patients with high treatment expectancy ratings (Estimate=0.43, S.E.=0.6, $p=0.03$), especially under the high expectancy and positive neurofeedback condition (Estimate=0.56, S.E.=0.28, $p=0.04$).

Conclusions: In patients with depression, antidepressant treatment expectancies interact with unfolding reinforcement. Specifically, mood improves when positive expectancies are confirmed by positive reinforcement.

Supported By: NARSAD, K23

Keywords: Expectancy, Reinforcement Learning, Mood

O40. Attention and Reward-Related Decision-Making Deficits Differentiate Youth With Bipolar Disorder From Healthy Individuals: A Machine Learning Study

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Background: Our previous work shows that young and old adults with bipolar disorder (BD) display poor reward-associated decision making (RDM). RDM in youth with BD is a largely unexplored research area. This study uses a component-wise gradient (CGB) machine learning algorithm to identify cognitive measures that can accurately differentiate youth with BD from a healthy comparison group.

Methods: 108 healthy controls (HC; 10.36±3.28 yo, 67F) and 119 children and adolescents with BD (13.31±3.02 yo, 52F) completed the CANTAB cognitive battery. Available data was split into two partitions for algorithm training (80%) and testing (20%). The algorithm was tuned using 10-fold cross validation and evaluated using classification accuracy and area under the receiver operating characteristic curve (AUROC). Algorithm training provided variable selection and measures of variable importance for model interpretation.

Results: After algorithm tuning, CGB achieved accuracy of 73.2% and an AUROC of 0.785 in classifying individuals as either BD or non-BD on a held-out data set for testing. The strongest cognitive predictors of BD were selective and sustained attention, RDM deliberation time, and quality of RDM.

Conclusions: Performance on attention and RDM tasks differentiate youth with BD from HC. This finding will need to be replicated in independent cohorts for generalization purposes. Further studies in high-risk individuals are needed to determine whether deficits in these cognitive domains are related to the disorder or are markers of vulnerability to BD.

Supported By: NIMH

Keywords: Bipolar Disorder, Reward Processing, Children and Adolescence, Machine Learning

O41. CREB-Zfp189 Interactions Regulate a Resilient-Specific Transcriptional Network in Animal Models of Depression

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Background: Major Depressive Disorder (MDD) is associated with abundant transcriptional alterations. RNA sequencing studies in animal depression models corroborate these findings, but find quantitatively more changes in stress resilient animals. Despite this, most studies of resilience have focused on single genes, and the mechanism by which sets of genes interact to induce resilience is currently unknown.

Methods: To address this, we performed weighted gene co-expression network analysis (WGCNA) on RNA transcripts following 10 days of chronic social defeat stress (CSDS).

Results: We identified a network of genes unique to the resilient phenotype. Zfp189, which encodes a previously uncharacterized zinc finger protein, was the most connected gene in this resilient-specific network and was differentially expressed in the prefrontal cortex (PFC) of resilient mice. Consistent with these findings, Zfp189 overexpression in mouse PFC was both pro-resilient and antidepressant, and RNA sequencing of virally infected tissue showed preferential changes in the network from which Zfp189 originates. We found that CREB is a predicted upstream regulator of our resilient network and ChIP-chip data found that CSDS decreased CREB binding to Zfp189, a phenomenon that was reversed by the antidepressant imipramine. Accordingly, knockout of CREB in the PFC increased susceptibility to stress, but the deleterious effects of CREB knockout were ablated by Zfp189 overexpression. Additionally, we utilized CRISPR to direct activated CREB to the Zfp189 locus in the PFC, and this too was sufficient to increase resilience.

Conclusions: These findings suggest that CREB interacts with Zfp189 to regulate a resilient-specific transcriptional network in PFC that induces behavioral resilience.

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Keywords: Major Depressive Disorder (MDD), Transcriptomics, Gene Networks, CREB, Antidepressant Response

O42. Gene-Environment Correlation Does not Explain Away the Association Between Childhood Trauma and Psychopathology: A Monozygotic Twin Differences Approach

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ORAL SESSION
Depression & Psychosis
3:00 p.m. — 5:00 p.m.
Chair: Dan Iosifescu

¹KU Leuven, ²Ghent University, ³Maastricht University, ⁴UMC Utrecht

Background: It is generally assumed that childhood trauma (CT) is a causal risk factor for psychopathology. However, studies have shown that baseline psychopathology may actually increase risk for subsequent victimization, suggesting that exposure to CT is not random but may result from pre-existing vulnerability. Therefore, studies testing whether the association between CT and psychopathology persists when accounting for gene-environment correlation are much needed.

Methods: A monozygotic (MZ) twin differences approach was used to examine whether differences in CT exposure among MZ twin pairs would be associated with MZ differences in symptoms. As MZ twins are genetically identical, within-pair correlations between CT exposure and psychopathology would rule out the possibility that the association is solely attributable to gene-environment correlation. 146 monozygotic twin pairs (n=292) recruited from the general population were selected for this study.

Results: In the whole sample, CT was associated with symptoms of psychopathology ($B=43.13$; $SE=6.27$; $p<.001$). There were meaningful differences within MZ twin pairs in CT exposure and symptoms. These within-pair differences in CT exposure were associated with within-pair differences of overall psychopathology ($B=29.22$; $SE=12.24$; $p=.018$) as well as specifically symptoms of anxiety ($B=0.65$; $SE=0.21$; $p=.002$), depression ($B=0.37$; $SE=0.18$; $p=.043$), and psychosis ($B=0.35$; $SE=0.16$; $p=.024$).

Conclusions: While it is not unlikely that pre-existing vulnerability may increase the risk for traumatic exposures, such gene-environment correlation does not explain away the association between CT and psychopathology. The present findings thus suggest that at least part of the association between CT and psychopathology may be causal.

Supported By: Other

Keywords: Childhood Trauma, Twins, Gene X Environment, Psychopathology

O43. Cognitive and Emotional Biomarkers of Anxious Major Depressive Disorder: An iSPOT-D Report

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Background: Major depressive disorder (MDD) commonly co-occurs with one or more anxiety disorders or with clinically significant levels of anxiety symptoms. While evidence

suggests these anxious forms of MDD present with more severe clinical profiles and are prognostic of poorer antidepressant treatment outcomes, little is known of their cognitive and emotional functioning. We compared cognitive and emotional functioning in various forms of anxious MDD and assessed whether functioning could predict antidepressant treatment outcome.

Methods: 1,008 adults with MDD and 336 healthy controls completed IntegNeuro: a computerized cognitive and emotional functioning assessment battery. Participants were then randomised to one of three antidepressants and reassessed at 8 weeks regarding 17-item Hamilton Depression Rating Scale (HRSD17) and 16-item Quick Inventory of Depressive Symptomatology-Self-Rated (QIDS-SR16) remission and response. Anxious MDD was defined using common criteria (i.e., MDD with one or more anxiety disorders, or a HRSD17 Anxiety subscale score > 7) and theoretically driven novel criteria (i.e., MDD with severe/extremely severe Depression Anxiety Stress Scales (DASS) Anxiety and Stress subscale scores).

Results: Syndromal anxious MDD had poorer working memory, HRSD anxious MDD had better emotion identification, and DASS anxious MDD had poorer working memory and cognitive flexibility compared to their non-anxious counterparts. Baseline functioning in people with HRSD anxious MDD also predicted QIDS-SR16 response (74% cross-validated accuracy).

Conclusions: Cognitive and emotional functioning in anxious MDD varied depending on its definition, but generally compounded existing MDD deficits with anxiety related deficits (i.e., executive functions). Subtyping by anxious MDD can also help develop cognitive and emotion-based treatment prediction biomarkers.

Supported By: The Brain Resource Company, NSW Health PhD Scholarship

Keywords: Major Depressive Disorder (MDD), Anxiety, Cognition, Emotion

O44. Effort and Reward Evaluation in Remitted Depression: A Preliminary Report on a Possible Predictor of Relapse

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Background: Relapse after antidepressant medication (ADM) discontinuation is high (30% in 6 months) and no established predictors exist. The role of anhedonia, one of the core