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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