P136. Trauma Exposure, Endocannabinoid Signaling, and Variation in Frontolimbic White Matter Pathways in Children

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Background: The endocannabinoid system plays a key role in modulating brain development throughout the lifespan, including myelination. Recent studies link a common variant (C385A) in the fatty acid amide hydrolase (FAAH) gene to higher endocannabinoid levels, lower anxiety, and altered frontolimbic development. Frontolimbic pathways demonstrate a protracted maturational course across childhood and adolescence, are associated with anxiety, and are sensitive to environmental stressors (e.g., trauma exposure). Here, we examined the impact of trauma exposure and the FAAH C385A variant on anxiety and frontolimbic white matter integrity in children.
Methods: We leveraged data from the Adolescent Brain Cognitive Development (ABCD) study (n=10,774; M±SD age=9.92±0.62 years; 47.9% female). Saliva samples were used for genotyping and parents reported on their child's anxiety symptoms (Child Behavior Checklist) and trauma exposure (Kiddie Schedule for Affective Disorders and Schizophrenia). Fractional anisotropy (FA) was estimated from DTI data for frontolimbic pathways.
Results: Forty-five percent of youth were FAAH A-allele carriers (55% non-carriers) and 36% were exposed to trauma (64% unexposed). Relative to controls, trauma-exposed youth demonstrated higher anxiety symptoms and higher FA of the right and left uncinate ($p<0.05$). There was no main effect of FAAH C385A or trauma-by-FAAH interaction on anxiety symptoms. Compared to non-carriers, A-allele carriers demonstrated higher FA in the left and right fornix and parahippocampal cingulum ($p<0.05$). There were also trauma-by-FAAH interactions for FA in the left and right fornix, and left parahippocampal cingulum ($p<0.05$).
Conclusions: Results highlight the role of trauma exposure and endocannabinoid signaling in modulating frontolimbic development and anxiety risk in children.
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Keywords: Endocannabinoids, Childhood Trauma, Diffusion Tensor Imaging, Gray Matter, White Matter, Resting State

P137. Differential Effects of Early Life Stress During Sensitive Periods of Development on Anxiety-Like Behavior and Gene Expression Response in Adult Mice

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Background: Preclinical ELS models (e.g., maternal separation) have been extensively used to investigate biomolecular changes underlying the behavioral outcomes in response to stress exposure during early postnatal period. However, it still unclear how the reprograming effects of these early stress experiences could interact with the exposure to a second stressor during later periods of development, such as adolescence. To address that, this study investigated how maternal separation would interact with chronic adolescence stress exposure on anxiety-like response, gene and protein expression of GR and FKBP5 in the hippocampus.
Methods: Balb/c mice were submitted to prolonged maternal separation (MS); unpredictable chronic stress (UCS); second hit stress model (MS+UCS) or animal facility rearing (AFR) conditions. Two independent cohorts were run to evaluate baseline biomarker parameters and behavioral phenotype using three classical anxiety-like behavior tasks. Corticosterone levels (CORT), gene expression of glucocorticoid receptor (GR) and FKBP5, as well as GR protein levels were measured.
Results: As expected we found a robust effect of UCS condition revealing an increase on anxiety-like parameters, CORT response and GR and FKBP5 gene expression. Interestingly, MS+UCS animals showed an inhibited behavioral and biological response in GR and FKBP5 mRNA expression and in GR protein levels. GR protein were found increased in cytosol, while reduced in the nucleus.
Conclusions: Our findings suggested that animals exposed to MS exhibited a blunted reactivity response when challenged with a second stressor in adolescence. Blunted stress response could reflect a differential second hit effect failing to adequate the biological and behavioral response to the environmental challenge.
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Keywords: Early Life Stress, Animal Model, Maternal Separation, Unpredictable Chronic Mild Stress, Anxiety-Like Behavior

P138. Prefrontal Connections to the Extended Amygdala and Their Role in Early-Life Inhibited Temperament in Adolescent Rhesus Monkeys

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Background: The extended amygdala has been implicated in the expression of fear and anxiety, and is thought to mediate early-life risk for psychopathology. How these regions interact with newly expanded areas of the primate frontal cortex remains largely unknown. Using a well-validated primate model, we leverage a multimodal neuroimaging to explore the contributions of prefrontal-connections in early-life inhibited temperament, a risk factor for the future development of stress-related psychopathologies