database. Static rs-FC was explored with the independent component analysis and the sliding window approach was employed to calculate dynamic functional network connectivity (DFNC). A principal component analysis was conducted on clinical and cognitive scores.

Results: Compared to HC, FEP showed increased static rs-FC in the bilateral striatum, bilateral superior temporal gyrus, left superior frontal gyrus, left inferior parietal gyrus, and right postcentral gyrus, as well as reduced rs-FC in the right precentral gyrus, right precuneus, and left superior occipital gyrus. We found a negative correlation in FEP between emotion regulation and right striatum rs-FC ($p=0.009$), along with a negative correlation between negative symptoms and right striatum ($p=0.019$) and precuneus ($p=0.032$) rs-FC. All DFNC parameters were altered in FEP relative to HC, but no correlations with clinical variables were observed.

Conclusions: Our findings support the view that psychosis is characterized by complex alterations in intrinsic static and dynamic functional connectivity, that may ultimately result in emotion dysregulation and negative symptoms.

Keywords: First episode psychosis (FEP), functional Magnetic Resonance Imaging (fMRI), Functional brain connectivity, Dynamic functional network connectivity (dFNC)

40. Novel Pet Ligand [18F]PF974 can Measure Inflammatory Activation of Phosphodiesterase-4B (PDE4B) in Rat Brain

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Background: The cyclic adenosine monophosphate (cAMP) theory of depression posits that low cAMP signaling predisposes to major depressive episodes. Increased cAMP signaling phosphorylates and activates phosphodiesterase-4 (PDE4), which increases radioligand affinity tenfold; thus, cAMP signaling can be indirectly detected by radioligand binding of PDE4. Inhibition of the PDE4B subtype has antidepressant-like properties in animals and anti-inflammatory properties in animals and humans. The novel positron emission tomography (PET) radioligand PF974 was developed to visualize PDE4B in vivo. This study sought: 1) to evaluate PF974 as a dynamic biomarker specific for PDE4B by imaging its distribution and pharmacokinetics in rats; 2) to determine whether inflammatory changes affect PDE4B binding; and 3) whether these changes could be measured in living animals using PF974.

Methods: Three 120-minute PET scans were conducted in rats using PF974: 1) one day after separate hemispheric lipopolysaccharide (LPS) and saline injections; 2) eight days after LPS injection; and 3) one day after separate hemispheric LPS and saline injections, with the PDE4 inhibitor rolipram introduced via a penile vein after 50 minutes.

Results: At Day 1, LPS injection increased PF974 binding to PDE4, an effect that had resolved by Day 8 post-injection. Rolipram displaced PF974 binding, suggesting that PF974 was indeed binding to PDE4B. This increased binding may be due to increased PDE4B phosphorylation, which future studies could measure with ELIZA.

Conclusions: Taken together, the data suggest that PF974 can act as a dynamic biomarker for cAMP signaling secondary to neuroinflammation.

Funding Source: This work was supported by the Intramural Research Program of the National Institute of Mental Health, National Institutes of Health.

Keywords: Neuroinflammation, PET imaging, Depression, cAMP

41. Neurodevelopmental Processes Supporting Social Behavior: Associations Between Brain Network Connectivity and Pubertal Timing, Pubertal Status, Hormones, and Age

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Background: Puberty and age are associated with both neurodevelopment and social behavior. Healthy social behavior is essential for mental health, making the link between puberty, age, and the brain a critical area of research. Here, we identified associations involving brain network connectivity during a peer-evaluation fMRI task and pubertal status, timing, hormones, and age. The study goal was to identify specificity of brain network connectivity associations with puberty and age outcomes.

Methods: 99 girls (ages 9-15, $M=12.38$) completed a peer-evaluation fMRI task, self-reported pubertal status, and provided saliva for hormonal assay. Connectivity was calculated using correlations between brain regions, and Dehydroepiandrosterone (DHEA), testosterone, estradiol, and progesterone hormone levels were combined into one latent factor. Pubertal timing was computed by extracting residuals from age predicting status. Multivariate partial least squares regression was used to identify associations involving within/between brain network connectivity and our four developmental factors: pubertal status, timing, latent hormone factor, and age.

Results: Of the seven large-scale social-affective, cognitive-control and attention networks assessed, within default connectivity was the strongest predictor across all developmental factors. Within Reward connectivity was most linked to perceived pubertal status and age. In contrast, Default - Ventral Attention connectivity was associated with timing while Dorsal Attention - Reward was related to hormones. Associations reported are all Cohen's $d > .2$ and $p < .001$, corrected for multiple comparisons.

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Conclusions: Results suggest specificity in how puberty and age relate to communication among brain networks during peer evaluation, with implications for neurodevelopmental models of social behavior and psychopathology.
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Keywords: Puberty, Functional network connectivity, Peer evaluation

42. Confirming Computational Synaptic Pruning Model Predictions in Adolescent Longitudinal EEG Data

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Background: Adolescence is a critical period for both behavioral and brain development with extensive synaptic pruning. A previously published computational model linked improvements in working memory and cognitive control to more stable brain dynamics derived by pruning of network connections. We test this model's predictions in a longitudinal flanker task EEG dataset from 181 children (aged between 12 and 20 years old).
Methods: After initial preprocessing through the MADE pipeline, data dimensionality was reduced with PCA and down sampled to 30 Hz. For each recording we estimated temporal stability of the ERPs time-locked to flanker stimulus presentation and motor response. We tested the eigenvalues summarizing trial-level temporal dynamics for effects of age and task performance with a linear mixed effects model including a random effect of subject. Significance level was corrected with Bonferroni (alpha=0.05/12) and temporal clustering (N=10,000 bootstrap sample).
Results: We found significant effects of age on the eigenvalue representing the time evolution of the central-parietal principal component, with older children showing more stable dynamics in the stimulus locked (peak cluster fixed effect estimate -0.160 [SD 0.031], DF 322) and response locked conditions (-0.195[SD 0.035], DF 305). The same eigenvalue predicted accuracy (-0.209[SD 0.057]) and RT in the response condition (0.228[SD 0.055]) and RT in the stimulus condition (0.239[SD 0.051]).
Conclusions: We found confirmation of our model predictions in EEG data: older children showed significantly more stable ERP dynamics, which correlated with improved behavioral responses. These results add to the evidence supporting the mechanistic link between synaptic pruning, network efficiency and behavioral changes during adolescence.
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Keywords: Adolescent Development, Computational modelling, Electroencephalography (EEG)

43. Resting State Functional Connectivity of the Basal Ganglia as a Marker of First Onset Internalizing Disorder in High-Risk Youth

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Background: While research has linked alterations in functional connectivity of the basal ganglia at rest to depressive and anxiety disorders, little research has examined whether these alterations may be premorbid vulnerabilities. This study examined resting state functional connectivity of basal ganglia nuclei as markers of risk for a first lifetime onset of an internalizing disorder in adolescents at high familial risk for these disorders.
Methods: Participants were adolescents aged 11-17 with one parent with a history of depressive or anxiety disorders, but with no such history themselves. 119 youth completed T2*-weighted resting state fMRI scans, as well as the Mini International Neuropsychiatric Interview-Kid (MINI-Kid) and the Youth Self Report internalizing symptoms scale at baseline. The MINI-Kid was completed again at 9- or 18-month follow-up for 99 participants to assess onset of internalizing disorders.
Results: Analyses consisted of multiple regressions controlling for sex, age, and baseline symptoms, making the analysis highly conservative. Decreased connectivity between the left putamen and the paracingulate gyrus (pFDR = .02) and between the left pallidum and the precentral gyrus (pFDR = .03) at baseline predicted first episode onsets of an internalizing disorder at follow-up.
Conclusions: Even adjusting for pre-existing subclinical symptoms, altered resting state functional connectivity between the dorsal striatum and emotional processing regions and the pallidum to the motor cortex may represent a premorbid risk factor for developing a clinically significant onset of an internalizing disorder. Results may have implications for understanding the neural bases of internalizing disorders episodes and for early identification and prevention efforts.
Funding Source: Brain and Behaviour Research Foundation, Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada.
Keywords: mood disorders, familial high risk, longitudinal study, resting state functional connectivity, basal ganglia

44. Contrastive Connectivity Profiles of Resting-State EEG Link With Symptom Dimensions in Autism

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