that self-reported euphoria, fear or anxiety during ketamine's psychoactive period mediates antidepressant response. We predicted that greater euphoria and lower anxiety and fear would predict reduced depressive symptom-severity one (D1) and seven (D7) days following infusion.

Methods: We administered a standard adverse events (AE) questionnaire (scored from zero-three) that included "euphoria," "fearful," and "anxiety" items measured immediately after 40-minute infusions of 0.5 mg/kg ketamine and saline. Our primary outcome was the Montgomery Asberg Depression Rating Scale (MADRS). We used drug*AE-interactions from mixed models to test mediation hypotheses. Covariates included diagnosis and baseline MADRS.

Results: We did not detect any drug*AE interactions associated with D1 MADRS-scores. While greater anxiety was associated with higher D1 MADRS for ketamine and placebo, ($p= 0.007$), main effects of fear ($p=0.062$) and euphoria ($p=0.059$) were weaker. We did not detect D7 interactions or main effects.

Conclusions: Our results do not support a role for peri-infusion, psychoactive experiences in ketamine's antidepressant mechanism. Short-lasting associations between experiences and response observed with ketamine and placebo is consistent with extra-pharmacological effects. Further research is warranted since this analysis is post-hoc and had limited measures of psychoactive experiences.

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Keywords: Ketamine, Treatment-resistant Depression, Non-specific Effects, Behavioral Biomarkers, Psychoactive Effects

Assessing the Link Between Schizophrenia and Antisocial Behavior in Not Guilty by Reason of Insanity (NGRI) Acquittees

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Background: Schizophrenia is considered one of the most impactful psychiatric disorders leading to serious mental illness (SMI) classification. To date, there is mixed evidence linking schizophrenia to antisocial behavior, with some research supporting the association and some not. Research is needed to understand what mechanisms may explain schizophrenia-related antisocial behavior. This study tested if psychopathy, a well-known risk factor for antisocial behavior, mediates the link between schizophrenia symptoms and violent crime, nonviolent crime, aggression, and antisocial behavior in Not Guilty by Reason of Insanity (NGRI) acquittees.

Methods: In a sample of 82 NGRI acquittees (Mage=37 years; 78% male), we assessed psychopathy using the Psychopathy Checklist: Revised (PCL-R; Hare, 2003), schizophrenia symptoms, antisocial behavior, and aggression were measured using the Personality Assessment Inventory (Morey, 2007), and criminal history was coded using criminal files.

Results: No significant direct effects were found for schizophrenia on violent crime or nonviolent crime. There was a significant indirect effect for psychopathy fully mediating the link between schizophrenia and violent crime (b=.01, SE=.01, 95% CI[.01,.03]) and nonviolent crime (b=.02, SE=.01, 95% CI [.01,.05]). A direct effect was found for aggression ($p<.001$) and antisocial behavior ($p<.001$), and psychopathy partially mediated the link between schizophrenia and aggression (b=.05, SE=.03, 95% CI[.01,.11]) and antisocial behavior (b=.07, SE=.04, 95% CI[.01,.17]).

Conclusions: The present study suggests that mixed evidence linking schizophrenia to antisocial behavior may be due, in part, to psychopathic traits. Even in patients where rates of SMI are high, psychopathy explains the link between past and future risk of antisocial behavior for those with schizophrenia.

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Keywords: Schizophrenia, Psychopathy, Violence, Serious Mental Illnesses, Not Guilty by Reason of Insanity

Associations Between Trauma Exposure, Internalizing Symptoms, and Functional Connectivity in Youth

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Background: Traumatic early-life experiences can have lasting effects on brain and behavior, including altered functional connectivity. However, it remains unclear whether trauma-related patterns of altered connectivity can be observed in children, and whether individual differences in connectivity can predict psychopathology symptoms. Clarifying these links could provide insight into the etiology of trauma-related brain changes, and their relation to psychiatric symptoms.

Methods: Here, we use data from 3,691 youth ages 9-10 (49.4% female) enrolled in the Adolescent Brain Cognitive Development Study (Release 2.0, DOI: 10.15154/1503209; Release 1.1, DOI: 10.15154/1412097) to examine associations between trauma exposure, functional connectivity at rest (fast-track data), and internalizing symptoms.

Results: Using the Network Based Statistic, we identified a network that differed between trauma-exposed and non-exposed participants ($p<.001$). Linear mixed-effects models revealed a negative association between trauma exposure and mean network connectivity ($p<.001$). Mean network connectivity did not predict internalizing symptoms, but exploratory within-network analyses revealed that mean connectivity of edges connected to bilateral amygdalae were positively associated with trauma exposure ($p=.033$), and an interaction between participant sex and mean amygdala connectivity predicted internalizing symptoms ($p=.038$).

Conclusions: These findings support prior evidence that trauma exposure in childhood is associated with altered neural connectivity. We advance previous work by identifying a network that significantly differs between trauma-exposed and non-exposed participants, and demonstrate that connectivity

within limbic regions is associated with internalizing symptoms in a sex-specific manner. This work highlights the complex interactions between brain and symptoms during development, and supports previous work implicating limbic connectivity as a potential biomarker for psychiatric symptoms.
Supported By: NIH and additional federal funding for the ABCD study, Jacobs Foundation, NIMH, BBRF
Keywords: Childhood Trauma, Resting State fMRI, Brain Networks, Child Internalizing Symptoms, Adolescent Brain Cognitive Development (ABCD) Study

Bayesian Network Modeling Suggests Adolescent Cannabis Use Causes Accelerated Dorsal Prefrontal Thinning

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Background: While neurobiological differences have been found in cannabis users relative to non-users, it is unclear if these differences are caused by cannabis use. Here we investigate if adolescent cannabis use causes cortical thinning using Bayesian causal network modeling, which leverages conditional probabilities among variables to estimate the strength and direction of associations in a directed acyclic graph.
Methods: We examined data from 697 adolescents from the IMAGEN dataset with structural MRI data at ages 14 and 19. All participants had never used cannabis at age 14; by age 19, 47% had used cannabis at least once. Structural MRI data was used to derive cortical thickness, which we tested vertexwise for differences in cannabis initiators. Then, we extracted average thickness for each participant in regions differentiating cannabis initiators from non-users and conducted 10,000 Bayesian causal network modeling simulations for each of five network structure learning algorithms.
Results: At age 19, participants who had initiated cannabis use had thinner dorsolateral and dorsomedial prefrontal cortices, even after accounting for alcohol and tobacco use. In all five algorithms, greater than 70% of simulations indicated that the initiation of cannabis use between 14 and 19 was causing dorsal prefrontal cortex thinning, rather than dorsal prefrontal thinning causing cannabis use.
Conclusions: The current results leverage the temporal sequence of longitudinal data and Bayesian modeling of conditional probability to provide evidence that adolescent cannabis use causes accelerated thinning of the dorsal prefrontal cortex. Further research should confirm these findings in larger samples and using other approaches.
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Keywords: Cannabis, Adolescence, Structural MRI, Causal Inference, Cortical Thickness

Behavioral and Biological Resilience Modulates Stress Effects on Epigenetic Aging

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Background: Our society is currently going through a stress epidemic, and this has led not only to negative psychological impacts, but physical outcomes as well. Cumulative stress has been linked to negative long-term health outcomes, raising the possibility that stress is related to accelerated aging.
Methods: In this study, we use a recently developed epigenetic clock, "GrimAge," to ask whether epigenetic aging is affected by cumulative stress (as measured by the CAI) and psychological resilience (measured via DERS and B-SCS scales) in a cross-sectional study of a healthy community population between the ages of 18-50. We then assess correlations between these findings and physiologic resilience factors.
Results: We find that stress is associated with accelerated GrimAge, even after accounting for demographic and behavioral covariates. This effect is directly moderated by emotion regulation, while self-control influences this relationship by moderating the effect of stress on insulin resistance. We also identify correlations between stress, GrimAge acceleration, and physiological resilience factors (HPA and insulin signaling) which suggest broad impacts of stress on the physiology of aging.
Conclusions: Together, these results demonstrate that the influence of cumulative stress acts through physiologic and behavioral factors to accelerate epigenetic aging. previous associations between GrimAge acceleration and increased mortality suggest those with poor emotion regulation and high stress may be at up to a 50% increased relative risk of death. Further studies could determine if interventions to address these psychological and biological resilience factors may alter the course of epigenetic aging acceleration and break the link between stress and aging.
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Keywords: Accelerated Aging, Chronic Stress, Emotion Regulation, Epigenetic Aging, Insulin Resistance

Changes in Personal Space During the COVID-19 Pandemic

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Background: Personal space, as defined by the distance that people prefer to maintain from others, is determined by trait-like, individual preference and contextual factors. During the COVID-19 pandemic, the practice of "social distancing" has been adopted to decrease the likelihood of virus transmission, but it is unknown whether personal space preferences (which have high test-retest reliability) have been altered as a result. Here we measured personal space characteristics in healthy individuals using the well validated Stop Distance Paradigm (SDP), at two time points: before and after the onset of the COVID-19 pandemic. Personal space measurements, as