT HAPPENED WHEN THE WORLD SHOOK?
Iris Manor, Geha MHC

Overall Abstract: Dr. Manor's plenary provides us with the pause and reflection we need to digest the impact of the pandemic on our social world, our patients with ADHD and ourselves as clinicians. At this, our first post COVID in person meeting, this plenary helps us look back and look forward to gain perspective on the changes we have seen for the better and for the worse.
Learning Objective 1: To document the historical impact of COVID on our social world.
Learning Objective 2: To examine the ways in which patients with ADHD were more or less impacted by the pandemic.
Learning Objective 3: To identify how we, as clinicians, have processed these changes using the five stages of grief.

CONCURRENT SYMPOSIA

10:15 A.M. - 11:45 A.M.

21. LEVERAGING MOBILE TECHNOLOGY TO ENHANCE INTERVENTIONS FOR ADHD
Traci Kennedy, University of Pittsburgh

21.1 OBJECTIVE MEASUREMENT OF HYPERACTIVITY WITH MOBILE SENSING, MACHINE LEARNING, AND CONTEXT MODELING
Riku Arakawa, Carnegie Mellon University, Human-Computer Interaction Institute

21.2 A DHEALTH TOOL FOR IMPROVING PARENT ADHERENCE TO BEHAVIORAL PARENT TRAINING FOR ADHD
Linda Pfiffner, University of California - San Francisco

21.3 DEVELOPMENT OF A DIGITAL TOOL TO PROMOTE ADOLESCENTS' ENGAGEMENT IN ORGANIZATIONAL SKILLS INTERVENTIONS
Melissa Dvorsky, Children's National

21.4 SYMPTOM TRACKING FOR ADHD IN REAL TIME (START SMART): A PROMISING MHEALTH INTERVENTION FOR YOUNG ADULTS WITH ADHD
Traci Kennedy, University of Pittsburgh

Overall Abstract: Although numerous efficacious interventions for ADHD exist (Sibley et al., 2014), several barriers limit their real-world effectiveness (Corkum et al., 2015). A key

challenge is the need to transport ADHD interventions from the clinic into the real-world moments and contexts in which support is needed. Individuals with ADHD often possess skills to manage inattention, hyperactivity, and impulsivity, but they struggle to execute them when they are needed (Barkley, 2015). Traditional office-based ADHD treatment is removed from these everyday moments and situations, and therefore may not optimize outcomes. Mobile technology (e.g., smartphone apps and smartwatches) can provide a promising bridge to facilitate in-the-moment application of skills acquired in the clinic. Digital tools also offer scalability, affordability, and increased treatment access, furthering their appeal for ADHD (Bush et al., 2019).

This symposium highlights exciting findings from four cutting edge pilot studies that leverage digital technology to make treatment for ADHD more in-the-moment and in-context across populations: children, adolescents, young adults, and parents. Shaaban and colleagues will describe their innovative smartwatch app designed to objectively measure hyperactivity in school-age children in context using machine learning. Complementing this work, Pfiffner and colleagues are developing a digital tool to make parent training for ADHD more in-the-moment by increasing skill use between sessions. Similarly, Dvorsky and colleagues will present a novel smartphone app that augments behavioral treatment for adolescents with ADHD by strengthening treatment engagement and daily skill use. Lastly, Kennedy and colleagues' smartphone-based intervention for young adults with ADHD aims to increase symptom awareness via self-monitoring and personalized feedback throughout the day. These formative pilot studies all employ user-centered design and offer clear, immediate clinical relevance for practitioners seeking to make support for ADHD more in-the-moment. Together, these novel findings indicate that digital tools hold promise for enhancing real-world ADHD treatment across the lifespan.

Learning Objective 1: Participants will identify three benefits of mobile technology for enhancing the efficacy of treatment for ADHD.

Learning Objective 2: Participants will be able to describe several novel digital tools for augmenting treatment for ADHD.

22. ADHD AND INFLAMMATION THROUGH THE LENS OF SOMATIC COMORBIDITIES

Margaret Weiss, Cambridge Health Alliance

22.1 INFLAMMATION, COGNITION, AND ATTENTION DEFICIT HYPERACTIVITY DISORDER

Beth Krone, Icahn School of Medicine at Mount Sinai

22.2 CLINICAL AND SOCIO-DEMOGRAPHIC VARIABLES ASSOCIATED WITH LONG COVID SYNDROME IN YOUTH: A POPULATION-BASED STUDY

Iris Manor, Geha MHC

22.3 ADHD, SLEEP AND INFLAMMATION

J.J. Sandra Kooij, PsyQ, Program Adult ADHD, The Hague

22.4 DOES MAST CELL INFLAMMATION LINK HYPERMOBILITY AND ADHD?

James Kustow, United Kingdom Adult ADHD Network

22.5 SHOULD MAST CELLS BE CONSIDERED THERAPEUTIC TARGETS IN THE TREATMENT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER?

Anne Maitland, Icahn School of Medicine at Mount Sinai

Overall Abstract: This symposium brings together expertise on the role of inflammation in mediating the relationship between ADHD and various somatic conditions, including Long COVID Syndrome, Ehlers Danlos Syndrome, and Sleep Disorders. Beth Krone will introduce a current. review of the psycho-neuro-immuno-endocrinological model of cognition that may contribute to the coaggregation of somatic illness and ADHD. Iris Manor presents a recent research study which finds a statistically significant association between Long Covid Syndrome and ADHD, urticaria and allergic rhinitis suggesting inflammatory processes may be the common mechanism. James Kustow provides a review of the bilateral association between ADHD and Ehlers Danlos Syndrome (Hypermobility Syndrome) suggesting that multi-system inflammation could be causing the neuropsychiatric manifestations we understand to be ADHD in these patients, with a focus on mast cell activation as a mediator or this association. Sandra Kooij notes that sleep disorders are over-represented in ADHD and that sleep loss leads to inflammation, which might explain the increased risk for autoimmune processes, allergies, and COVID. Her literature review indicates that sleep loss impacts the immune system through neuroendocrine, microbiomal, and autonomic pathways that connect the immune system with inflammatory peptides. Anne Maitland, a Fellow of the American College of Allergy, Asthma and Immunology will provide a discussion of the relationship between mast cell disease and ADHD as mediated by Super Somatic Syndrome.
Learning Objective 1: Comprehend the role of the immune system in mediating an association between ADHD and various somatic conditions, and new data on the impact of mast cell activation syndrome on neuropsychiatric conditions.
Learning Objective 2: Summarize new data on the association between ADHD and Long COVID Syndrome, urticaria and rhinitis.
Learning Objective 3: Recognize the association between sleep disorders and immune dysfunction.
Learning Objective 4: Review mast cell activation syndrome as a mediator of the relationship between ADHD and Hypermobility Syndrome and between ADHD and the immune system.

OTSUKA INDUSTRY SPONSORED SYMPOSIA

12:45 P.M. – 1:45 P.M.

23. IS THERE A NEW CLASS FOR TREATING ADHD?

Chair: Ann Childress, Center for Psychiatry and Behavioral Medicine, Inc.

23.1 ADULT ADHD PHARMACOLOGIC TREATMENT LANDSCAPE – FOCUS ON CENTANAFADINE

Jeffrey Newcorn, Mount Sinai Medical Center

23.2 UNMET NEEDS IN ADHD

Ann Childress, Center for Psychiatry and Behavioral Medicine, Inc.

23.3. NEUROPSYCHOPHARMACOLOGY IN ADHD

Stephen Faraone, SUNY Upstate Medical University

Overall Abstract: Of children with attention-deficit/hyperactivity disorder (ADHD), >90% display persistent symptoms into adulthood (1). Symptoms and economic burden of ADHD together with treatment-emergent adverse events (TEAEs), such as sleep disorders and emotional impulsivity, significantly reduce patients' quality of life (QoL) (2,3). Current pharmacotherapies include stimulants (methylphenidate and amphetamines) and non-stimulants (atomoxetine, viloxazine, guanfacine, and clonidine) (4,5). Although stimulants are used as first-line treatments, they are potentially liable to abuse (4). These factors highlight the need for effective novel therapies that alleviate symptoms, improve QoL, and minimize abuse liability.

Centanafadine is a triple dopaminergic–noradrenergic–serotonergic reuptake inhibitor that may address ADHD symptoms via a similar mechanism to stimulants, improve symptoms of anxiety and depression, and mitigate TEAEs such as sleep disturbances and loss of appetite (6). Furthermore, centanafadine may have less abuse potential than stimulants commonly prescribed for ADHD (6).

Centanafadine has demonstrated efficacy and tolerability in adults with ADHD across the clinical development program. Phase 2 trials showed that centanafadine treatment was associated with improvements in ADHD symptoms and was generally well tolerated (6). No cases of drug abuse, dependence, diversion, or euphoria were reported (6).

Two Phase 3 randomized, double-blind, placebo-controlled trials evaluated efficacy and safety of 200 or 400 mg/d centanafadine in adults with ADHD (7). Primary and secondary endpoints included change from baseline at Day 42 in the Adult ADHD Investigator Symptom Rating Scale (AISRS) and Clinical Global Impression–Severity of Illness Scale (CGI-S), respectively (7). Both doses of centanafadine led to significant improvements in AISRS and CGI-S scores (7). AISRS total scores were maintained to the end of treatment and effect sizes versus placebo were -0.28 for 200 mg/d and -0.24 for 400 mg/d in study 1, and -0.37 for 200 mg/d and -0.40 for 400 mg/d in study 2 (7). Centanafadine was generally well tolerated with a low incidence of TEAEs; of which, the majority were considered to be mild or moderate. The most common TEAEs were headache and decreased appetite (7). No cases of TEAEs indicated misuse (7). Longer term tolerability of centanafadine has been demonstrated in a 52-week, open-label extension trial (8).

Learning Objective 1: Describe the disease state of ADHD, gain awareness on the impact of ADHD and its existing pharmacotherapy on patients' health-related quality of life, and identify the unmet needs in ADHD to understand the rationale for needing novel therapies.

Learning Objective 2: Recognize how centanafadine differs from current pharmacological treatments for ADHD and the benefits that centanafadine treatment may deliver.

Learning Objective 3: Value the promising results on efficacy and tolerability of centanafadine, as demonstrated in pivotal clinical trials.

SATURDAY, JANUARY 14, 2023

LUNCH & POSTER SESSION
11:00 A.M. - 12:30 P.M.

*Denotes Presenting Author

S1. RESPONSIVENESS OF AN OBJECTIVE MEASURE OF COGNITION TO TREATMENT WITH ENDEAVORRX®, A NOVEL DIGITAL THERAPEUTIC IN PEDIATRIC ATTENTION-DEFICIT HYPERACTIVITY DISORDER

Elena Canadas*[1], Katie Mercaldi[1], Deborah Farlow[1], Vandana Menon[1], Ann Childress[2]

[1]Akili Interactive, [2]Center for Psychiatry and Behavioral Medicine, Inc.

Hypothesis/Objective: Attention-deficit/hyperactivity disorder (ADHD) is a common neurodevelopmental disorder. Traditional treatments for ADHD include medication and psychological interventions. EndeavorRx® is a digital therapeutic indicated to treat inattention in children aged 8-12, with ADHD with demonstrated attention issues. In a randomized controlled trial, EndeavorRx demonstrated significant improvement in an objective measure of attention. Tools to better assess the responsiveness of new treatment modalities could enhance caregivers' and healthcare providers' ability to design and adapt treatment plans. This study evaluated a validated computerized assessment (Gradual-Onset Continuous Performance Test (GradCPT) by TestMyBrain) as a measure of attention.

Methods: Open-label, single-center study in children aged 8-12, with inattentive/combined ADHD. Participants were instructed to play EndeavorRx, at home, for approximately 25 minutes/day, 5-days/week, for 4-weeks. GradCPT was administered on-site, pre-and post-intervention. Responsiveness to GradCPT was evaluated by mean change in scores after 28 days of treatment.

Results: 41 participants completed GradCPT. Mean age was 10 (SD=1.4) years old, 29% female, 21% non-white/Hispanic/Latino ethnicity, and predominantly combined type ADHD (79%).

Participants completed 89% of the intended treatment course. Statistical improvements in GradCPT were observed in reaction time (Cohen's $d=-1.2$, $p<0.0001$) and reaction time variability ($d=-0.4$,$p=0.02$), but not d' or accuracy scores.

Conclusions: The GradCPT is a short, validated, computerized cognitive assessment that can be administered remotely via a secure web platform. This study provides initial evidence of the responsiveness of several metrics within GradCPT to a 4-week intervention with EndeavorRx. Remote cognitive assessments may have the potential to help inform caregivers and healthcare providers' decision-making in a routine clinical setting.

S2. PHARMACOGENOMICS IN THE TREATMENT OF ADHD WITH METHYLPHENIDATE IN CHILDREN

Philip Melchert[1], Jeffrey Newcorn[2], Mark Stein[3], Tanya Froehlich[4], Beth Krone[5], Taimour Langaee[1], Qingchen Zhang[1], John Markowitz*[1]

[1]University of Florida, College of Pharmacy, [2]Mount Sinai Medical Center, [3]University of Washington, [4]Cincinnati Children's Hospital Medical Center, [5]Icahn School of Medicine at Mount Sinai

Hypothesis/Objective: Methylphenidate (MPH) is considered a first-line medication for ADHD and been in clinical use over 50 years. A number of reports document variability in MPH treatment response and tolerability which may be associated with pharmacokinetic (PK) and pharmacodynamic (PD) genetic polymorphisms. However, there remains a gap in understanding the role of these genes as potential biomarkers of MPH treatment response. Carboxylesterase 1 (CES1) is the major enzyme catalyzing MPH clearance. Genetic variants of CES1 may represent a major reason for MPH therapeutic outcome variability. Additionally, other PK and PD genes may also influence drug response. The aim of this study is to identify key associations between genetic variants and the PK/PD of MPH in ADHD pediatric patients.

Methods: Approximately 500 DNA samples from patients from three clinical sites were used to genotype the polymorphisms in 14 candidate genes associated with PK/PD of MPH by TaqMan and Pyrosequencing genotyping methods.

Results: Preliminary results show that none of the assessed variants deviated from the Hardy Weinberg Equilibrium (HWE). The CES1 gene SNP (rs71647871) that was shown to play an important role in the metabolism of MPH has a minor allele frequency (MAF) of <2% which is consistent with previous published reports.

Conclusions: Based on the preliminary results and analysis only results for SNP SNAP25 rs3746544 deviated from HWE. Moreover, the MAF was consistent with those reported on publicly available genomic databases. Ultimately, we will cross reference each specific SNP and archived PD data of a diverse patient population. These results will aid in individualizing treatment.

S3. CARDIOMETABOLIC COMORBIDITIES IN ADHD: A RETROSPECTIVE COHORT STUDY FROM ELECTRONIC MEDICAL RECORDS

Yanli Zhang-James*[1], Stephen Faraone[1]

[1]SUNY Upstate Medical University

Hypothesis/Objective: Attention-deficit/hyperactivity disorder (ADHD) is a common neurodevelopmental disorder frequently co-occurring with other psychiatric and medical conditions. Although psychiatric comorbidity among patients with ADHD has been very well documented, few large systematic studies had assessed the link between ADHD and somatic comorbidities. In this study, we utilized electronic health records (EHR) from the TriNetX Research Network to investigate the cardiometabolic outcomes in patients with ADHD.

Methods: We identified 1.2 million patients with diagnoses of ADHD and a cohort of 3.3 million non-ADHD patients who were matched with the ADHD patients by demographic characteristics (age, sex, race, and ethnicity) and marital status (1:3 matching ratio). We then used the Cox proportional-hazards model to compare the risks of acquiring diagnoses of various cardiometabolic disorders later in life in the ADHD vs. non-ADHD cohort.

Results: We found that overall patients with ADHD have increased risks of getting diagnosed with cardiometabolic disorders with adjusted hazard ratios ranging from 1.1 ~ 1.8 (all p<.0001).

Conclusions: ADHD is associated with increased risk of cardiometabolic comorbidities later in life.

S4. PREDICTION OF INTERNALIZING AND EXTERNALIZING SYMPTOMS IN LATE CHILDHOOD FROM ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS IN EARLY CHILDHOOD

Agnieszka Mlodnicka*[1], Maxwell A. Mansolf[2], Aruna Chandran[3], Izzuddin M. Aris[4], Shaikh Ahmad[5], Allison Shapiro[6], Bibiana Restrepo[7], Rebecca Schmidt[7], Irva Hertz-Picciotto[7], Deborah Bennett[7], T. Michael O'Shea[8], Leslie Leve[9], Julie B. Schweitzer[10]

[1]Private Practice, [2]Northwestern University Feinberg School of Medicine, [3]Bloomberg School of Public Health, Johns Hopkins University, [4] Harvard Pilgrim Health Care Institute and Harvard Medical School, [5] University of California, San Francisco, [6]University of Colorado Anschutz Medical Campus, [7]University of California, Davis, [8] University of North Carolina, Chapel Hill, [9]Prevention Science Institute, University of Oregon, [10]MIND Institute, University of California Davis School of Medicine

Hypothesis/Objective: Attention-deficit/hyperactivity disorder (ADHD) is a prevalent neurodevelopmental disorder with high comorbidity for internalizing and externalizing disorders. Limited analyses based on national samples have assessed whether early ADHD symptoms predict later internalizing and externalizing symptoms in youth. Even less is known about the potential influence of sex and pubertal timing on psychiatric symptoms within the context of early ADHD symptoms, which in turn can impact the diagnosis of ADHD and internalizing and externalizing symptoms.
Methods: The current study was conducted with a subset of data (n=1808) collected from the Environmental influences on Child Health Outcomes (ECHO) Program, a large national cohort funded by the National Institutes of Health (NIH). Analyses were conducted with exposure data from early childhood (mean age=4.9 years) using parent report of ADHD symptoms to predict rates of internalizing and externalizing symptoms from late childhood to adolescence (mean age=12.5 years). Age at peak height velocity (APHV) was used as a proxy to assess pubertal timing.
Results: The results demonstrated that early childhood ADHD symptoms predicted later symptoms in multiple areas of psychopathology (i.e., anxiety, depression, aggressive behavior, conduct problems, oppositional defiant disorder, rule-breaking behavior) with similar outcomes for both males and females. Earlier APHV was associated with an increase in aggressive behavior from late childhood to adolescence for females only. However, APHV did not appear to moderate internalizing or externalizing symptoms.
Conclusions: Therefore, when working with peripubertal youths, providers should be vigilant in identifying, diagnosing, and potentially treating internalizing and externalizing symptoms in individuals who had an early diagnosis of ADHD.

S5. COMPONENTS OF COGNITIVE CONTROL ARE DIFFERENTIALLY IMPAIRED IN GIRLS AND BOYS WITH ADHD

Beatrice Ojuri[1], Alyssa DeRonda[1], Micah Plotkin[1], Stewart Mostofsky[2], Keri Rosch*[2]

[1]Kennedy Krieger Institute, [2]Kennedy Krieger Institute/Johns Hopkins

Hypothesis/Objective: There is growing evidence of distinct neurobehavioral profiles among girls and boys with attention-deficit/hyperactivity disorder (ADHD) that relate to differences in clinical presentation and functional impairments. The current study expanded on our published findings of ADHD-related sex differences in go/no-go (GNG) task performance of

ADHD boys and girls relative to typically developing (TD) controls and includes additional tasks measuring cognitive control.
Methods: Participants (ages 8-12) with ADHD (n=201, 58 girls) and TD controls (n=99, 37 girls) completed three computerized neurocognitive tasks: a GNG, flanker, and stop signal task (SST). We examined effects of diagnosis within sex on measures of response inhibition (commission error rate [ComRate] and SST stop signal delay [SSD]), response speed, and response variability.
Results: As compared to their same-sex TD peers, for GNG, ADHD boys made more commission errors (p=.008, d=0.41) and showed higher response variability (p=<.001, d=0.57), whereas ADHD girls showed higher response variability (p=.029, d=0.46) but did not make more commission errors (p=.938, d=0.02).
For SST, ADHD girls responded slower (p=.060, d=0.40) but displayed intact response inhibition (ComRate: p=.515, d=0.14; SSD: p=.445, d=0.16), whereas ADHD boys displayed poorer response inhibition (ComRate: p=.010, d=0.40; SSD: p=.002, d=0.47) but responded as quickly (p=.167, d=0.21).

For Flanker task, children with ADHD showed a greater congruency effect on errors than did TD children (Diagnosis*Congruency: p=.008) regardless of sex (ADHD girls, d=1.18 vs. TD girls, d=0.83; ADHD boys, d=1.19 vs. TD boys, d=0.94).

Conclusions: ADHD girls and boys show distinct task-dependent patterns of impairment in cognitive control, particularly for GNG and SST tasks.

S6. GENETIC CHARACTERIZATION OF THE COMPAS COHORT: A POLYGENIC RISK SCORE ANALYSIS IN ADULT ADHD

Aylin Mehren*[1], Friederike S. David[1], Carlo Maj[2], Börge Schmidt[3], Markus M. Nöthen[1], Axel Krug[1], Andreas Forstner[1], Alexandra Philipsen[1]

[1]University Hospital Bonn, [2]University of Marburg, [3]University of Duisburg-Essen

Hypothesis/Objective: To perform a genetic characterization via polygenic risk score (PRS) analyses of a well-characterized sample of adult patients with ADHD.
Methods: For 330 cases of the German Comparison of Methylphenidate and Psychotherapy in Adult ADHD Study (COMPAS), genome-wide genotyping with the Illumina GSA and standard data quality control using Plink was conducted. Joint imputation with a population-based control cohort (subset of Heinz Nixdorf Recall Study, n=4140) was performed using Eagle and Minimac based on the 1000 Genomes reference panel. PRS were calculated for multiple psychiatric phenotypes and behavioral traits and tested for association with ADHD case-control status using PRSice-2.
Results: We found a positive association of the PRS for ADHD with case-control status, which did not remain significant after correction for multiple testing. Significant positive associations were observed for PRS of major psychiatric disorders (affective disorders, schizophrenia, Tourette), and the PCG cross-disorder PRS. PRS for educational years, intelligence and cognitive performance were higher in patients compared to controls. Based on those findings and above-average IQ (mean=113) in our patient sample, adjusted PRS for ADHD conditioned on educational attainment were estimated. The conditioned PRS explained more variance in our sample compared to the pure ADHD PRS and was significantly positively associated with case-control status, indicating a confounding effect of education on ADHD PRS association.
Conclusions: Our sample represents a highly educated ADHD sample, which is possibly caused by recruitment bias via University hospitals. Nevertheless, this study provides further

insights into the genetic background of adult ADHD, which is still underrepresented in the majority of studies.

S7. SOCIAL FUNCTIONING IN CHILDREN WITH COGNITIVE DISENGAGEMENT SYNDROME (SLUGGISH COGNITIVE TEMPO): FINDINGS FROM TWO STUDIES USING CATEGORICAL AND DIMENSIONAL APPROACHES

Joseph Fredrick*[1], Stephen Becker[1]

[1]Cincinnati Children's Hospital Medical Center

Hypothesis/Objective: Cognitive disengagement syndrome (CDS, previously referred to as sluggish cognitive tempo) includes excessive mind-wandering, mental fogginess, and slowed behaviors that are distinct from ADHD inattention (ADHD-I). Although evidence shows CDS symptoms to be uniquely associated with social withdrawal, the majority of studies have relied on ad-hoc CDS ratings, single domains of social withdrawal, and studies not sampling children based on CDS elevations. The current study used parent/teacher ratings of CDS, social functioning, and real-life recess observations to examine the social functioning of school-aged children recruited based on categorical or dimensional elevations in CDS.
Methods: Study 1 included 207 school-aged children (37% girls; 88% White) with half elevated in CDS. Study 2 included 265 school-aged children (58% male; 75%) recruited with the full dimension of CDS. Study 1 included teacher-ratings of CDS elevations, whereas Study 2 used dimensional ratings of parent/teacher reported CDS symptoms. Across studies, parents and teachers completed various ratings of social functioning.
Results: Controlling for key demographic factors and ADHD-I, children in the high CDS group or elevated in CDS had greater teacher-reported withdrawal, shyness, and preference for solitude compared to ADHD-I. Whereas ADHD-I symptoms were associated with social skills problems, children high in CDS were rated as less assertive and were observed to spend more time alone and disengaged in social interaction during recess.
Conclusions: Children elevated in CDS are more withdrawn and disengaged from the peer group, including in real-life interactions with peers during recess, which is an important area of assessment and intervention for clinicians, researchers, and educators.

S8. TEMPERAMENT CORRELATES OF COGNITIVE DISENGAGEMENT SYNDROME (SLUGGISH COGNITIVE TEMPO) AND ADHD INATTENTIVE SYMPTOMS IN SCHOOL-AGED CHILDREN

Joseph Fredrick*[1], Stephen Becker[1]

[1]Cincinnati Children's Hospital Medical Center

Hypothesis/Objective: Cognitive disengagement syndrome (CDS, previously referred to as sluggish cognitive tempo) is a set of symptoms, including excessive mind-wandering, mental fogginess, and slowed behaviors, that are distinct from ADHD inattention (ADHD-I) and associated with internalizing symptoms, social withdrawal, and academic difficulties. Despite evidence supporting CDS as a separate construct, no study has clearly identified temperament correlates of CDS that may be shared or unique from ADHD-I. The current study tested behavioral activation (BAS), behavioral inhibition (BIS), and fight/flight/freeze systems (FFFS) in relation to CDS and ADHD-I symptoms in two samples of school-aged children recruited based on categorical or dimensional elevations in CDS.

Methods: Study 1 included 207 school-aged children (ages 7-11; 37% girls; 88% White) with approximately half elevated in CDS. Study 2 included 263 school-aged children (ages 8-12; 58% male; 75%) recruited with the full dimension of CDS represented. Across both studies, parents completed ratings of temperament, whereas both teachers and parents reported on CDS and ADHD-I symptoms.
Results: Controlling for key demographic characteristics (e.g., sex, income, and medication status), greater FFFS-fear/shyness was most consistently related to parent and teacher ratings of CDS symptoms, whereas BAS-impulsivity/fun-seeking was associated with ratings of ADHD-IN. Further, lower BAS-drive was uniquely associated with teacher ratings of CDS but unrelated to ADHD-I.
Conclusions: Findings are the most comprehensive to date of temperamental correlates associated with CDS and ADHD-I symptoms across two independent samples of children. Identifying temperament correlates and predictors of CDS may help researchers and clinicians understand the heterogeneity of ADHD presentations, comorbidities, and impairments.

S9. ADHD DURING PERIMENOPAUSE AND MENOPAUSE

Jeanette Wasserstein*[1], Mary Solanto[2], Gerry Stefanatos[3]

[1]Mt. Sinai Medical College, [2]Hofstra-Northwell School of Medicine, [3]Temple University

Hypothesis/Objective: There is little data regarding the impact of the hormonal changes of menopause on ADHD and associated symptoms. This study examines this issue.
Methods: Information was obtained from a reader survey sponsored by ADDitude Magazine. Responses were received from 2,945 women who had experienced perimenopause or menopause, and of whom 85% had been diagnosed with ADHD. Respondents ranged in age from 46 to 94 (mean=53). Respondents were asked to indicate their age at diagnosis and the impact of each of 11 different symptoms or associated problems of ADHD at each of 5-time intervals: 0-9 years, 10-19 years, 20-39 years, 40-59 years and 60+years.
Results: The largest group of respondents (43%) were diagnosed between ages 41 and 50. Sixty-one percent reported that ADHD had the greatest impact on their daily lives between 40 and 59 years of age. The reported prevalence of inattention, disorganization, poor time-management, emotional dysregulation, procrastination, impulsivity, and poor memory/brain fog increased over the life span. The subset of symptoms/problems that increased most markedly during the critical menopausal/perimenopausal window included: Inattention, poor memory/'brain fog', disorganization, procrastination, and a general sense of 'overwhelm'.
Conclusions: Hormonal change during the climacteric is associated with worsening cognitive complaints. Our results suggest that the increased complaints can lead to a first diagnosis of ADHD during this period, as well as a worsening of symptoms in those previously diagnosed. Moreover, this hormonal shift may underlie the diagnosis of ADHD in a subset of the individuals currently characterized as having "late-onset" ADHD.

S10. QELBREE® (VILOXAZINE ER) EFFICACY IN ADULTS WITH ADHD INATTENTIVE OR COMBINED PRESENTATIONS

Andrew Cutler*[1], Ann Childress[2], Andrea Formella[3], Christian Teter[3], Jami Earnest[3], Peibing Qin[3], Joseph Hull[3], Azmi Nasser[3], Jonathan Rubin[3]

[1]Neuroscience Education Institute, [2]Center for Psychiatry and Behavioral Medicine, Inc., [3]Supernus Pharmaceuticals, Inc.

Hypothesis/Objective: Stimulant medications are widely believed to be equally effective for different ADHD presentations (predominantly inattentive [PI], predominantly hyperactive/impulsive [PHI] or combined [C]); however, questions remain regarding nonstimulant efficacy, particularly for inattentive symptoms. Still, few studies specifically evaluate efficacy by ADHD presentation. Here, the efficacy of the novel nonstimulant, viloxazine extended-release (Qelbree®; VLX-ER), to reduce ADHD symptoms was evaluated by baseline ADHD presentation in adults.
Methods: Using phase 3 study data, the change from baseline (CFB) in Adult ADHD Investigator Symptom Rating Scale (AISRS) Total score at Week 6 (EOS) was analyzed using MMRM, by ADHD presentation (assigned using a proxy of 5 or more items rated ≥2 on either or both AISRS subscales).
Results: Of 354 subjects, 269 were categorized ADHD-C, 79 ADHD-PI, 5 ADHD-PHI*, and 1 uncategorized* (*not analyzed due to small sample). The CFB AISRS Total score at Week 6 (EOS) showed greater reduction (improvement) in VLX-ER group compared to placebo in both subgroups; the difference [LS mean ± SE, p-value; ES] was statistically significant in the ADHD-C subgroup (-3.8±1.54, p=0.015; EF=0.32), though not the ADHD-PI subgroup (−3.9±2.21, p=0.0813; ES=0.43). Improvement in ADHD symptoms over time in both subgroups showed a similar pattern. VLX-ER separated from placebo as early as Week 3 in ADHD-C and Week 1 in ADHD-PI.
Conclusions: Overall, subjects who met ADHD-C criteria showed a significant improvement at endpoint. However, most likely due to small sample size, subjects who met ADHD- PI criteria showed significant early improvement in clinical symptoms that was not statistically significant at endpoint.

S11. SERDEXMETHYLPHENIDATE/DEXMETHYLPHENIDATE FOR CHILDREN WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER: REDUCTION IN DISORDER SEVERITY FROM A LABORATORY CLASSROOM STUDY

Ann C. Childress[1], Scott Kollins[2], Andrew C. Barrett[3], Rene Braeckman[3], Sven Guenther[3], Travis C. Mickle[3], Charles Oh*[4], Matthew Brams[5]

[1]Center for Psychiatry and Behavioral Medicine, [2]Duke University School of Medicine, [3]KemPharm, Inc., [4]Corium, LLC, [5]Bayou City Research

Hypothesis/Objective: To evaluate changes in attention-deficit hyperactivity disorder (ADHD) severity in children (aged 6-12 years) posttreatment with serdexmethylphenidate/dexmethylphenidate (SDX/d-MPH) in a laboratory classroom setting.
Methods: During a 3-week open-label, dose-optimization phase, subjects (N=150) were titrated to a final SDX/d-MPH dose of 26.1/5.2 mg, 39.2/7.8 mg, or 52.3/10.4 mg based on tolerability and best individual response. During the subsequent 7-day double-blinded treatment period, subjects received once-daily SDX/d-MPH or placebo. The primary efficacy end point was mean change from baseline in Swanson, Kotkin, Agler, M-Flynn, and Pelham-Combined (SKAMP-C) scores averaged over the laboratory classroom day (0.5-13 hours postdose). The Conners 3rd Edition-Parent (C3P) score, an exploratory end point, assessed weekly changes in ADHD severity during the dose-optimization and treatment phases.
Results: During the treatment phase, SKAMP-C scores improved significantly with SDX/d-MPH vs placebo (least-squares mean treatment difference [95% CI], −5.4 [−7.1, −3.7]; P<.001), indicating fewer symptoms with SDX/d-MPH versus placebo. Changes in ADHD severity, based on mean C3P scores, were significantly improved from baseline at each visit during the dose-optimization phase for each subscale (P<.001). During the treatment phase,

C3P scores significantly improved from baseline for SDX/d-MPH versus placebo in the subscales of inattention (−11.2 [−15.7, −6.7]), hyperactivity/impulsivity (−9.9 [−14.4, −5.3]), executive functioning (−9.0 [−13.3, −4.7]), and learning problems (−5.4 [−8.9, −1.8]; all P≤.003). No significant difference was seen in the subscales of defiance/aggression and peer relations. SDX/d-MPH had no concerning safety signals.
Conclusions: SDX/d-MPH demonstrated significant reductions in ADHD severity in children based on the C3P scores.

S12. SERDEXMETHYLPHENIDATE/DEXMETHYLPHENIDATE (SDX/D-MPH) OPTIMIZED DOSE LEVELS AND EFFECTS ON ADHD-RATING SCALE-5 (ADHD-RS-5) RESPONSE RATES IN CHILDREN WITH ADHD

Andrew J. Cutler[1], Meg Corliss[2], Andrew C. Barrett[3], Charles Oh*[4]

[1]SUNY Upstate Medical University and Neuroscience Education Institute, [2]Corium, Inc., [3]KemPharm, Inc., [4]Corium, LLC

Hypothesis/Objective: To evaluate treatment responder rate (RR) using the ADHD-RS-5 score based on optimized dose level of SDX/d-MPH.
Methods: During a 21-day dose optimization phase of a classroom study, 155 patients initiated treatment with 39.2/7.8 mg SDX/d-MPH in the first week and then were titrated to an optimum dose (1/3 available doses); 5 patients were downtitrated to 26.1/5.2 mg, 76 were uptitrated to 52.3/10.4 mg, and 69 remained at the 39.2/7.8-mg optimized dose level during the following 2 weeks. Responder threshold values were 30% and 50% based on the percent change from baseline (day [D] 0) to D7, D14, and D21 in the ADHD-RS-5 score.
Results: Of the 5 patients optimized at 26.1/5.2 mg, ≥80% of patients across all days had ≥50% RR. Of the 69 patients optimized at 39.2/7.8 mg, 72.5% had ≥50% RR at D7, and 81.2% had ≥50% RR by D21. Of 76 patients optimized to 52.3/10.4 mg, 22.4% had ≥50% RR at D7 (initiated at 39.2/7.8 mg), and 72.4% had ≥50% RR by D21. Patients having a suboptimal response to methylphenidate to the initial 39.2/7.8-mg dose may need titration to a higher dose or require longer treatment duration to achieve ≥50% RR.
Conclusions: Responders are evident after the first week of SDX/d-MPH treatment at the 26.1/5.2-mg and 39.2/7.8-mg final dose levels, with small increases in the proportion of responders thereafter. The 52.3/10.4-mg final dose level continued to increase in the proportion of responders after titration to the 52.3/10.4-mg final dose level.

S13. UNDERLYING MECHANISMS OF ADHD PREDICT ANXIETY SEVERITY: A PRELIMINARY ANALYSIS

Sachinthya Lokuge*[1], Kathryn Fotinos[1], Sherinne Clarissa[1], Coltan Bains[1], Tia Sternat[1], Irvin Epstein[1], Martin Katzman[1]

[1]START Clinic for Mood and Anxiety Disorders

Hypothesis/Objective: Studies indicate up to 25% of individuals with ADHD also suffer from generalized anxiety disorder (GAD). Moreover, executive dysfunction and reward-related deficits may affect anxiety severity. Additionally, intolerance of uncertainty perpetuates symptoms of anxiety. Thus, the aim of this study was to investigate the underlying mechanisms of ADHD and GAD.
Methods: Adult psychiatric outpatients (n = 39) were assessed for ADHD and GAD using the MINI Plus ADHD module 5.0.0. GAD severity was assessed by the GAD-7. Additionally,

executive dysfunction was assessed by the Barkley Deficits in Executive Functioning Scale (BDEFS), reward-processing deficits were measured by the Snaith-Hamilton Pleasure Scale (SHAPS), and intolerance of uncertainty was measured by the Intolerance of Uncertainty Scale (IUS).
Results: A multiple linear regression was conducted to determine whether the BDEFS, SHAPS and IUS predicted GAD-7 severity in individuals with ADHD and GAD. The overall model was significant, $R2 = 0.585$, $F(3, 35) = 16.439$, $p < 0.001$. All three variables added statistical significance to the prediction. The independent variables did not show multicollinearity (BDEFS, Tolerance = 0.755, VIF = 1.135; SHAPS, Tolerance = 0.836, VIF = 1.196; IUS, Tolerance = 0.881, VIF = 1.135).
Conclusions: This preliminary analysis supports the idea that symptoms of ADHD can lead to anxiety. In particular, these findings suggest reward processing deficits, executive dysfunction and intolerance of uncertainty independently contribute up to 58.5% of the variance seen in anxiety severity. These results highlight the importance of identifying mechanisms that connect psychopathology and aims to promote targeted treatment options.

S14. RESILIENCY AND EGO-UNDERCONTROL AS PREDICTORS OF ADHD SEVERITY OVER TIME

Katharine Selah*[1], Joel Nigg[1]

[1]Oregon Health and Sciences University

Hypothesis/Objective: Comparatively little research on ADHD has looked at its intersection with developing personality/temperament trait features in childhood and adolescence despite extensive theoretical reason to do so. Ego resiliency and ego control are two venerable traits related to a range of child outcomes. This study aims to clarify the role of temperament and gender variation in predicting ADHD symptoms over time.
Methods: Participants were 849 children (ADHD N=509, 61% boys, ages 7-11) and a primary caregiver participating in a case-control design. Parents completed the California Child Q-Sort across three time points over six years, which were scored by similarity to conceptual prototype profiles created by Block and Block. Cross-lagged panel models examined relationships between these temperament descriptors and ADHD symptoms across time.
Results: Time 1 Ego-Undercontrol and Ego-Resilience were weakly correlated with Time 1 ADHD (Undercontrol: r=.20, p<.001, 95% CI: .14, .26; Resilience: r=-.24, p<.001, 95% CI: -.3, -.17). In cross-lagged models, Time 1 ADHD predicted more Undercontrol at Time 2. Time 1 Undercontrol predicted more Time 2 ADHD severity in girls but not in boys, but as the children aged into adolescence, Time 2 Undercontrol predicted higher Time 3 ADHD in boys but not girls. For ego-resiliency, no differences were seen by gender of the child.
Conclusions: Variability in temperament influences ADHD symptom severity differentially for girls versus boys with ADHD.

S15. ARE THERE HETEROGENEOUS TEMPERAMENT TRAITS IN ADHD BEYOND MIDDLE CHILDHOOD? AN EXPLORATORY STUDY WITH EMERGING ADOLESCENTS

Michael Kozlowski*[1], Hannah Morton[1], Joel Nigg[1], Sarah Karalunas[2]

[1]Oregon Health and Sciences University, [2]Purdue University

Hypothesis/Objective: Child temperament, or the dispositional traits that underlie personality development, has been promising in the understanding of behaviors associated with ADHD (e.g., Martel et al., 2022; Nigg, 2022) with two or three distinct regulatory profiles emerging consistently in ADHD populations in the critical developmental period of early to middle childhood when most ADHD is identified (Goh et al., 2020; Karalunas et al., 2014, 2019). A key question has been the way this picture may change with development into early adolescence.
Methods: Parents (75% mothers) of participants diagnosed with ADHD (n = 225) completed the Early Adolescent Temperament Questionnaire-Parent Revised Form (Ellis, 2002). Structural validity for a seven-factor structure was found in an independent discovery dataset with diverse demographics features but identical recruitment and identification procedures. Community detection methods were used to differentiate temperament profiles and compared them with classifications obtained via latent profile analysis.
Results: Results suggested a two-class assignment within the ADHD sample reflecting (1) a high irritability, risk-taking profile and (2) a withdrawn, depressed profile with moderately good agreement across LCA and community detection methods (k = 0.58). Follow-up analyses revealed class assignments obtained in both methods had similar variation with more impairment in executive functioning, peer relationships, and inattentive symptoms in Class 2 ($p = 0.01$).
Conclusions: We provide replicated support for temperament trait differentiation in in ADHD adolescence. Rather than positive and negative valence groups, at this age differentiation was based on types of negative emotion dysregulation.

S16. ASSOCIATION BETWEEN ADHD AND COVID-19 INFECTION AND CLINICAL OUTCOMES: A RETROSPECTIVE COHORT STUDY FROM ELECTRONIC MEDICAL RECORDS

Kathleen Heslin*[1], Aminat Haruna*[2], Regina George[3], Shiyu Chen[4], Ishak Nobel[5], Kathryn Anderson[6], Stephen Faraone[1], Yanli Zhang-James[1]

[1]SUNY Upstate Medical University, [2]University of Pittsburgh Medical Center, [3]University of Alabama, Tuscaloosa, [4]VA Boston-Harvard South Shore, Brockton, [5]Northwell Health at Staten Island University Hospital, [6]Institute for Global Health and Translational Sciences, SUNY Upstate Medical University; SUNY Upstate Medical University

Hypothesis/Objective: Though psychiatric illnesses have been associated with increased COVID-19 infection risk, limited information exists about the relationship between ADHD and COVID-19. This study examines the effect of ADHD diagnosis and treatment on COVID-19 infection rate and severity.
Methods: Using the TriNetX COVID-19 Research Network and a sample of 1,124,774 patients diagnosed with COVID-19 before the start of US COVID-19 vaccinations, we examined the impact of ADHD diagnosis and recent pharmacologic treatment (within two months prior to COVID-19 diagnosis) on COVID-19 infection rates and short-term (60-day) severe outcomes (death, hospitalization, and mechanical ventilation). We also examined the effect of ADHD diagnosis on COVID-19 risk across five race categories and between male/female groups. Cohorts were balanced for demographic, medical, psychiatric, and social factors using propensity score-matching.
Results: ADHD patients had greater risk of COVID-19 (risk ratio (RR) 1.11, 95% CI [1.09, 1.12]). Increased risk was higher in females than males, and highest among Asian and Black patients. Within 60 days after COVID-19 diagnosis, ADHD patients had lower rates of

hospitalization (RR 0.91, 95% CI [0.86, 0.96]) and mechanical ventilation (RR 0.69, 95% CI [0.58, 0.83]), and a nonsignificant reduced death rate (RR 0.65, 95% CI [0.42, 1.02]). Patients who recently received ADHD medication (within two months prior to COVID-19 diagnosis) had higher rates of COVID-19 (RR 1.13; 95% CI [1.10, 1.15]), with non-significant findings for hospitalization, mechanical ventilation, and death rates.
Conclusions: ADHD is associated with increased risk for COVID-19 but reduced risk of severe outcomes. ADHD medications modestly impacted COVID-19 risk.

S17. MODELING PSYCHOLOGICAL NETWORKS OF DISTRACTION IN ATTENTION DEFICIT HYPERACTIVITY DISORDER

Jahla Osborne*[1], Han Zhang[1], Madison Carlson[1], Priti Shah[1], John Jonides[1]

[1]University of Michigan

Hypothesis/Objective: Adults with Attention-Deficit/Hyperactivity Disorder (ADHD) are easily distractible, yet few studies have investigated whether these distractions manifest from external or internal sources (e.g., mind-wandering, repetitive negative thinking). The current study aims to discover if ADHD symptoms are differentially associated with one source of distraction.
Methods: Participants completed questionnaires that measure external distraction (EXT), repetitive negative thinking (RNT), spontaneous mind-wandering (MW), and ADHD symptomatology. Our data included two non-clinical samples (N=651, N=569) and one clinically diagnosed sample (ADHD=30, Control=30). We conducted network analyses to estimate psychological networks that showcase the relationships between individual ADHD symptoms (18) and sources of distraction in our non-clinical samples. Our clinically diagnosed sample was too small for network analysis. Therefore, we used dominance analysis to indicate the relative importance of internal and external distraction predictors of ADHD symptoms.
Results: Estimated psychological networks suggest heterogeneity among ADHD symptoms and their association with distraction. For example, "difficulty sustaining attention" showcases a stronger association with MW compared to its associations with RNT or EXT. Conversely, "misplacing things" did not indicate significant differences in association with distraction. Dominance analysis in our clinically diagnosed sample offers converging evidence with respect to which sources of distraction are relatively more important in explaining the symptom of interest.
Conclusions: These findings highlight the importance of better understanding distractibility in relation to ADHD symptoms. These findings should ignite future research to examine the relationship between ADHD subtypes and sources of distraction in larger clinically diagnosed samples to inform solutions for combating distraction in real world settings.

S18. ASSOCIATION BETWEEN CUMULATIVE PSYCHOSOCIAL ADVERSITY IN THE FAMILY AND NEURODEVELOPMENTAL DISORDERS

Aleksandra Kanina*[1], Mina Rosenquist[1], Henrik Larsson[2], Arvid Sjölander[1], Agnieszka Butwicka[1], Miriam Martini[1], Mark Taylor[1], Paul Lichtenstein[1], Brian D'Onofrio[3]

[1]Karolinska Institute, [2]Karolinska Institute and Örebro University, [3]Indiana University

Hypothesis/Objective: The aim of this study is to investigate the association between cumulative psychosocial adversity during the first year of life in the family and

neurodevelopmental disorders in offspring, using family-based study designs to control for unmeasured confounding.
Methods: We used a population-based cohort of 1,877,901 individuals born in Sweden between 1990 and 2009. Participants were followed from the age of 3. We created a cumulative index based on 7 psychosocial adversity factors. We used Cox regression to estimate the hazard ratios (HRs) relating ADHD and autism to cumulative psychosocial adversity. To address familial confounding, the analyses were repeated in groups of relatives of different kinship: siblings and half-siblings, cousins, and half cousins.
Results: In the general population, the cumulative psychosocial adversity index was associated with ADHD in a dose-response relationship, with adjusted HRs for ADHD ranging from 1.55 to 2.61. No clear dose-response relation was observed for autism. HRs of ADHD and autism decreased with increasing kinship between the relatives. Separate analysis with stratification by sex showed that girls had a higher risk of getting diagnosed with autism but not ADHD compared to boys.
Conclusions: Our findings show that exposure to cumulative psychosocial adversity in the family during the first year of life is associated with a greater risk of developing ADHD in general population and attenuated towards 0 with increasing relatedness due to unmeasured familial confounding. We advocate for using family-based designs to account for unmeasured familial confounding when conducting studies on etiology of ADHD.

S19. PREDICTING ADHD AT 8-21 YEARS FROM EARLY CHILDHOOD DEVELOPMENT IN CHILDREN WITH AUTISM, INTELLECTUAL DISABILITY AND OTHER NEURODEVELOPMENTAL CONCERNS

Julie Schweitzer*[1], Yuny Ren[1], Agnieszka Mlodnicka[1], Crystal Herrera[1], Irva Hertz-Picciotto[1]

[1]University of California, Davis

Hypothesis/Objective: While it is very difficult to diagnose ADHD in children younger than five years old, factors in preschool children can associate with ADHD diagnoses at later ages. Using data from the ReCHARGE study, this analysis seeks to understand factors predictive of children's ADHD diagnoses at ages 8-21 years, using their early childhood neurodevelopmental characteristics (ages 2-5 years).
Methods: This analysis included 645 participants with: a diagnosis of ADHD or not based on the Mini International Neuropsychiatric Interview (MINI) or Diagnostic Interview Schedule for Children (DISC); one of four clinically confirmed outcomes from the CHARGE study at 2-5 years: Autism Spectrum Disorder (ASD) Developmental Delay (DD), other early concerns (OEC); or typical development (TD); and mental age of at least six years. Predictor variables included demographics, clinically confirmed diagnosis, and family background, all obtained by the CHARGE study.
Results: In multivariate logistic regression models, child sex and early childhood developmental outcome were strong predictors, as was parental ADHD. Sociodemographic characteristics tended to have weaker associations. In our predictive model, the CHARGE diagnosis group is the main predictor of ADHD, and the highest risk for an ADHD diagnosis at later ages was ASD, followed successively by OEC, DD, and TD (lowest risk), with prevalence of, respectively, 51.0%, 41.4%, 35.7%, and 20.6%. Subdividing ADHD by the combined or hyperactive, and inattentive presentation, results were similar to the overall analysis: the CHARGE diagnostic group strongly predicted both subtypes.
Conclusions: These results emphasize the potential for early interventions that might alter the trajectory of ADHD, in early childhood.

S20. A MACHINE LEARNING APPROACH TO PREDICTING HYPERACTIVE/IMPULSIVE SYMPTOMS USING IRRITABILITY

Julie Schweitzer*[1], Saeedeh Komijani[1], Dipak Ghosal[1], Prerona Mukherjee[1]

[1]University of California, Davis

Hypothesis/Objective: There is limited existing research investigating the relation between irritability and hyperactive/impulsive symptoms in adolescents with attention-deficit/hyperactivity disorder (ADHD).
Methods: We applied statistical and machine learning (ML) models to investigate if irritability can predict hyperactive/impulsive symptoms in a longitudinal analysis. We used the DSM Hyperactive/Impulsive subscale of the Conners' Parent Rating Scale and irritability symptoms. We explored the relation between irritability, impulsivity, and other ADHD symptoms to determine if irritability could predict impulsivity and other psychiatric symptoms. We applied Gaussian Graphical Modeling (GGM) with EBIC GLASSO using the q-graph package in R and observed high correlations between symptoms of irritability and impulsivity. We analyzed data for 80 participants (48 males) aged 12-16 years for two consecutive years, T1 and T2. Analysis of raw data showed that higher irritability scores are correlated with a higher hyperactive/impulsive score. We applied a regression model using age, gender, and irritability along with hyperactive/impulsive raw scores at T1, as predictor variables, to predict hyperactive/impulsive scores at T2.
Results: Preliminary results showed irritability predicted higher scores of hyperactivity/impulsivity in later teenage years, particularly in females (1 unit increase in irritability predicts 0.88 increase in hyperactivity/impulsivity in later years).
Conclusions: Irritability needs to be considered as a predictor of impulsivity. Ongoing work includes consolidating self-report rating scale to increase the sample size and exploring gender differences, family history, and socio-economic status (SES) on predictability of symptoms. Additionally, we will apply random forest regression to investigate interpretability of model for prediction of hyperactive/impulsive symptoms in later years.

S21. THE EFFECTS OF NOTETAKING MODALITY AND SYMPTOMS OF ADHD ON LECTURE LEARNING

Gabrielle Shimko*[1], Karin James[1]

[1]Indiana University

Hypothesis/Objective: College students with attention/deficit-hyperactivity disorder (ADHD) exhibit difficulty with taking notes during lectures. There is evidence suggesting that college students with ADHD have slower handwriting speed than their peers, which may disrupt the note-taking process and lead to less learning. Thus, increasing transcription speed by typing notes may lead to gains in encoding during lecture notetaking in individuals with higher ADHD symptoms. This study assessed how fine motor dexterity (FMD), transcription speed, sustained attention, and ADHD symptoms affected learning during the lecture notetaking process within different notetaking modalities. It was hypothesized that students with higher ADHD symptoms would exhibit increased recall of lecture material if they took typed notes, while individuals with lower ADHD symptoms would exhibit increased recall of lecture material if they took handwritten notes.
Methods: N = 136 college students with self-reported ADHD symptoms watched a 15-minute lecture and took handwritten notes, typed notes, or no notes. Participants took a quiz later in the session to assess recall of lecture material.

Results: Results indicated that individuals with higher ADHD symptoms recalled significantly more lecture material in the typed note condition than in the no note condition. Individuals with worse FMD recalled significantly less from the lecture in the handwritten note condition than in the no note condition. Worse sustained attention significantly predicted less lecture recall. Finally, slower handwriting speed significantly predicted higher ADHD symptoms.
Conclusions: These results illustrate an important role of FMD during note taking and provide evidence that difficulties in handwriting are associated with ADHD symptoms in college.

S22. THE MALADAPTIVE COPING CYCLE: A INTEGRATED MODEL FOR UNDERSTANDING ACADEMIC AND SOCIAL FAILURE IN CHILDREN WITH ADHD

Martha Wise*[1], Barbara Wise[2], Sarah Jones[2]

[1]Ohio University, [2]Indiana Wesleyan University

Hypothesis/Objective: Drawing from a wide variety of fields, this poster seeks to collect in a diagram the research describing how core ADHD symptomology spirals out into deficits in the academic, social, and coping skills of individuals with ADHD in a classroom setting.
Methods: Using equivalent keywords from roughly 100 journal articles from various related professions, including Neurobiology, Education, Nursing, Sociology, Business etc., investigators synthesized previously unconnected research to build a conceptual model that presented an overview of the cascading consequences of core ADHD symptomatology on functionality within the classroom.
Results: Core ADHD symptoms impair both critical coping, academic, and social competencies. These deficits form a feedback loop that drastically reduces the performance of students with ADHD in the classroom. Maladaptive behavior patterns emerge from these continuous struggles and outside pressures which exasperate these maladaptations into a negative spiral that erodes performance and resiliency.
Conclusions: While the research surrounding ADHD indicates that student's maladaptations form a functionality-deteriorating cycle, there are points of intervention that may allow practitioners to make these synergistic elements work FOR the student instead of AGAINST the student. Given the severity of the negative outcomes associated with ADHD, such as reduced graduation rate, increased incarceration likelihood, high smoking risk etc., it is vital that practitioners from different disciplines collaborate to understand the relationships between these barriers-to-functionality to better identify intervention points. The role of negative intrusive thoughts, stereotype threat, self-efficacy, reward pathways, frustration threshold, sympathetic system activation, motivational attributes, depression and anxiety comorbidities, emotional clarity, help-seeking behaviors, and more are explored.

S23. PRACTICE CONSIDERATIONS FOR CHILDREN DIAGNOSED WITH ADHD AND DYSGRAPHIA

Lisa Anderson*[1]

[1]Family Wellness Center

Hypothesis/Objective: Children diagnosed with ADHD often have handwriting difficulties, but messy handwriting should not be disregarded. Rather, a specific learning disability in written expression, or dysgraphia, should be considered to further provide a biopsychosocial approach for treatment purposes of children diagnosed with comorbid ADHD and dysgraphia.

This presentation reviews the literature to discuss the similarities and challenges of diagnosing comorbid ADHD and dysgraphia and appropriate treatment interventions.
Methods: A literature review of the evidence was performed to examine the psychopathology and neurobiology, diagnostic assessment, and a biopsychosocial treatment approach for children diagnosed with ADHD and dysgraphia.
Results: ADHD and dysgraphia have several similarities from a psychological and neurobiological perspective. Handwriting difficulties are not a prerequisite for the diagnosis of ADHD, although a careful and thorough diagnostic assessment of ADHD may warrant further assessment for dysgraphia. Treatment considerations for a child diagnosed with both ADHD and dysgraphia have some overlap with the biopsychosocial model of intervention.
Conclusions: ADHD and dysgraphia have multiple similarities when comparing the intricacies of each diagnosis. Professionals working with children in a psychiatric or mental health capacity should be aware of these intricacies when assessing for either ADHD or dysgraphia. Implementing appropriate measures that encompass a biopsychosocial approach to address both diagnoses is recommended.

S24. FATIGUE AND ADULT ADHD: ANALYZING THE RELATIONSHIP

Joel Young[1], Richard Powell*[1], Jaime Saal[1], Anna Powell[1], Lisa Welling[2]

[1]The Rochester Center for Behavioral Medicine, [2]Oakland University

Hypothesis/Objective: This study investigated a hypothesis of whether adult ADHD is a significant predictor of co-occurring clinically significant fatigue. We hypothesized predictive relationships between ADHD and fatigue severity and between ADHD and the degree to which fatigue interferes in daily life functioning.
Methods: The de-identified results of 925 psychological assessment reports were analyzed. The assessments were administered between September 2021 and October 2022 as a part of the initial phase of treatment at a large outpatient psychiatric center. We conducted ANOVA and regression analyses to test the study hypotheses.
Results: 1x1 ANOVA analyses demonstrated a significant difference between positive and negative ADHD screen conditions in mean measurements of fatigue interference ($F(1) = 47.46$, $p < 0.001$, Cohen's $D = 0.45$), and fatigue severity ($F(1) = 46.00$, $p < 0.001$, Cohen's $D = 0.26$). Multiple linear regression analyses found that ADHD predicted fatigue interference and severity, taking into account the variance explained by the common co-occurring clinical problems insomnia, anxiety, and depression; fatigue interference: $R (908) = .702$, $R2 = .492$, $p < .001$; fatigue severity: $R (910) = .655$, $R2 = .429$, $p < .001$.
Conclusions: ADHD predicted a reported stronger subjective intensity of fatigue and a higher level of daily life interference from fatigue. Also, ADHD's influence on fatigue may not be better explained by other clinical conditions. Of note, the primary ADHD screen assessment used relies heavily on an adult's recollection of childhood patterns. ADHD's impact on fatigue in adulthood may be a critical consideration for treatment planning.

S25. ADHD AND BINGE EATING DISORDER: INVESTIGATING THE RELATIONSHIP WITHIN A LARGE CLINICAL POPULATION

Joel Young[1], Richard Powell*[1], Anna Powell[1], Jaime Saal[1], Lisa Welling[2]

[1]The Rochester Center for Behavioral Medicine, [2]Oakland University

Hypothesis/Objective: This study had a principle aim of investigating whether a relationship exists between ADHD and binge eating disorder in a clinical outpatient adult population. We hypothesized that ADHD would positively predict binge eating symptoms.
Methods: De-identified results of 913 psychological assessment reports were analyzed. All assessments were administered between September 2021 and October 2022 at the onset of treatment. Chi-square and regression analyses were used to test the study hypothesis.
Results: The Chi-Square test found a significant relationship between screen results for ADHD and Binge Eating Disorder, $\chi 2(1) = 8.23$, $p = 0.003$. A binary logistic regression analysis found that ADHD predicted Binge Eating Disorder, $\chi 2\ (1) = 8.62$, $\beta = 0.47$, Nagelkerke $R2 = 0.014$, $p = 0.003$. A multiple regression analysis found that ADHD severity measurements predicted binge eating severity when accounting for variance in binge eating measurements explained by common co-occurring clinical problems, $R\ (896) = 0.66$, $p < 0.001$.
Conclusions: The presence and severity of ADHD signs and symptoms positively predicted the presence and severity of binge eating symptoms. These findings should advise clinicians to screen for and actively monitor their ADHD-positive patients for binge eating disorder symptoms and choose treatment regimens that provide cross-benefits for both conditions. Even though a significant relationship between the two disorders was detected, there was variation in the presence and absence of binge eating amongst ADHD patients. Future research should investigate what intervening variables are at play that predict whether one adult with ADHD will develop binge eating symptoms and another will not.

S26. SLEEP PHYSIOLOGY AMONG ADOLESCENTS WITH ADHD: ASSOCIATIONS WITH COGNITION

Jessica Lunsford-Avery*[1], Scott H. Kollins[1], Leah Jackson[1], Noyuri Tominaga-Brown[2], Venkata Ramana Thalasila[2], Andrew Krystal[2]

[1]Duke University Medical Center, [2]University of California San Francisco School of Medicine

Hypothesis/Objective: Sleep disturbances are common among adolescents with ADHD; however, few studies have characterized the nature of ADHD-related sleep problems using the gold-standard sleep measure, polysomnography (PSG), in adolescence. Additionally, the potential role of sleep in contributing to cognitive impairment in adolescent ADHD is unknown. This study investigates differences in PSG-measured sleep among adolescents with ADHD versus healthy controls (HC) and associations with cognition.
Methods: Sixty-two adolescents aged 13-17 (31 ADHD, mean age=15.3, 50% female) completed a psychiatric evaluation and 3 nights of ambulatory PSG. Following the third night, participants completed the Cambridge Neuropsychological Test Automated Battery. Linear regressions controlling for demographics examined group differences in PSG and spectral sleep-EEG indices as well as relationships between PSG/spectral indices and cognition within the ADHD group.
Results: Adolescents with ADHD displayed reduced slow wave sleep percentage (SWS%) ($F(4,50)=10.21$, $p=.002$), increased stage 2 percentage (N2%) ($F(4,50)=10.54$, $p=.002$), increased relative sigma power ($F(6,45)=10.50$, $p=.002$) and reduced relative delta power ($F(6,45)=4.99$, $p=.03$) compared to HC. Within the ADHD group, reduced N2% ($r=-.56$), greater relative delta power ($r=.48$), steeper delta decline overnight ($r=-.54$), and reduced relative theta ($r=-.49$) and beta ($r=-.61$) power were associated with better cognition (p's$<.05$).
Conclusions: Adolescents with ADHD exhibited abnormalities in sleep stage distribution and non-REM EEG frequency spectral indices, including reduced SWS and low frequency power and increased stage 2 sleep and high frequency power, compared to HC. Similar parameters

were associated with cognition, suggesting sleep may contribute to cognitive deficits in ADHD. Future studies may clarify whether sleep treatments improve cognition in this population.

S27. COMORBID PSYCHOLOGICAL, NEURODEVELOPMENTAL, AND SOMATIC SYMPTOMS IN CHILDREN WITH AND WITHOUT SLUGGISH COGNITIVE TEMPO IN AUTISM, ADHD, AND POPULATION-BASED SAMPLES

Raman Baweja*[1], Susan D. Mayes[1], Susan L. Calhoun[1], Rachel Kallus[1], Daniel Waschbusch[1]

[1]Penn State College of Medicine

Hypothesis/Objective: Symptoms of sluggish cognitive tempo (SCT) include sluggish, underactive, slow moving, lethargic, drowsy, spacey, blank staring, daydreaming, in own world, in a fog, and confused. Research demonstrates that SCT is a clinical syndrome with convergent and divergent validity, internal consistency, and measurement invariance over time. SCT is associated with multiple symptoms and disorders, but no studies have investigated the comparative prevalence of comorbid problems in children with versus without SCT in ADHD-Combined, ADHD-Inattentive, autism, and general population samples.
Methods: Mothers rated 987 children with autism, 700 with ADHD-Combined, and 303 with ADHD-Inattentive and 665 elementary school children on the Pediatric Behavior Scale. IQ tests were also administered.
Results: Comorbid problems significantly more prevalent in children with versus without SCT in all or three of the four diagnostic groups in order of significance were cognitive problems, gross motor incoordination, depression, somatic complaints, excessive sleep, anxiety, inattention, insomnia, academic impairment, bully victimization, autism, dysgraphia, and overweight. Nonsignificant comorbidities in all or most groups were hyperactivity, impulsivity, oppositional behavior, irritability/temper outbursts, aggression, bullying, suicide ideation and attempts, incontinence, underweight, seizures, and low IQ.
Conclusions: Given SCT's association with multiple comorbid problems and functional impairment across clinical and population-based samples, its general population prevalence similar to that of other childhood disorders, and its high frequency in clinical children, it is important to expand our understanding of SCT through continued research and to evaluate SCT symptoms and comorbidity in referred children and intervene when symptoms are present.

S28. EFFICACY ASSESSMENTS DURING LONG-TERM TREATMENT WITH VILOXAZINE EXTENDED-RELEASE (QELBREE®) IN ADULTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: RESULTS: FROM AN OPEN-LABEL EXTENSION SAFETY TRIAL

Azmi Nasser*[1], Joseph Hull[1], Zulane Maldonado-Cruz[1], Tesfaye Liranso[1], Peibing Qin[1], Jonathan Rubin[1]

[1]Supernus Pharmaceuticals, Inc.

Hypothesis/Objective: Viloxazine ER (viloxazine extended-release capsules, Qelbree®) is FDA-approved in children and adults ≥6 years of age with ADHD. The objective was to assess the efficacy of viloxazine ER in adults with ADHD during an ongoing, open-label extension (OLE) trial.
Methods: The ADHD Investigator Symptom Rating Scale (AISRS) Total score and Clinical Global Impression-Severity of Illness scale (CGI-S) score were assessed during a 6-week, Phase 3, double-blind trial (Baseline, Weeks 1–4 and 6) and during an OLE trial (Weeks 2, 4,

and every 8 weeks thereafter; up to Week 52). The change from baseline (CFB) AISRS Total score and CFB CGI-S score was assessed by visit and at subject's last on-study visit in the OLE. Subjects took 200 mg/day Weeks 1-2 in OLE (n=58; titrated up to 400mg/day after Week 1). After Week 2, based upon the subject's clinical response and tolerability, investigator could adjust dose (50 to 200 mg/day/week between 200 and 600 mg/day).
Results: At time of data cut (30Mar2021), 157 subjects received viloxazine ER in OLE trial; median planned dose at last on-study visit was 400 mg. The CFB AISRS Total score and CFB CGI-S score improved across OLE study visits. At last on-study visit, the mean (±SE) CFB AISRS Total score (-18.0 ± 0.94; n=140) and CFB CGI-S score (-1.6 ± 0.10; n=139) was significantly improved ($p<0.0001$).
Conclusions: Subjects continued to show improvement in ADHD symptoms during long-term viloxazine ER treatment.

S29. ATTNKARE-D: A VIRTUAL REALITY AND ARTIFICIAL INTELLIGENCE BASED TOOL FOR MEASURING ADHD SYMPTOM SEVERITY

Ha Min Son*[1], Joonhui Lee[1], Minsu Pak[1], Beth Krone[2], Jeffrey Newcorn[2], Tai-Myoung Chung[1]

[1]Hippo T and C, [2]Icahn School of Medicine at Mount Sinai

Hypothesis/Objective: Virtual Reality (VR) is a promising tool for assessing symptoms of mental disorders, as recent technological advances allow for simulation of realistic, isolated, and deterministic settings. Here we provide initial validation of AttnKare-D, an investigational objective measure for ADHD symptom severity/diagnosis in VR.
Methods: AttnKare-D is designed to measure ADHD symptom severity in settings intended to approximate home, school, and playgrounds through performance, eye and hand movement, and voice variables. We constructed variables by selecting behavior in VR most likely to reflect severity of DSM-5 ADHD symptoms. We collected data from a nonclinical group of 612 children ages 7–12 (μ=9.83,σ=1.53,47.5% Male) from March to September 2022. We examined convergent validity with the Korean Parent ADHD-RS-IV (N=612,μ=11.60,σ=7.91). Two methods of analysis were used. First, on the entire dataset, we compared VR variable distributions between a low score group (<20,N=513,μ=8.97,σ=5.19) and a high score group (>=20,N=99,μ=25.21,σ=5.14). Second, we randomly split our samples into a stratified training-validation dataset (80%-to-20%) with a balanced proportion of high score samples to train a Poisson Regression model.
Results: We confirmed significant difference of the unweighted sum of all VR variable z-scores between low and high scores (μ=-0.50, σ=6.03 vs. μ=7.85, σ=6.62 ($p=0.004$)). Furthermore, on the validation dataset, we confirmed moderately strong correlation ($R=0.67$, $p<0.0001$) between parent scores and our Poisson Regression model predictions.
Conclusions: Our results show AttnKare-D to reliably predict rating scores in a nonclinical sample. Future research will examine whether AttnKare-D can reliably predict symptom severity in clinical populations and serve as an aid in ADHD diagnosis.

S30. ADHD AND COMORBID MENTAL HEALTH OUTCOMES FOR CHILDREN AND ADOLESCENTS WITH COVID-19

Rachel Aber*[1], John Clay[1], Stephen V. Faraone[1], Yanli Zhang-James[1]

[1]SUNY Upstate Medical University

Hypothesis/Objective: There is extensive research on the negative effects of the COVID-19 pandemic on mental health, but the COVID-19 infection and its psychiatric sequelae in adolescents remain less explored. In this study, we investigated mental health outcomes of the COVID-19 infection on adolescents, specifically Attention-deficit/hyperactivity disorder (ADHD) and its comorbidities.
Methods: We used de-identified medical records from the TriNetX Research Network to examine the association of the COVID-19 infection on the subsequent diagnosis of ADHD and its comorbidities in 3.8 million adolescents, aged 13-21 at the index event of COVID-19 infection. We excluded those with known psychiatric diagnoses (ICD-10 F01-F99) prior to contracting COVID-19. We used Kaplan-Meier survival analysis to compare the incidence of new psychiatric diagnoses between COVID-19-infected adolescents with and without post-COVID-19 ADHD.
Results: We found that adolescents diagnosed with COVID-19 were 6 times more likely to be diagnosed with ADHD, compared to those who never had COVID-19 (HR 5.83, 95% CI: 5.16, 6.59). Of these patients with COVID-19 and ADHD, compared to COVID-19 patients without ADHD, there is increased risk for developing other mental health outcomes, such as conduct disorder (HR 14.805, 95% CI: 13.454, 16.292), depression (HR 7.209, 95% CI: 6.788, 7.656), anxiety, autism, and suicidal ideations.
Conclusions: The COVID-19 infection poses a significant risk for adolescents to develop mental health outcomes, and those who are later diagnosed with ADHD have a higher risk for developing psychiatric comorbidities. This highlights the need for mental health services for at-risk youth, as well as awareness of and adherence to COVID-19 safety guidelines.

S31. WORKING MEMORY MEDIATES THE RELATIONSHIP BETWEEN CHILDHOOD DEPRESSION AND ADOLESCENT SUICIDALITY FOR THOSE WITH AND WITHOUT ADHD

Hannah Morton*[1], Michael Kozlowski[1], Joel Nigg[1], Sarah Karalunas[2]

[1]Oregon Health and Science University, [2]Purdue University

Hypothesis/Objective: Suicide is the second leading cause of death in adolescence (Curtin, 2020), with particular vulnerability for youth with ADHD when depressed mood is elevated (Garas and Balazs, 2020). Decreased working memory may further accentuate risk (Richard-Devantoy et al., 2015) and specifically in ADHD (Bauer et al., 2018). Cross-sectional interaction of ADHD with mood disorders may increase suicidality (Forte et al., 2021). However, working memory may also directly relate to depression and suicidality. Here, we examined whether working memory mediated the relationship between self-reported childhood depression symptoms and adolescent suicidality for youth with and without ADHD.
Methods: Data for 849 community-recruited youth (ages 7-13; nADHD = 509) were collected at 12 annual timepoints. Youth completed laboratory measures of working memory (digit span forward/backward, CANTAB spatial span forward/backward, N 1-back/N 2-back). Parent- and youth-report questionnaires characterized the highest level of suicidality across ages 13-23 as none, moderate (thoughts of death or suicidal ideation), or severe (ideation+plan/intent) based on K-SADS-PL, SCID, CDI, and Youth/Adult Self Report.
Results: Baseline depression was associated with lower working memory (β=-0.192, SE=.038, $p<.001$) and more severe subsequent suicidality (β=.185, SE=.044, $p<.001$), whereas higher baseline working memory protected against future suicidality (β=-.094, SE = .043, p=.029). Effects were nominally stronger in ADHD but did not differ significantly in ADHD and non-ADHD groups.

Conclusions: Working memory mediates prospective relationships between depression and suicidality in children with ADHD. Longitudinal modeling of suicidality risk should be extended to include youth with ADHD as a highly vulnerable group particularly when working memory is impaired.

S32. DO FIDGET INSTRUMENTS ENHANCE ATTENTIONAL CONTROL AND COMPREHENSION IN 6-13 YEAR-OLDS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD)?

Jennifer Persia*[1], Lori Schweickert[1], Steven Buzinski[2]

[1]3-C Family Services, [2]UNC Chapel Hill

Hypothesis/Objective: For children with ADHD, fidget gadgets have been shown to contribute to fewer area, but greater attentional, violations in the classroom (Grazino et al., 2020). On the other hand, fNRI research indicates that fidgets may actually decrease cognitive load (Koiler, 2020). To help clarify the mixed literature, this study was developed to examine the impacts of fidgets on attention. We hypothesized that fidgets improve attentional control and comprehension in children with ADHD.
Methods: Participants were a sample (N=21) of children diagnosed with ADHD through clinician referrals and flyer postings. Parents indicated their child's ADHD subtype and completed the ADHD Rating Scale-IV: Home Version. Participants were randomly assigned to a fidget selection, or no fidget (control) group, and completed a computer-administered 2-back version of the n-back attentional control task, as well as a multiple-choice video comprehension test.
Results: An independent t-test indicated no significant differences in 2-back scores between fidget (M=0.47, SD=0.24) and control (M=0.53, SD= 0.15) groups, $t(17)= 0.70$, $p = .404$, $d= 0.32$. ADHD subtype ($p= 0.034$) and ADHD-RS scores ($p= 0.019$) were significant covariates impacting visual scores. A second t-test examining multiple choice correctness revealed no significant difference between fidget (M= 5.50, SD= 2.27) and control (M= 6.64, SD= 1.29) groups on comprehension measures, $t(19)= 1.43$, $p = 0.166$, $d=0.62$.
Conclusions: The use of a fidget gadget did not significantly affect 2-back correctness measures or video comprehension scores. Results may be related to a lack of statistical power from the small sample size, or an unanticipated attentional drain from fidget use.

S33. U.S. TRENDS IN PREVALENCE OF NON-PHARMACOLOGICAL TREATMENT AND EDUCATION SERVICES AMONG CHILDREN AND ADOLESCENTS AGED 3–17 YEARS WITH ADHD, 2016–2021

Melissa Danielson*[1], Angelika Claussen[1], Rebecca Bitsko[1], Kimberly Newsome[1]

[1]Centers for Disease Control and Prevention

Hypothesis/Objective: The COVID-19 pandemic disrupted access to treatment and services for mental disorders beginning in 2020. This study describes trends in non-pharmacological treatment and services for children with ADHD from 2016–2021.
Methods: Data are from the National Survey of Children's Health, an annual, nationally representative survey. Parents reported whether their child currently had ADHD, if their child received behavioral treatment for ADHD in the past year, and if their child was currently receiving services under a special education or early intervention plan. Treatment and service

use prevalence was estimated among children with current ADHD aged 3–17 years annually from 2016–2021; trends were tested using joinpoint analysis.
Results: Less than half of children with current ADHD received behavioral treatment or education services in 2016–2021. Joinpoint analyses detected a change in trend for both indicators in 2019. The percentage of children receiving behavioral treatment increased from 46.4% in 2016 to 51.8% in 2019 but decreased to 42.9% in 2021. Similarly, the percentage of children receiving education services increased from 40.7% in 2016 to 45.3% in 2019 but decreased to 41.5% in 2021.
Conclusions: There is evidence of decreasing use of non-pharmacological treatment and education services for children with ADHD during the COVID-19 pandemic, which might be due to reduced access to in-person care and differing needs during the pandemic. Families of children with ADHD and their providers can evaluate current treatment needs to ensure that children with ADHD are able to access evidence-based care and services.

S34. DIABETES GLYCEMIC CONTROL IN ADULTS WITH TYPE 2 DIABETES MELLITUS AND ADHD

Dahlia Leshno*[1], Liat Lev Shalem[2], Revital Perlove[2]

[1]Tel Aviv University, [2]Maccabi Institute of Research and Innovation, Maccabi Healthcare Services, Israel

Hypothesis/Objective: Attention Deficit Disorder impairs quality of life and functioning in many areas of life. Patients with ADHD are caracterized, among other things, by managerial difficulties, which can affect the adherence and persistence of treatment. The aim of this study is to evaluate the possible association of ADHD and diabetes glycemic control among adults with type 2 diabetes in MACCABI HMO.
Methods: We conducted a retrospective cross-sectional study using electronic medical records form Maccabi health service database between the years 2010-2020.
. We compared a group of 1,582 patients with DM without ADHD and 1,582 patients with DM and ADHD. For the analysis, a propensity score was prepared for the variables of age, gender and duration of diabetes

Results: We found that the variance in the distribution of HbA1c in patients with ADHD is significantly greater than the variance in patients with non-ADHD.
The proportion of patients with HbA1c values above 10 in the group of patients with ADHD was 4.7-5.9 times higher than in patients without ADHD. Also for the mean HbA1c values of the patients in each of the groups the proportion of patients with an average HbA1c value greater than 10 was 3.7 times in the group of patients with ADHD compared to the group of patients without ADHD. This rate is also found in logistical regression with additional variables.

Conclusions: The findings extend the knowledge on the relationship between ADHD and Diabetes and highlight the need for further research to improve treatment.

S35. EFFECT OF A SINGLE DOSE OF AMPHETAMINE EXTENDED-RELEASE TABLET ON DRIVING PERFORMANCE IN YOUNG ADULT DRIVERS WITH ADHD: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY USING A LABORATORY DRIVING ENVIRONMENT

Joseph Biederman[1], Ronna Fried[1], Antonio Pardo[2], Stephanie Duhoux*[2], Roberto Gomeni[3], Judith Kando[2], Bruce Mehler[4]

[1]Clinical and Research Program in Pediatric Psychopharmacology and Adult ADHD, Massachusetts General Hospital, [2]Tris Pharma, Inc., [3]PharmacoMetrica, [4]Center for Transportation and Logistics – AgeLab, Massachusetts Institute of Technology

Hypothesis/Objective: ADHD is a risk factor for motor vehicle accidents, including injuries and fatalities, traffic citations and license suspension. This study assessed the impact of a single dose of amphetamine extended-release (DYANAVEL® XR) tablets (AMPH ER TAB) on driving performance in young adult drivers with ADHD in a laboratory-based simulation environment.
Methods: This single-center, randomized, double-blind, placebo-controlled, parallel study evaluated driving performance predose, 45-minutes and 10-hours postdose, emulating typical morning and evening commutes, and taking AMPH ER TAB efficacy data, as early as 30 minutes and as late as 13 hours postdose, into consideration. The study evaluated relative crash risk of drivers with ADHD who took AMPH ER TAB vs. placebo. The primary endpoints were the difference from placebo of the Minimum Time to Collision, Braking Percent, and Highest Braking Intensity. The key secondary endpoint was Total Crash Count during the last drive.
Results: Forty-one male and female drivers aged 18-25 years who met DSM-V criteria for ADHD completed the study. Assessment of driving performance during postdose drives demonstrated that Median Minimum Time to Collision and Maximum Highest Braking Intensity were statistically significantly improved with AMPH ER TAB at both 45-minutes and 10-hours postdose. Generally, drivers with ADHD who received AMPH ER TAB had numerically improved outcomes across all measures. Single dose of AMPH ER TAB was well tolerated with no dropouts due to adverse events.
Conclusions: Drivers with ADHD who took AMPH ER TAB showed improved behavior in the driving simulation associated with a lower crash risk relative to subjects who took placebo.

S36. POPULATIONPHARMACOKINETIC-PHARMACODYNAMIC (PK/PD) MODELING OF VARIABLE WEAR TIMES FOR A DEXTROAMPHETAMINE TRANSDERMAL SYSTEM (D-ATS)

Kanan Balakrishnan[1], Mariacristina Castelli*[1], Marina Komaroff[l], Suzanne Meeves[1], Kyle T. Baron[2], John T. Mondick[2], Stephen V. Faraone[3], Gregory W. Mattingly[4]

[1]Noven Pharmaceuticals, Inc., [2]Metrum Research Group, [3]SUNY Upstate Medical University, [4]Washington University School of Medicine, Midwest Research Group

Hypothesis/Objective: In a pivotal study in pediatric ADHD patients, d-ATS met primary and secondary efficacy endpoints. Nine-hour patch applications resulted in SKAMP score improvements 2-12 hours post-dose. This analysis describes the d-ATS exposure-response relationship and explores outcomes for wear times ≤9 hours under varying assumptions.
Methods: A population PK model was developed to describe amphetamine disposition following d-ATS administration. This model was used to construct a population PK/PD model for SKAMP total score data from two pediatric studies to characterize onset and duration of d-ATS's effect. The integrated PK/PD model describes the d-ATS exposure-response relationship and potential impact of d-ATS wear times by simulating amphetamine PK and SKAMP profiles for wear times ≤9 hours using several amphetamine absorption assumptions.
Results: Data from 81 children and 41 adolescents, ages 6-17, were included. The model provided a reasonable description of the SKAMP score over time, showing initial declines ~2

hours after patch application (max decline ~4 hours). Earlier simulated removal was associated with reduced systemic exposure and earlier return to near-baseline scores across the assumptions tested. With moderate/conservative assumptions, following a 9-hour wear time, SKAMP scores reached 90% of baseline in ~49% of subjects by 12 hours and ~80% by 16 hours. Following a 4-hour wear time, percentages were ~74% by 12 hours and ~95% by 16 hours.
Conclusions: Simulations suggest d-ATS efficacy duration may be related to wear time, which can be adjusted according to treatment needs. Controlling exposure with a transdermal patch allows individualized treatment duration, providing flexibility in optimizing ADHD treatment.

S37. SERDEXMETHYLPHENIDATE/DEXMETHYLPHENIDATE EFFECTS ON SLEEP IN CHILDREN WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER

Greg Mattingly[1], Ann C. Childress[2], Andrew J. Cutler[3], José Estrada[4], Meg Corliss*[4]

[1]Washington University School of Medicine, Midwest Research Group, [2]Center for Psychiatry and Behavioral Medicine, [3]SUNY Upstate Medical University and Neuroscience Education Institute, [4]Corium Inc.

Hypothesis/Objective: To determine sleep behavior during serdexmethylphenidate/ dexmethylphenidate (SDX/d-MPH) treatment in children with attention-deficit hyperactivity disorder (ADHD).
Methods: This was a 12-month, dose-optimized, open-label safety study in 6–12-year-old subjects, including new subjects and those rolled over from a previous double-blind study (J Child Adolesc Psychopharmacol. 2021;31:597). The primary end point was safety and tolerability of SDX/d-MPH. A secondary end point was sleep behavior based on the Children's Sleep Habits Questionnaire (CSHQ) consisting of 8 sleep domains (bedtime resistance, sleep-onset delay, sleep duration, sleep anxiety, night wakings, parasomnias, sleep-disordered breathing, and daytime sleepiness).
Results: Of 282 subjects enrolled (212 new; 70 rolled over), 238 were included in the sleep analysis. At baseline, mean (SD) CSHQ total sleep disturbance score was 53.4 (5.9). After 1 month of treatment, the overall mean CSHQ score significantly decreased to 50.5 (5.4; least-squares mean change from baseline [95%CI], −2.9 [−3.5, −2.4]; P<.0001) and remained significantly decreased for up to 12 months, indicating overall sleep improvement. Mean sleep-score changes from baseline to 12 months were statistically significant (P<.0001) for 6 of 8 sleep domains. There was no significant worsening for sleep duration and sleep-disordered breathing. Daytime sleepiness and parasomnias sleep domains had the greatest mean improvement from baseline to 12 months (−2.0 [−2.4, −1.7] and −1.1 [−1.3, −0.9], respectively).
Conclusions: Significant improvements in most CSHQ sleep domains were observed with SDX/d-MPH use in children with ADHD after 1 month and lasting up to 12 months of treatment. Importantly, the use of SDX/d-MPH did not worsen sleep problems.

S38. ASSESSMENT OF PEDIATRIC WEIGHT AND HEIGHT TRAJECTORIES DURING LONG-TERM VILOXAZINE ER (QELBREE®) TREATMENT: INTERIM RESULTS FROM AN OPEN-LABEL EXTENSION TRIAL IN ADHD

Azmi Nasser*[1], Joseph Hull[1], Jami Earnest[1], Jennifer Koch[1], Tesfaye Liranso[1], Zulane Maldonado-Cruz[1], Jonathan Rubin[1], Ann Childress[2]

[1]Supernus Pharmaceuticals, Inc., [2]Center for Psychiatry and Behavioral Medicine, Inc.

Hypothesis/Objective: Viloxazine ER (viloxazine extended-release capsules; Qelbree®) may have pharmacological properties distinct from other approved ADHD treatments and may not impact growth in the same manner. The objective was to examine the effects of long-term viloxazine ER treatment on growth trajectories in pediatric patients.
Methods: Weight (kg) and height (cm) were measured at baseline and end of study in 5 double-blind placebo-controlled (DBPC), Phase 2 and 3 clinical trials and every 3 months in an ongoing open-label extension (OLE) safety trial. Weight and height were converted into percentile and corresponding z-score values using Centers for Disease Control (CDC) Growth Charts. The allowed viloxazine ER dose range in the OLE was 100-400mg/day (6-11 yrs) or 100-600mg/day (12-17 yrs). Growth-related adverse events (AEs) were also evaluated.
Results: 1097 subjects received at least one dose of viloxazine ER in OLE study [66.4% male, 58.8% age 6-11 yrs; mean (SD): age 10.8 (3.06) yrs, BMI 18.80 (3.42) kg/m2, weight 42.05 (16.01) kg, height 146.66 (17.46) cm]. The mean (SE) z-score for weight and height was within a normal range relative to expected values. At OLE Month 12 (n=338), the mean (SD) change from baseline weight-for-age z-score was -0.2 (0.5) and height-for-age was -0.1 (0.4). AEs (≥ 1% subjects) were decreased appetite (5.8%), vomiting (2.7%), nausea (2.4%), weight decreased (2.3%), and weight increased (2.0%).
Conclusions: During long-term viloxazine ER treatment, pediatric subjects' weight and height remained within the normal range. However, pediatric patients' weight should be monitored during viloxazine ER treatment.

S39. EVALUATING THE POTENTIAL IMPACT OF CAFFEINE EXPOSURE ON THE SAFETY PROFILE OF VILOXAZINE EXTENDED-RELEASE CAPSULES (QELBREE®) TREATMENT IN ADULTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER

Azmi Nasser*[1], Roberto Gomeni[2], Joseph Hull[1], Zulane Maldonado-Cruz[1], Lilian Adeojo[3], Jami Earnest[1], Jonathan Rubin[1]

[1]Supernus Pharmaceuticals, Inc., [2]PharmacoMetrica, [3]Formerly Supernus Pharmaceuticals, Inc.

Hypothesis/Objective: Viloxazine ER (viloxazine extended-release capsules, Qelbree®) is a novel, nonstimulant, FDA-approved treatment for individuals ≥6 years of age with ADHD. Viloxazine ER inhibits cytochrome P450-1A2, the enzyme responsible for caffeine metabolism. The objective was to evaluate the impact of caffeine consumption on viloxazine ER safety in adults with ADHD.
Methods: Total week caffeine amount (mg) and incidence of known caffeine-associated adverse events (AEs) were evaluated in a Phase 3 double-blind (DB), placebo-controlled trial and an ongoing open-label extension (OLE) trial in adults. For caffeine-associated AEs occurring in >5% of viloxazine ER-treated subjects (200-600 mg/day) who reported caffeine use, a logistic regression model was used to estimate the probability of AE occurrence as a function of viloxazine ER dose and caffeine amount.
Results: Of 372 subjects, ~85% reported caffeine use during the DB trial; mean: 859 mg/week, viloxazine ER; 1034 mg/week, placebo. There was no correlation between viloxazine ER dose and caffeine amount. There were 44 DB placebo, 79 DB viloxazine ER, and 33 OLE viloxazine ER subjects reporting any caffeine-associated AEs. Most common (>5%) caffeine-associated AEs (*combined preferred terms) were insomnia*, fatigue, nausea, headache*, decreased

appetite, and somnolence*. The probability of experiencing insomnia-related AEs was high (p=0.02) in viloxazine ER-treated subjects who reported caffeine use.
Conclusions: Except for insomnia, the likelihood of experiencing caffeine-related AEs is low with caffeine use during viloxazine ER treatment. Prescribers should consider suggesting caffeine intake reduction if patients taking viloxazine ER experience potential caffeine-related AEs.

S40. CHARACTERIZATION OF VILOXAZINE'S SEROTONERGIC EFFECTS AT DOSES RELEVANT FOR ADHD TREATMENT

Jami Earnest*[1], Jennie Garcia-Olivares[1], Brittney Yegla[1], Vladimir Maletic[2], Chungping Yu[1], Jonathan Rubin[1]

[1]Supernus Pharmaceuticals, [2]University of South Carolina School of Medicine, Columbia

Hypothesis/Objective: The objective of this study was to conduct a series of experiments to determine whether viloxazine engages serotonergic receptors and modulates serotonin levels at clinically relevant concentrations and in species with close physiology to humans.
Methods: In vitro binding competition and functional activity assays assessed viloxazine effects at human isoforms of 5-HT receptors. Microdialysis was conducted, in rats, to determine viloxazine concentrations in the interstitial fluid (ISF) and concentrations of NE, DA, 5-HT, and their metabolites in the prefrontal cortex (PFC). PET imaging using a 5-HT2A/2C receptor radioligand agonist, [11C]CIMBI-36, was conducted in non-human primates (NHPs) to determine if viloxazine binds these receptors and/or increases 5-HT release.
Results: Binding competition and functional activity assays indicated viloxazine binding at 5-HT2C (partial agonism) and at 5-HT7 (antagonism) receptors. At a clinically relevant dose of viloxazine in rats, NE, DA, and 5-HT levels were increased over baseline. NE metabolite (DHPG) levels were decreased, confirming norepinephrine transporter inhibition; however, 5-HT metabolite (5-HIAA) levels were unchanged indicating lack of 5-HT transporter inhibition. At a clinically relevant dose of viloxazine in NHPs, changes in binding potential of [11C]CIMBI-36 indicated viloxazine binds directly to 5-HT2C receptors (60-72%). These preclinical doses approximated unbound plasma concentrations in pediatric ADHD patients.
Conclusions: Thus far our experiments show, at clinically relevant concentrations, viloxazine may act on certain 5-HT receptors and augment 5-HT in the rat PFC; these serotonergic effects may also occur in NHPs.

Previously presented at ACNP.

S41. GROWTH TRAJECTORIES OF YOUTH WITH ADHD TREATED WITH DELAYED-RELEASE/EXTENDED-RELEASE METHYLPHENIDATE: A PILOT DATABASE ANALYSIS OF REAL-WORLD DATA

Stephen Faraone*[1], Vamshi Ruthwik Anupindi[2], Mitchell DeKoven[2], Marina Komolova[3], Michelle Po[3], Cassandra Uchida[3], Lewis Warrington[4]

[1]SUNY Upstate Medical University, [2]IQVIA Health Economics and Outcomes Research – Real World Insights, [3]Ironshore Pharmaceuticals Canada Inc., [4]Ironshore Pharmaceuticals Inc.

Hypothesis/Objective: Stimulants are associated with a slowed growth rate in youth with attention-deficit/hyperactivity disorder (ADHD). DR/ER-MPH (JORNAY PM®) is an

evening-dosed, delayed-release and extended-release methylphenidate released in the colon; it has no immediate-release component and provides a dose-dependent duration of effect. We report real-world weight and height changes in patients newly prescribed DR/ER-MPH versus two branded stimulants, osmotic release oral system (OROS) MPH (Concerta®) and lisdexamfetamine dimesylate (LDX; Vyvanse®).

Methods: Patients (aged 6–17y) newly prescribed DR/ER-MPH, OROS MPH, or LDX between July 2019 and June 2020 were retrospectively identified from professional fee (Dx) and prescription claim (Rx) databases (New Data Warehouse, IQVIA). Differences in weight and height trajectories based on data from a linked electronic medical records database (Ambulatory EMR, IQVIA) were modeled with repeated measures mixed effects models (DR/ER-MPH vs OROS MPH or LDX).

Results: Analyses included 83, 240, and 403 patients prescribed DR/ER-MPH, OROS MPH, and LDX, respectively. There were no significant differences in growth measures at baseline. After 1 year of treatment, model-adjusted weight (+6.1kg vs +5.3kg, P=0.50) and height (+5.7cm vs +5.1cm; P=0.57) trajectories increased numerically for DR/ER-MPH versus OROS MPH. Versus LDX, height trajectory (+5.7cm vs +4.9cm; P=0.23) of DR/ER-MPH increased numerically and weight trajectory (+7.2kg vs +2.7kg; P<0.0001) increased significantly.

Conclusions: In its introductory year, patients prescribed DR/ER-MPH showed a numerical (non-significant) increase in growth trajectories versus OROS MPH and LDX after 1 year of treatment, with weight trajectory significantly increased versus LDX. These preliminary findings warrant further study with larger sample sizes.

S42. A RANDOMIZED, FIVE-WAY CROSSOVER STUDY TO EVALUATE BIOEQUIVALENCE OF THE DEXTROAMPHETAMINE TRANSDERMAL SYSTEM (D-ATS) AT FIVE APPLICATION SITES IN HEALTHY ADULTS

Houda Haj-Ibrahim[1], Marina Komaroff[1], Kanan Balakrishnan[1], Suzanne Meeves[1], Mahwish Khan*[1], Mariacristina Castelli[1], Gregory W. Mattingly[2], Stephen V. Faraone[3]

[1]Noven Pharmaceuticals, Inc., [2]Washington University School of Medicine, Midwest Research Group, [3]SUNY Upstate Medical University

Hypothesis/Objective: In a pivotal study, d-ATS applied to the hip met primary and secondary efficacy endpoints for ADHD in children and adolescents. Although no discontinuations from application-site reactions occurred, additional site options may minimize dermal reactions, increasing tolerability. This study evaluated amphetamine pharmacokinetics and safety following d-ATS application across five sites in healthy adults.

Methods: In this open-label crossover study, healthy adults aged 18-45 were randomized to 1 of 5 application sites (left/right hip [reference], upper back, chest, upper arm, flank) during each study period. One d-ATS patch (20 mg/19.05 cm²) was applied for 9 hours, with a 7-day washout between periods. Pharmacokinetic parameters (Cmax, AUC0-t, and AUC0-inf) and dermal safety were assessed. For bioequivalence between application sites, 90% confidence intervals (CIs) for test-to-reference treatment ratios of the geometric means of Cmax, AUC0-t, and AUC0-inf must fall within FDA-specified limits of 80%-125%.

Results: Demographics and baseline characteristics were balanced across treatment groups in the safety population (N=50). All 90% CIs of test-to-reference ratios for Cmax, AUC0-t, and AUC0-inf were within 80%-125%. d-ATS-related erythema occurred in <3% of subjects, with no marked differences between sites. No subject reported more than moderate discomfort, with most reporting mild or no discomfort, and minimal irritation. No new safety concerns were identified.

Conclusions: In this study, bioequivalence was observed between all five d-ATS application sites tested. No new safety concerns were identified, with comparable dermal evaluations across sites. With bioequivalence across sites, patients can choose from 10 d-ATS application sites (including left/right choices) to minimize dermal reactions.

S43. ADHD AS A CONTRIBUTING FACTOR TO MISCONDUCTS AND THE EFFICACY OF STIMULANTS AS AN INTERVENTION IN PRISON SETTINGS.

Gunter Lorberg[1], Sherinne Clarissa*[2], David Runnalls[1], Sachinthya Lokuge[2], Geneva Mason[2], Kathryn Fotinos[2], Tia Sternat[2], Martin Katzman[2]

[1]Central North Correctional Centre (CNCC), [2]The START Clinic for Mood and Anxiety Disorders

Hypothesis/Objective: Research has found that 26.1% of incarcerated individuals suffer from ADHD, which is substantially higher than the prevalence in non-offender populations. Furthermore, inmates with ADHD are more likely to engage in misconduct compared to their non-ADHD counterparts. While stimulant medications are considered first-line interventions for ADHD, there may exist barriers for access to medications for inmates with ADHD. Therefore, this poster aims to explore whether introducing stimulants to inmates with ADHD impacts the number of misconducts that they commit.
Methods: A chart review was conducted from a maximum-security prison in Ontario, Canada. Data collected included inmates with ADHD (n=96) treated with lisdexamphetamine dimesylate or methylphenidate and inmates with ADHD without treatment, as well as the number of violent and general misconducts.
Results: Results show that inmates treated with stimulants ($M = 45.83$, $SD = 22.33$) committed significantly fewer misconducts compared to inmates without stimulants ($M = 965.33$, $SD = 443.60$), $t(5) = -201.75$, $p < 0.001$. Additionally, inmates without treatment had significantly greater numbers of general $v(5) = 21$, $p = 0.03$, and violent misconduct compared to inmates with treatment $t(5) = -148.33$, $p < 0.001$.
Conclusions: To conclude, stimulants such as lisdexamphetamine dimesylate and methylphenidate may serve as an appropriate intervention for ADHD in prison settings. Appropriate intervention is expected to improve the behavior of inmates, provide health economics benefits, reduce recidivism rate, and improve the effectiveness of rehabilitation efforts. These results aim to destigmatize the use of stimulant therapy in prison settings.

S44. SYMPTOM TRACKING FOR ADHD IN REAL TIME (START SMART): A QUALITATIVE CONTENT ANALYSIS OF ADHD SYMPTOM MANAGEMENT STRATEGIES IN YOUNG ADULTS

John Gnalian*[1], Sarah Pedersen[2], Brooke Molina[2], Traci Kennedy[2]

[1]Frank H. Netter MD School of Medicine at Quinnipiac University, [2]University of Pittsburgh

Hypothesis/Objective: Young adults with ADHD experience numerous impairments (e.g., Hechtman et al., 2016), potentially due to low self-awareness and inhibitory control underlying ADHD symptoms (Barkley, 2015). We developed an mHealth intervention to reduce ADHD symptom severity by increasing awareness of ADHD symptoms via ecological momentary assessment (EMA) and personalized symptom feedback. We aim to use qualitative data to describe the strategies young adults with ADHD use to manage their symptoms.

Methods: Young adults with ADHD (N=68; age=18-21; 67% women, 23% men, 10% nonbinary; 75% White, 14% Black, 10% Asian American, 5% other races) completed open-ended reflections after receiving feedback on what strategy to use to manage their unchanging, improving, or worsening ADHD symptoms. Participants were randomized to receive either 1 or 5 daily prompts via smartphone over 21-days. We coded open-ended response data using inductive qualitative content analysis that coded participant strategies into larger categories (Cho and Lee, 2014). The frequency of each category was summed.
Results: We coded 3774 instances of 11 categories from the open-response data. The 4 largest categories Attention (680 instances), Unsure (654), Organization (607), and Productivity (520) account for 65% of the data set. The largest strategy "I don't know" under the Unsure category accounted for 15.3% of all responses. Example strategies will be discussed (e.g., Assignment book- "Write things down more", Stay on task- "Focus on work I need to do").
Conclusions: Given the large number of unsure responses, real-time strategies should be recommended via the mobile-health intervention. These strategies will be developed using these pilot data.

S45. STEPPED CARE FOR ADOLESCENT ADHD: TELE-GROUP IMPLEMENTATION OF LOW-DOSE BEHAVIOR MANAGEMENT TRAINING

Tess Gabert*[1], Devin Kennedy[2], Fiona Macphee[2], Jessica Jenness[2], Margaret Sibley[3], Mark Stein[3], Erin Gonzalez[2]

[1]Alpert Medical School, Brown University, [2]Seattle Children's Hospital, [3]University of Washington

Hypothesis/Objective: Behavior management training (BMT) is the leading behavioral treatment for childhood ADHD but has rarely been studied as stand-alone treatment in adolescence (e.g., Barkley et al., 2001). Moreover, families face innumerable barriers to access evidence-based care for adolescent ADHD. We piloted low-dose BMT for families of adolescents with ADHD as an initial step in an eventual "stepped-care" treatment approach.
Methods: The 4-session telemedicine First Approach Skills Training – Parenting Teens (FAST-P) program educates parents about ADHD, behavior management strategies, communication/emotion coaching, and screen time boundaries. Adolescents ages 13-17 with ADHD were recruited using Electronic Medical Record searches. The idiographic Top Problems interview was administered at pre- and posttest. Acceptability of FAST-P and telemedicine delivery was measured by the Consumer Satisfaction Scale, program-specific questionnaires and qualitative interviews.
Results: A total of 23 caregiver-adolescent dyads participated and 18 completed posttest measures. Teens' most common top problems were concentration and productivity (34.6%), interpersonal challenges (14.1%), and concomitant anxiety/depression (11.5%). Caregiver attendance averaged 3.33 of 4 sessions. In interviews, 85% of caregivers noted that their parenting perspective, confidence, or knowledge improved, and 40% reported improved parent-teen relationship. Overall satisfaction was moderate-to-high and 89% would recommend FAST-P to other families.
Conclusions: FAST-P shows promise as an engaging and acceptable low-dose BMT telemedicine intervention as part of a stepped-care model for adolescent ADHD treatment. There is a need to support this population not only with challenges related to their ADHD, but interpersonal difficulties and broader mental health.

S.46 THE EFFECTS OF PUNISHMENT AND REWARD SENSITIVITY ON INTERVENTION EFFICACY FOR PROCRASTINATION IN UNIVERSITY STUDENTS WITH ADHD TENDENCIES: SINGLE-CASE EXPERIMENTAL DESIGN SERIES

Mana Oguchi*[1], Hiroaki Kumano[1]

[1]Waseda University

Hypothesis/Objective: University students with ADHD diagnosis have some academic problems in their daily life. One of their problems is procrastination, which is irrational delay even though recognizing the delay causes negative consequences (Steel, 2007). Procrastination increases mental problems, such as depression moods, low self-efficacy. However, there are few studies to examine procrastination intervention for ADHD students. Therefore, this study aims to clarify the effect of procrastination intervention and the influences of reward and punishment sensitivity to intervention effects.
Methods: Twenty-four university students who have ADHD tendencies, ages ranging from 19 to 25, completed the study (Female = 16, Average of age = 20.42, SD = 1.50). Single-Case Experimental Design consisted of two phases, about three weeks baseline and six weeks intervention. Participants completed measurements of procrastination, depression (PHQ, CESD), and reward/punishment sensitivity (BIS/BAS, EROS) pre and post of study. And they also answered the GPS and PPS twice weekly, in baseline and intervention phases.
Results: As a result, procrastination scores decreased from pre- to post-intervention. The amount of changes in procrastination is positively related to the changes in depression symptoms. However, the BIS/BAS was not significantly related to all variables. On the other hand, the increasing EROS was negatively related to the change in procrastination and depressive symptoms.
Conclusions: The procrastination intervention has the effect of improving procrastination and depression among university students with ADHD tendencies. However, the reward and punishment did not influence procrastination intervention. This study revealed decreasing procrastination, which means increasing the action needed, making perceived rewards cause decreasing depression.

S.47 EARLY EXPERIENCE WITH DELAYED-RELEASE/EXTENDED-RELEASE METHYLPHENIDATE FOR THE TREATMENT OF ADULTS WITH ADHD: A RETROSPECTIVE ELECTRONIC MEDICAL RECORD ANALYSIS

Amy Stevenson1, Perry Roy*1, R. Derek Brugman1

1Carolina Attention Specialists

Hypothesis/Objective: DR/ER-MPH (formerly HLD200; trade name: JORNAY PM®) is an evening-dosed, delayed-release and extended-release methylphenidate for the treatment of individuals 6 years and older with attention-deficit/hyperactivity disorder (ADHD). Data on the use of DR/ER-MPH in adults are limited. This retrospective study explored the real-world use of DR/ER-MPH from three practitioners who treat adults with ADHD.

Methods: A dual-center, retrospective, electronic medical record (EMR) analysis of patients with ADHD was conducted in September 2022. All patients identified in the EMR aged ≥16

years with ADHD and prescribed DR/ER-MPH before July 2022 were included (N=50). Data collected included patient demographics, treatment/dosing history, and the Adult ADHD Self-Report Scale (ASRS).

Results: The population was 64% female with a mean age of 36 years (range: 16–56) and a high incidence of comorbid anxiety (82%) and depression (20%). Only three patients were treatment-naïve. Mean starting dose was 53.6 mg/d and mean last dose (≥3 months of follow-up) was 81.9 mg/d. Eight patients discontinued (lost to follow-up, tolerability, efficacy). Mean (SD) ASRS scores improved from 36.5 (13.7) at DR/ER-MPH initiation to 30.9 (13.6) at last follow-up with DR/ER-MPH (P=0.001, repeated measures analysis, paired t-test). Sixteen patients reported side effects (reported in ≥5 patients: increased appetite, pre-existing condition aggravated).

Conclusions: This retrospective database analysis of adult patients corroborated pediatric Phase 3 trial results, where an optimized dose of DR/ER-MPH resulted in ADHD symptom improvement with a safety profile consistent with methylphenidate products. The findings support DR/ER-MPH as an effective treatment option in a stimulant-experienced adult population.

S.48 EVALUATING A DISPENSER DEVICE FOR PRECISE AND FLEXIBLE DOSING OF PELLETS

Laura Steinecker1, Emelie Svensson2, Firat Koca2, Marie Wiechert1, Simon Bock*1, Maresa Eckhardt1

1AET Pharmaceuticals, 2OnDosis AB

Hypothesis/Objective: Various solid dosage forms exist for oral application of drugs. In comparison to tablets and capsules, drug-loaded pellets offer smaller dosing increments. However, dosing pellets accurately is a challenge that complicates their clinical use. This work aims at evaluating the capabilities of a device under development in terms of precise and flexible dose adjustments. Moreover, it investigates whether pellets could match properties of a reference dosage form (tablet) in terms of bioavailability.

Methods: The evaluation included testing procedures with pre-defined sampling schemes and specified acceptance criteria for precise and flexible dosing of pellets. To investigate the comparability of the used pellets with a reference tablet, a comparative study in 14 healthy subjects was conducted.

Results: For the targeted low-dose (50 mg), testing 28 different cartridges and control units resulted in an average mass output of 51.8 mg (720 dispenses, RSD = 2.8%). For the targeted high-dose (30 mg), the average mass output for 90 individual dispenses was 300.9 mg (RSD = 1.6%).

A comparative bioavailability study in 14 healthy subjects showed that the developed drug pellets and an approved reference drug product are comparable regarding Cmax and AUC. The co-administration of mixed amphetamine salts showed a slightly lower peak- and slightly higher partial exposure.

Conclusions: This work revealed that the device under development allows for precise and flexible dose-to-dose adaption. In addition, the investigation indicated that using pellets can result in acceptable bioavailability compared to approved tablets. Further research should target usability studies with the device and its assessment in a clinical environment.

S.49 LESS SEX AND GENDER ALIGNMENT IN ADOLESCENTS WITH ADHD IS RELATED TO GREATER ADHD AND INTERNALIZING SYMPTOM SEVERITY AND SELF-HARM

Laura Rice1, Alyssa DeRonda1, Kathryn Van Eck1, Christopher Hammond2, Stewart Mostofsky3, Keri Rosch*3

1Kennedy Krieger Institute, 2Johns Hopkins, 3Kennedy Krieger Institute / Johns Hopkins,

Hypothesis/Objective: The goal of the present study is to examine how the alignment of biological sex (assigned at birth) with gender expression relates to symptoms of attention-deficit/hyperactivity disorder (ADHD) and internalizing problems in adolescents with ADHD. We hypothesized that less sex/gender alignment would be associated with increased severity of ADHD and internalizing symptoms.

Methods: Adolescents (ages 12-17) with ADHD (n=43; 17 females) and typically developing (TD) controls (n=32; 16 females) completed gender expression questionnaires including the YGISH (from the ABCD study) and the Traditional Masculinity/Femininity (TMF) scale in addition to measures of ADHD symptoms (Conners), internalizing symptoms (BASC Depression, Anxiety), and self-harm (ISAS). Gender assessments were analyzed in the context of diagnosis and biological sex. Within the ADHD group, dimensional analyses were conducted across ADHD symptoms and internalizing symptoms as a function of sex/gender alignment.

Results: TMF and YGISH scores revealed that individuals with ADHD showed less alignment than TD. Compared to the TMF, the YGISH was limited in dimensionality, particularly for biological males.

Less alignment in males with ADHD was associated with greater Inattentive symptoms ($r[20]=.39$), and less alignment in females with ADHD was associated with greater hyperactive-impulsive symptoms ($r[15]=.64$).

Less alignment among adolescents with ADHD was correlated with increased self-reported depression (Females $r[14]=-.45$, Males $r[24]=0.37$), anxiety (Females $r[14]=-.41$, Males $r[24]=.45$), and self-harm ($OR[33]=6.67$, $p=.07$; females>males).

Conclusions: These findings suggest that adolescents with ADHD generally show less sex/gender alignment, which is correlated with increased ADHD symptoms, anxiety, depression, and self-harm. Furthermore, TMF may provide greater sensitivity for assessing alignment in adolescents with ADHD.

S.50 PREVALENCE OF SLEEP DISORDERS AND ASSOCIATIONS WITH COMORBID PSYCHIATRIC DISORDERS IN A CLINICAL SAMPLE OF ADHD ADULTS

Mirte van der Ham1, Denise Bijlenga2, Mylène Böhmer1, Sandra Kooij1, J.J. Sandra Kooij*1

1PsyQ Expertise Center Adult ADHD, The Hague, 2SEIN Sleep-Wake Center,

Hypothesis/Objective: Sleep disorders are common in adults with ADHD, and affect ADHD and other psychiatric symptoms adversely. In this observational study we investigated the prevalence of sleep disorders, and the association between sleep disorders and other psychiatric disorders in adults with ADHD.

Methods: We included adult patients diagnosed with ADHD from all PsyQ locations in the Netherlands, who had filled out the Holland Sleep Disorders Questionnaire (HSDQ) at time of assessment. The HSDQ was used to screen for insomnia, parasomnia, hypersomnia, delayed sleep phase syndrome (DSPS), restless legs syndrome (RLS)/periodic limb movement disorder (PLMD), and sleep breathing disorder (SBD). Data on HSDQ screening, age, sex, and psychiatric comorbidity were retrieved from electronic patient files.

Results: Of the 3,691 adults with ADHD included, 63% had clinically relevant sleep problems, of which DSPS, insomnia, and RLS/PLMD most frequently screened positive (36%; 30%; 29%). Comorbid depression and PTSD were significantly associated with a positive screening for all sleep disorders, whereas anxiety disorder was associated with a positive screening for hypersomnia, insomnia, parasomnia and DSPS, but not RLS/PLMD and SBD.

Conclusions: This study showed a high prevalence of clinically relevant sleep problems in adults with ADHD. They most often screened positive for DSPS, insomnia, and RLS/PLMD. Comorbid depression, anxiety disorder and PTSD were associated with a positive screening for most sleep disorders. When diagnosing a patient with ADHD, practitioners should keep in mind the high probability of comorbid sleep disorders, especially in patients with other comorbidities.

S51. DO TREATMENTS FOR ADULT ADHD IMPROVE EMOTIONAL BEHAVIOR?

Craig Surman*1, Daniel Walsh2

1Massachusetts General Hospital / CHADD, 2Massachusetts General Hospital

Hypothesis/Objective: Dysregulated emotional behavior occurs often in adults with ADHD. Systematic analysis of prior clinical trials may guide clinical intervention and future research.

Methods: Controlled trials of adult ADHD measuring emotional behavior were included if another study offered a comparable analysis of the same treatment method. Standardized Mean Difference (SMD) of effects were calculated, and the size of effects for emotional and non-emotional ADHD behavior were compared.

Results: 13 out of 14 studies of methylphenidate, atomoxetine, and lisdexamfetamine demonstrated significant improvement in emotional behavior measures, with small to high SMDs. The proportional effect on emotional versus non-emotional behavior ranged from 46% to 110% for methylphenidate, 56% to 129% for atomoxetine, and 36% to 96% for lisdexamfetamine.

Conclusions: Psychopharmacological treatments for ADHD are likely to improve emotional behavior, and available scales are sensitive to these effects. Studies dedicated to treatment of this domain of function can further refine clinical approaches.

S52. POSTER WITHDRAWN

S53. VILOXAZINE INDUCES DOSE-DEPENDENT INCREASES IN INTERSTITIAL LEVELS OF NOREPINEPHRINE, DOPAMINE, AND SEROTONIN IN RAT MEDIAL PREFRONTAL CORTEX

*Chungping Yu1, Jennie Garcia-Olivares1, Brittney Yegla1, Jami Earnest1, Frank Bymaster2, Jonathan Rubin1

1Supernus Pharmaceuticals, Inc., 2Bymaster Neuroscience Consulting

Hypothesis/Objective: Utilize microdialysis to evaluate dose-dependent effects of viloxazine on prefrontal monoamine concentrations at therapeutically relevant concentrations of viloxazine for ADHD.

Methods: Sprague-Dawley rats (5-6/group) were implanted with I-shaped microdialysis probes into the prefrontal cortex (PFC). Viloxazine (1, 3, 10, or 30 mg/kg) was administered (i.p.). Dialysate samples were collected from PFC interstitial fluid (ISF) and measured at baseline and post-viloxazine administration at 30 minutes intervals. ISF concentrations of viloxazine, norepinephrine (NE), dopamine (DA), serotonin (5-HT) and their respective metabolites 3,5-dihydroxyphenylglycine (DHPG), 3,4-dihydroxyphenylacetic acid (DOPAC), and 5-hydroxyindoleacetic acid (5-HIAA) were measured.

Results: Viloxazine demonstrated a dose-dependent increase in plasma and ISF concentrations. At 60 minutes, the 30 mg/kg dose of viloxazine induced PFC ISF and unbound plasma maximum concentrations of 3.5 ± 1.6 μM and 2.3 ± 0.7 μM respectively, approximating unbound plasma concentrations in pediatric ADHD patients (2.1-3.3 μM; 400 mg/day). At this clinically relevant dose, NE and 5-HT ISF levels reached 558% and 213% over baseline respectively. Decreases in DHPG concentrations corresponded with NE increases, reflecting viloxazine's inhibition of the norepinephrine transporter (NET). There was not a concomitant decrease in 5-HIAA levels, reaffirming viloxazine's lack of activity as a SERT inhibitor. At the same dose (30mg/kg, i.p.), DA levels were increased over baseline, but DOPAC levels were not consistently quantifiable.

Conclusions: Therapeutic effects of viloxazine ER may involve induction of noradrenergic, dopaminergic, and serotonergic activity in the PFC as clinically relevant doses of viloxazine were able to increase ISF NE, DA, and 5-HT levels in the rat PFC.

Previously presented at ACNP.

S54. ASSESSMENT OF SEROTONERGIC EFFECTS OF VILOXAZINE IN CYNOMOLGUS MONKEYS USING PET IMAGING WITH THE [11C]CIMBI-36 SEROTONIN RECEPTOR (5-HT2A/2C) AGONIST RADIOLIGAND

*Chungping Yu1, Jennie Garcia-Olivares1, Brittney Yegla1, Jami Earnest1, Jonathan Rubin1

1Supernus Pharmaceuticals, Inc.

Hypothesis/Objective: Assess the ability of viloxazine to modify serotonergic neurotransmission in the cortical regions and direct occupancy of 5-HT2C receptors using PET imaging with the radioligand agonist (for 5-HT2A and 5-HT2C receptors), [11C]CIMBI-36.

Methods: Four anesthetized cynomolgus monkeys (n=1-2/dose) were administered bolus infusions of viloxazine (1.0, 3.0, 4.5, 6.0, and 12.0 mg/kg). [11C]CIMBI-36 was administered 30 minutes after viloxazine, immediately prior to initiation of the scanning period. During image acquisition, arterial blood samples were drawn at eight timepoints (2-90 minutes) for quantification of the [11C]CIMBI-36 metabolite. Plasma concentrations of viloxazine were measured in blood samples collected at four timepoints (15-120 minutes) post-administration of viloxazine. Non-displaceable binding potential (BPND) was determined using spatial processing to define regions of interest and total volume of distribution.

Results: The effect of viloxazine administration on [11C]CIMBI-36 binding was dose-dependent. Plasma concentrations showed that the 3 mg/kg dose reached concentration levels of unbound-viloxazine (4.0-6.4 μM) that are comparable with pediatric ADHD patients administered viloxazine ER (2.2-3.3 μM). At this clinically relevant dose, viloxazine reduced BPND in the choroid plexus by 60%. Cortical region changes in [11C]CIMBI-36 may be attributed to either direct occupancy of 5-HT2A or due to interaction of increased synaptic 5-HT (induced by VLX) with the 5-HT2A receptor.

Conclusions: This PET imaging study suggests that viloxazine, at a clinically relevant plasma concentration, directly occupies 5-HT2C receptors in NHP brain. Therefore, these findings support viloxazine’s serotonergic modulatory effect which could play a role in its efficacy in the treatment of ADHD.

Previously presented at ACNP.