Life Sciences Seminar

Synaptic mechanisms underlying rapid antidepressant action

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Major depressive disorder is one of the most prevalent mental illnesses. Traditional antidepressants, which target the monoamine system, are commonly prescribed for the treatment of depression but they typically take several weeks to exert a clinical effect, with a sizable fraction of the patients failing to respond to treatment. This therapeutic delay in onset is a major limitation of traditional antidepressant therapies especially for individuals at risk for suicide. Thus, there has been a significant unmet need for the development of pharmacological therapies that can quickly and effectively alleviate symptoms associated with depression. Ketamine is a noncompetitive glutamatergic N-methyl-D-aspartate receptor (NMDAR) antagonist with rapid antidepressant efficacy for patients with treatment-resistant major depressive disorder. We have been investigating the mechanisms underlying the efficacy of rapid antidepressant action using preclinical animal models. We previously showed that ketamine blocks NMDARs activated by spontaneous glutamate release (also referred to as at rest) that couples to eukaryotic elongation factor 2 kinase (eEF2K) signaling. This signaling pathway subsequently results in increased protein synthesis including brain-derived neurotrophic factor (BDNF) and a-amino-3-hydroxy-5-methylisoxazole-4-propinic acid receptors (AMPARs) that results in a robust and persistent potentiation of AMPA receptor-mediated transmission in Schaffer collateral to CA1 synapses that is necessary for rapid antidepressant effects. This presentation will focus on the key synaptic mechanisms underlying rapid antidepressant action, including the specific role of eEF2K in synaptic function, as well as the long-term antidepressant effects.

Tuesday, November 16, 2021 03:30pm - 04:30pm

Online Event
(https://istaustria.zoom.us/j/97414233454?pwd=Y3FibW9LY21wQ29qMG9wZTJxQkF6dz09,
Meeting ID: 974 1423 3454, Passcode: 482716)

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