RELAPSE VULNERABILITY AS A BRAIN NETWORK STATE: STUDIES IN HUMANS AND RATS

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Bringing novel medications from preclinical to clinical development is challenging, especially when efficacy predictors are based on subjective assessments. Neuroimaging methods such as magnet resonance imaging (MRI) may allow for objective human-animal comparisons and thus to identify imaging signatures that are comparable between patients with alcohol use disorders (AUD) and animal models. Such signatures may represent ‘relapse prone’ network states that should be positively modulated (i.e. towards normal states) by effective pharmacological treatments.

Here, we report results from global mapping of brain activity using resting state functional MRI (rsfMRI) and manganese enhanced MRI (MEMRI) in an established rat model of abstinence from alcohol dependence (i.e. postdependent rats). We found abstinence related changes in brain regions known to be involved in the addiction circuitry but also regions currently not in the focus of alcohol research. The effects of naltrexone, a clinical approved treatment for relapse prevention in AUD, on brain activity patterns in postdependent rats were also investigated. Comparable rsfMRI experiments in alcoholic patients and healthy controls using rsfMRI point to altered connectivity in the default mode network and of limbic regions in alcoholics.

By integrating human and animal data we expect to develop a translational strategy for identifying relevant neuronal networks in AUD that can be targeted by potential therapeutic approaches.