outcomes is partially explained by deficits in executive control, or processes enabling self-regulation. Here, we test a novel executive neural target in three fMRI tasks and its relevance to shared psychopathology. METHODS/STUDY POPULATION: We studied 60 children [15 F/45 M; mean age (SD)=11.6 years (1.62)] with diverse diagnoses including attention deficit disorder (n=26) and autism spectrum disorder (n=22). We extracted a latent general factor of psychopathology using principal component analyses applied to parent-report Child Behavior Checklist syndrome scores. Subjects completed 3 executive control fMRI probes, tapping adaptive control, working memory, and inhibition. Correlational psychophysiological interaction (cPPI) analysis measured correlations between executive control-related modulations of activity in 414 network-affiliated parcels. We selected parcels exhibiting control-related cross-network correlations as well as control-related activity across all tasks and tested them for association with psychopathology. RESULTS/ANTICIPATED RESULTS: cPPI connectivity matrices were thresholded and graphs were identified using the Network-Based Statistic toolbox (p90th percentile PC) as well as control-related activation (>10% activated voxels; p DISCUSSION/SIGNIFICANCE: Our results examine cross-network interactions between brain regions during 3 fMRI tasks and their role in explaining individual variation in psychopathology. As executive control links to both comorbidity and life outcomes, identifying the clinically-relevant neural correlates of controlled behavior may lead to transdiagnostic treatments.

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Unraveling and targeting the innate immune response in Multisystem Inflammatory Syndrome in Children (MIS-C)

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OBJECTIVES/GOALS: The innate immune responses to Multisystem Inflammatory Syndrome in Children (MIS-C) are not fully known. Using samples from MIS-C, we will assess the cellular responses and develop a novel Tri-Specific Killer Engager (TRiKE) that engages innate immune cells to improve those responses. METHODS/STUDY POPULATION: We collected blood samples from 60 pediatric patients from which we isolated plasma and peripheral blood mononuclear cells. We received blood samples from 13 MIS-C, 32 severe acute COVID, 5 COVID-19 asymptomatic, and 15 COVID-19 negative patients. Using plasma, we then performed ELISAs to determine IgG antibody levels against SARS-CoV-2 and plaque reduction neutralization tests to determine neutralizing antibody functions. We isolated DNA to look at Fc receptor genetics. We also utilized utilize flow cytometry assays determine the phagocytosis and killing abilities of the innate cells from these patients. This data will be correlated with clinical outcomes. Additionally, we have developed a novel SARS-CoV-2 TRiKE which directs natural killer (NK) cell killing specifically to of COVID-19 infected cells. RESULTS/ANTICIPATED RESULTS: MIS-C patients had higher IgG antibody titers against SARS-CoV-2 compared to children with symptomatic or asymptomatic COVID. MIS-C patients also neutralized SARS-CoV-2 more effectively than children with acute symptomatic or asymptomatic COVID-19. We found natural killer cells and monocytes are dysfunctional in MIS-C patients and do not kill SARS-CoV-2 infected cells as well. Specifically, NK cells do not kill COVID-19 infected cells as well. To combat this, we have successfully generated and are now testing a Tri-Specific Killer engager (TRiKE) which binds one ends to NK cells, one end to the Spike protein on COVID-19 infected cells and contains IL-15 to improve NK cell function. We anticipate that we can improve NK cell killing of COVID-19 infected cells with this TRiKE. DISCUSSION/SIGNIFICANCE: We found that MIS-C patients have antibodies that can neutralize SARS-CoV-2 but that that innate immune cells that engage antibodies are dysfunctional. We are have successfully developed and are targeting this response with a TRiKE to improve innate immune cell functional; this may serve as an adjunctive therapeutic if proven successful.

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Upregulated Genes in Age-Related Lobular Involution Stagnation Represent Potential Biomarkers That Link To Increased Breast Cancer Risk*

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OBJECTIVES/GOALS: Age-related lobular involution (LI) is a physiological process of breast epithelial regression that occurs primarily during perimenopause (ages 45-55); women in this age range for which the process of LI is delayed, defined as LI stagnation, show significantly increased risk of breast cancer as compared to LI progression patients. METHODS/STUDY POPULATION: The Mayo Clinic Benign Breast Disease (BBD) cohort includes ~1000 women who had multiple sequential benign biopsies. 103 patients were found to have sequential biopsies during the perimenopausal period, of which 10 eventually progressed to breast cancer. These patients were assessed for LI stagnation vs LI progression by quantifying 10 lobules per slide and comparing median acini number and median lobule size between initial and subsequent biopsies from the same patients. RNA was derived from whole tissue sections from the initial biopsies, and profiled using NanoString IO360 and BC360, which were normalized using RUVg methods. Differentially expressed genes associated with LI stagnation were defined as having two-tailed, unpaired p-values less than 0.05. RESULTS/ANTICIPATED RESULTS: Analysis showed subsetting patient sets by time between biopsies improves classification of stagnant vs. progression. Differential gene analysis identified 37 genes associated with LI stagnation and LI progression, and 20 of these genes were found to overlap a set of 128 gnese that were differentially expressed between women who subsequently developed breast cancer vs remained cancer-free. These genes represent potential biomarkers of processes that link LI stagnation and increased breast cancer risk. DISCUSSION/SIGNIFICANCE: In future studies, we intend to study these genes that were shown to be upregulated in LI stagnation for their association with subsequent development of breast cancer in independent cohorts of women with BBD. We will use this knowledge to improve individualized risk assessment, which will help focus surveillance and prevention strategies.

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Using Assessments to Create a Translational Pipeline at a Science-Based Inpatient Addiction Treatment Facility

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OBJECTIVES/GOALS: Effective translation of data to inform real-time patient care is lacking in addiction inpatient settings. The

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current study presents the optimization of a Comprehensive Rehabilitation Assessment summary report that is used by clinicians to individualize treatment. METHODS/STUDY POPULATION: A multi-aim approach was taken that utilized aspects of various implementation science frameworks. Participants were clinical staff (N = 7; female = 71%). A quantitative survey was used for aims 1 and 2 to assess motives and context around the report as well as evaluate the design of it. Aim 3 focused on optimization via semi-structured interviews. Descriptive and modified content analyses were utilized appropriately for each aim. RESULTS/ANTICIPATED RESULTS: Five versions of the assessment report were created between February 2021 and August 2022, the most recent of was adapted into patients'electronic medical records based on study results. Each report version, participants'results/feedback, and researchers'perceived barriers to this translational process will be discussed. DISCUSSION/SIGNIFICANCE: The current study highlights a replicable approach for optimizing the translation of assessment data into treatment for patients with disorders of addiction.

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Using autism symptom profiles at intervention baseline to predict social cognitive outcomes

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Rush University Authorship has not yet been determined and finalized, but all will be at Rush University.

OBJECTIVES/GOALS: 1) Investigate the utility of pragmatic communication profiles in a sample of children with autism at baseline to predict response to treatment in a randomized clinical trial (RCT) of oxytocin augmentation and social cognitive skills training at week 12. 2) Determine if levels of anxiety or hyperactivity moderate child outcome performance. METHODS/STUDY POPULATION: 40 children (37M, 3F), aged 8-11(M=9.25, SD=1.10), with confirmed autism spectrum disorder (ASD), enrolled in an RCT(NCT02918864) were evaluated at baseline on: an assessment of ASD (Autism Diagnosis Observation Schedule, ADOS-2), a task of perspective taking, Theory of Mind ToM, (Reading the Mind from the Eyes Task), pragmatic communication (Pragmatic Rating Scale-School Aged; PRS-SA), IQ (WAIS_I, WISC-V) and anxiety and hyperactivity (Behavior Assessment Scales for Children-3; BASC-3). A Tobii T60 XL was used for eye-tracking visual patterns and attention during the RMET. The PRS-SA was coded by trained, reliable clinicians. Parent ratings indicated over half of the participants' had At Risk levels or higher on anxiety and hyperactivity on the BASC-3. Week 12 measures included all but the PRS-SA and ADOS-2. RESULTS/ANTICIPATED RESULTS: Baseline preliminary analysis indicated the participants spent more time looking at words (.41ms) than eye images on the RMET(.15ms, p DISCUSSION/SIGNIFICANCE: Findings at baseline suggest pragmatic communication skills are more related to ToM than gaze and attention on the RMET. This relationship will be further investigated over the time of the trial. Mental health indicators need to be considered further in this population. Child profiles at baseline may inform appropriate triage and treatment targets.

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Utilization of machine learning approaches on multimodal and ambulatory data to predict individualized symptom course in adults with obsessive-compulsive disorder.

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OBJECTIVES/GOALS: This study will collect multimodal and longitudinal data in adults with obsessive-compulsive disorder and healthy controls. A mixed effects random forest machine learning approach will be taken to develop a model that can predict individualized longitudinal OCD symptom burden. METHODS/STUDY POPULATION: Baseline resting state functional MRI (rsfMRI) and measures of symptom burden will be collected in adults with OCD and healthy controls. Longitudinal measures of behavior and physiology–such as heart rate, activity, and sleep metrics - will be collected using Fitbit Charge 5 tracker. Daily assessments of symptom burden and functional status will be collected through a smartphone app. Individuals with OCD will start pharmacotherapy during the study period and all participants will be followed for a total of 10 weeks. Repeat rsfMRI imaging will occur at study conclusion. Data will be analyzed using a mixed effects random forest machine learning algorithm with assessment of model performance. RESULTS/ANTICIPATED RESULTS: Prior studies of symptom severity in psychiatric illness and affect in non-clinical populations have found longitudinal features - such as lexical and acoustic measures, participant context, heart rate, and sleep metrics–that were predictive of these states over time. It is anticipated that the present study will extend these results to individuals with OCD and identify physiologic and behavioral features that track personalized symptom burden longitudinally in this patient population. A model able to predict when symptoms are elevated could allow for provision of additional treatment or interventions targeted to times of high symptom burden. DISCUSSION/SIGNIFICANCE: This study will be the first to collect and analyze longitudinal measures of behavior, symptoms, and physiology in patients with OCD with a goal of predicting symptom burden. Identification of elevated symptom burden would allow for implementation of just-in-time treatment, during these periods.

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Waste not, test more: Innovations in tissue processing to expand the testing of clinical specimens

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OBJECTIVES/GOALS: Clinical tissue specimens are primarily destined for formalin fixed, paraffin embedded processing to create a basis for diagnosis by microscopic examination. Innovations in specimen processing are required to expand its availability for inclusion as the substrate in assays that can contribute to the further development of

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