Results: We identified six robust psychopathology components that were consistently associated with multimodal neuroimaging components in the training sample ($r = 0.26$ to 0.40, $p < 0.0083$), the independent test sample ($r = 0.14$ to 0.26, $p < 0.05$), and in psychiatric patients ($r = 0.12$ to 0.19, $p < 0.05$). Among these components, each mapped to distinct symptom profiles that, in turn, had specific multimodal brain profiles ($q < 0.05$).

Conclusions: Our model integrates multimodal neuroimaging features revealing their relationships with shared psychiatric symptoms across disorders. Arguably, by linking these distinct symptoms components shared structural and functional neuroimaging features, we have provided biological characterization that may be used to identify targets for therapeutic intervention.

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Keywords: Psychopathology, Multimodal neuroimaging, cross-disorder analysis, Depression, Mood/Anxiety

28. Peripheral Inflammation and Reward-Related Corticostriatal Functional Connectivity: Interactive Roles in Components of Anhedonia During Adolescence

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Background: Anhedonia—diminished reward processing—often emerges in adolescence, leading to functional impairment and distress. However, current treatments are ineffective. Identifying untargeted mechanisms could inform effective intervention targets. Reward-related brain and immune functions may be such candidates. Prior literature has largely neglected these systems' interactive nature and anhedonia's multi-faceted nature. This study tested the hypothesis that their interaction was associated with anhedonia and explored its components.

Methods: Participants were 166 adolescents (ages 13–16; 41% female; 48% People of Color). Anhedonia components were measured using the Positive Valence Systems Scale (PVSS; anticipatory/consummatory anhedonia), Card Arranging Reward Responsivity Objective Test (CARROT; reward responsiveness), and Delay Discounting Task (temporal discounting). Serum IL6, IL8, TNFa, IL10, CRP, and suPAR levels formed an inflammatory composite score (ICS). Functional connectivity (FC) between nucleus accumbens (NAc) and prefrontal regions [orbitofrontal (OFC), ventromedial prefrontal (vmPFC), and ventrolateral prefrontal cortex (vlPFC)] was assessed via fMRI Monetary Incentive Delay task.

Results: Lower NAc-vlPFC FC during reward outcome was linked to higher PVSS anticipatory ($p=.034$) and consummatory ($p=.008$) anhedonia. Lower NAc-vlPFC FC ($p=.013$) and NAc-OFC FC ($p=.032$) during anticipation predicted lower delay discounting, while higher NAc-vmPFC FC ($p=.009$) predicted lower discounting during outcome. At higher ICS, lower NAc-vlPFC FC predicted higher anticipatory anhedonia ($p=.036$), and higher NAc-vmPFC FC was linked to lower CARROT responsiveness ($p=.018$).

Conclusions: Distinct corticostriatal activity in adolescents was associated with anhedonia components, with some effects observed only at higher inflammation, suggesting its amplifying role. This work underscores the nuanced pathways underlying anhedonia, shaped by the interplay between reward and inflammation, varying by component.

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Keywords: Inflammation, reward processing, Depression, Anhedonia, fMRI

29. Selective Serotonin Release Influences Decision-Making in Aversive Contexts

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Background: Understanding the role of serotonin in human behaviour relies on in vivo modification of synaptic serotonin. Investigating increased serotonin signalling in human behavioural models faces challenges due to limitations in experimental tools, like SSRIs. This study uses a now available method—directly elevating synaptic serotonin with a selective serotonin releasing agent (low-dose fenfluramine)—to observe potential changes in human behaviour.

Methods: Fifty-six healthy volunteers were randomly assigned in a double-blind fashion to fenfluramine or placebo (15mg b.i.d.) for 7±2 days. Reinforcement learning and response inhibition measures were collected at baseline and follow-up, analysed using computational models (reinforcement learning and drift diffusion). Analysis methods included baseline-adjusted ANCOVA and Estimated Marginal Means.

Results: Significant group:valence interactions were observed for optimal choices ($F[1,50]= 5.14$, $p < 0.05$) and outcome sensitivity ($F[1,50]=5.73$, $p=0.02$) during reinforcement learning. These interactions were driven reductions in optimal choices (EMM ± SE = -8.62±3.18 , $p < 0.01$) and outcome sensitivity (EMM = -0.90±0.43, $p < 0.05$) during loss in the SSRA group.

Significant group:valence interactions were observed for choice impulsivity ($F[2,95]=3.22$, $p < 0.05$) and initial choice bias (z^*a; $F[2,95]=3.45$, $p = 0.03$) during response inhibition. Specifically, the SSRA group showed greater bias for the impulse control boundary during aversive interference (EMM =-0.33±0.15, $p = 0.03$), which corresponded with a drop in choice impulsivity (EMM=21.3±4.71, $p < 0.0001$).

Conclusions: This study underscores the direct impact of increased synaptic serotonin on human behaviour. The findings emphasize the crucial role of serotonin in guiding decision-making within aversive contexts.

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