mTORC1 Is A Key Molecular Transducer Of Alcohol-Dependent Plasticity, Seeking And Relapse

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The serine and threonine kinase mammalian target of rapamycin in complex 1 (mTORC1) controls the translation of a subset of mRNAs. In the adult brain, mTORC1 plays an important role in synaptic plasticity and memory by activating the translational machinery at dendrites. We previously discovered that excessive alcohol intake activates mTORC1 in the nucleus accumbens (Nac) of rodents. We further showed that mTORC1 plays an important role in the mechanisms that underlie the development and maintenance of excessive alcohol consumption. This presentation will describe a series of studies suggesting that mTORC1-dependent translation of a selected group of synaptic proteins in the NAc produces orchestrated alterations in the synaptic structure that in turn drive the motivation to seek and consume alcohol. Next, the presentation will show that mTORC1 also plays a central role in mechanisms underlying relapse to alcohol use. Specifically, the presented data will demonstrate that reactivation of alcohol-related memories activates mTORC1 in discrete amygdalar and cortical regions, which is accompanied by increased protein levels of several synaptic proteins. Importantly, the presentation will show that the administration of a selective mTORC1 inhibitor can erase the memory of alcohol seeking. Together, these findings suggest that mTORC1 is a central molecular transducer of neuroadaptations that underlie alcohol seeking and relapse. The studies further indicate that the inhibition of mTORC1 or its downstream targets may be developed as novel strategies to combat alcohol abuse disorder.

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