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Longitudinal Multiparametric Magnetic Resonance Imaging of Outbred Rats with Variable Vulnerability to the Development of Oxycodone Addiction-like Behaviors

Advancements in neuroscience, including MRI, have substantially improved our understanding of substance use disorder and its impact on brain function. However, the marked heterogeneity of substance use disorders and the complexity of brain organization necessitate controlled, longitudinal approaches in diverse populations to characterize individual variability. In this study, we use longitudinal multi-parametric MRI to assess brain features associated with opioid use disorder in anesthetized, genetically diverse rats obtained from the Rat Oxycodone Biobank. Animals underwent a state-of-the-art intravenous oxycodone self-administration pipeline with behavioral characterization. Imaging is performed on a Bruker 7.0T/20 cm system equipped with a quadrature transmit volume coil and a 2×2 array brain surface coil. The protocol includes T2-weighted TurboRARE, diffusion tensor imaging echo-planar imaging (DTI-EPI), and T2*-weighted BOLD resting-state fMRI (rs-fMRI). All modalities are acquired at baseline, prior to drug exposure and following the paradigm, to capture both pre-existing differences and oxycodone-induced changes. Data preprocessing is conducted using RABIES (v0.5.1) and AFNI software, and images are registered to the Waxholm rat brain template. For preliminary proof of concept, we imaged 8 males of 5 of the HS founder strains using the same metrics, which show heritability. We will compare drug-exposed animals to their within-subject baselines and to age-matched naive controls. Together, longitudinal imaging will allow to disentangle pre-existing brain differences from those arising as a consequence of drug exposure. With a large and diverse sample size, this approach may enable predictive modeling of addiction-like behaviors, ultimately supporting more precise and personalized strategies for AUD prevention and treatment.

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