treatment may require a more intensive pharmaco-psychotherapeutic approach than was implemented in this study.
Funding Source: Swiss National Science Foundation under the framework of Neuron Cofund, Swiss Neuromatrix Foundation, and Heffter Young Investigator Fellowship Award
Keywords: Serotonergic Psychedelics, Alcohol Use Disorder (AUD), Psilocybin-assisted psychotherapy

596. Utilizing Baby and Adult Functional Brain Landscapes to Develop a Model-Free Measure of Neurocognitive Maturation in Adolescence

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Background: Early adolescence is a period of growth in cognitive performance and functioning. Here, we assess the maturation status of brain functional landscape in early adolescence by directly comparing an individual youth's resting state functional connectivity (rsFC) to the canonical early-life and adulthood communities. Specifically, we hypothesized that the degree to which a youth's connectome is better captured by adult networks compared to infant/toddler networks is predictive of their cognitive functioning and its development.
Methods: To test this hypothesis both across individuals and longitudinally, we utilized data from the Adolescent Brain Cognitive Development Study at baseline (9-10 years; n=6,489) and 2-year-follow-up (11-12 years; n=5,089). To construct our anchored rsFC maturation score (AFC), we measured the difference in system segregation (within-network minus between-network connectivity) when a connectome is arranged according to canonical adult vs. baby networks.
Results: Cross-sectionally, we found that higher AFC was associated with better performance in the N-back task across participants, adjusted for demographic and nuisance factors (adjusted_β=0.10**). Longitudinally, increased AFC was associated with improved task performance within participants (adjusted_β=0.09**). AFC was sensitive to age and aging, and statistically mediated age's relationship with task performance. Exploratory analyses with previously developed data-driven network predictors of cognition and substance use showed AFC was positively correlated with network predictors of NIH-Toolbox task (adjusted_β=0.06**) and negatively correlated with network predictors of early substance use initiation (adjusted_β= -0.09**).
Conclusions: We showed that a model-free index of the brain at rest that is anchored to both baby and adult connectivity landscapes predicts cognitive performance and development in youth.
Funding Source: National Institute on Drug Abuse K01 DA059598
Keywords: Neurocognitive development, Functional brain connectivity, Adolescence

597. Maternal Inflammation During Pregnancy and Adolescent Alcohol Use in Offspring: Exploring a Mediating Role of Childhood Internalizing and Externalizing Symptoms

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Background: Prenatal maternal inflammation (PNMI) has been associated with sex-specific psychiatric outcomes in offspring throughout development, including internalizing/externalizing symptoms in childhood. Both internalizing and externalizing symptoms have been associated with future alcohol use. This analysis explored the sex-specific effects of childhood internalizing/externalizing symptoms mediating the relationship between PNMI and adolescent alcohol use.
Methods: Data from 718 mother-offspring dyads from the Child Health and Development Studies cohort included first (T1) and second trimester (T2) maternal serum levels for inflammatory biomarkers [interleukin (IL)-6, IL-8, IL-1 receptor antagonist (IL-1RA), and soluble TNF receptor-II, offspring internalizing/externalizing behavior at ages 9-11, and frequency of offspring alcohol use at ages 15-17. Conditional processing models were conducted to examine the indirect effect of internalizing/externalizing symptoms on the relationship between PNMI and adolescent alcohol use, accounting for conditional effects of sex assigned at birth. Analyses controlled for maternal education.
Results: For male offspring, multiple biomarkers of T1 PNMI predicted increased alcohol use (IL-8: b=0.167, $p < 0.05$; IL-1RA: b=0.500, $p < 0.05$), and externalizing symptoms (IL-8: b=0.251, $p < 0.05$; IL-6: b=0.466, $p < 0.05$). For female offspring, T1 and T2 IL-6 predicted decreased alcohol use (T1: b=-0.411, $p < 0.05$; T2: b=-0.557, $p < 0.01$), while a different T2 PNMI predicted internalizing symptoms (IL-1RA: b=1.480, $p < 0.01$). Childhood internalizing and externalizing symptoms did not mediate the relationship between PNMI and adolescent alcohol use.
Conclusions: Findings suggest that different types of PNMI may exert independent sex-specific effects on adolescent alcohol use and internalizing/externalizing symptoms. Further research should examine additional mechanisms through which PNMI may contribute to offspring substance use.
Funding Source: This research was supported by grants from the National Institute of Mental Health (Grant nos. R01 MH096478; R01 MH118545) awarded to Dr. Lauren M. Ellman. This study was also supported by the Department of Health and Human Services Contract from the Eunice Kennedy Shriver National Institute of Child Health and Development, National Institutes of Health (Grant no. HHSN275201100020C).
Keywords: Maternal Inflammation, Adolescent Alcohol, Pregnancy, Child Internalizing, Externalizing Problems