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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
well as skin conductance data, were collected using both a standard and a virtual reality version of the SDP. We tested the hypothesis that personal space has been altered during the COVID-19 pandemic.

**Methods:** Personal space characteristics, skin conductance responses and self-report measures were collected at two time points in 11 healthy subjects in response to both real and virtual humans.

**Results:** Personal space size and its correlates were significantly increased after (versus before) the onset of the COVID-19 pandemic in response to both real and virtual humans (all p < .019). Moreover, this change, in both real and virtual space, was significantly correlated with participants’ worry about COVID-19 (all p < .022).

**Conclusions:** Even in a virtual environment, healthy individuals now maintain greater distances from others during (versus before) the COVID-19 pandemic. This type of behavioral change may represent an early marker of changes in social functioning related to the pandemic.

**Supported By:** Massachusetts General Hospital Executive Committee on Research Funds

**Keywords:** Personal Space, COVID-19, Virtual Reality, Skin Conductance, Social Functioning

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**Characterizing Reward System Neural Trajectories From Adolescence to Young Adulthood**

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**Background:** Mixed findings exist in studies comparing brain responses to reward in adolescents and adults. Beyond reward systems, adults typically demonstrate more efficient network properties compared to adolescents. However, no study with a large-sample longitudinal design has examined the trajectories of brain response and task-modulated network during reward processing.

**Methods:** Participants from the IMAGEN study performed a Monetary Incentive Delay task during fMRI at age 14 (BSL; n=1,304) and age 19 (FU2; n=1,241). Brain activation during reward anticipation and task-modulated networks constructed using gPPI and summarized with graph theory metrics were compared between BSL and FU2. To explore alcohol use in relation to development, participants with AUDIT<2 at BSL but ≥8 at FU2 were compared with AUDIT<2 at BSL and FU2.

**Results:** Lower brain activations in bilateral caudate, VS, thalamus, midbrain, dACC and left precentral and postcentral gyrus but greater activations in bilateral IFG, MFG and right precentral and postcentral gyrus were found at FU2 compared to BSL. Lower network shortest path length and greater strength were observed at FU2. Significant interactions between alcohol use and time (BSL vs. FU2) were found in network shortest path length and nodal degree in frontal regions.

**Conclusions:** Five years’ development from adolescence to young adulthood was characterized by reduced reward-related activity in subcortical areas (e.g., the ventral striatum) and increased activity in cortical areas (especially frontal cortex). Mirroring these regional changes, the brain network involved in reward anticipation also became more efficient. Notably, this developmental pattern was altered in those who increased their drinking during these years.

**Supported By:** R01DA047119

**Keywords:** Non-dependent Alcohol use, Developmental Trajectories, Adolescents, Reward Anticipation

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**Childhood Trauma, Emotional Dysregulation and Salivary Inflammatory Biomarkers**

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**Background:** Childhood trauma and emotional dysregulation represent two risk factors for the development of psychopathology later in life and childhood trauma has been associated with increased levels of blood immune biomarkers. Recent literature suggests measure of inflammatory markers in the saliva as a more feasible methodology for studies in childhood and adolescence. The aim of this study was to investigate the association between history of childhood trauma, the presence of emotional dysregulation in adolescents and salivary levels of the immune biomarker CRP as well as to understand the feasibility of using salivary biomarkers.

**Methods:** 182 adolescents (age 17.86 ± 0.91; 82.7% females) were recruited from Italian schools and clinically assessed with self-report questionnaires for both childhood trauma and emotional dysregulation. Saliva samples were collected by Salivette cotton swab and CRP levels measured by ELISA immuno-essay. IL-6 and IL-1β analyses are ongoing.

**Results:** Among the 182 adolescents, 57.1% reported at least one traumatic event and we found a positive correlation between emotional dysregulation and childhood trauma (R= .494, p<0.01). However, CRP levels were not significantly associated with childhood trauma or emotional dysregulation.

**Conclusions:** Our findings support that individuals who experienced childhood trauma are more likely to develop emotional dysregulation during adolescence. The lack of correlation between salivary CRP and childhood trauma could be explained by lack of sensitivity of this specific marker in saliva. Further research on other immune mediators will allow us to understand whether other salivary inflammatory markers could be more sensitive to the effect of childhood trauma.

**Supported By:** 5x1000 Italy

**Keywords:** Childhood Trauma, Emotional Dysregulation, Adolescent Depression, Salivary Biomarkers, Inflammatory Biomarkers

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**Abstract Withdrawn**

One abstract within this section of abstracts was withdrawn and deleted after this issue was completed.