mechanism of the Ext even in the PTSD. At the meeting, we will show the changes in the phosphorylation of TrkB (an receptor of BDNF) after the micro-infusion of BDNF.

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AMPK signaling in the dorsal hippocampus negatively regulates contextual fear memory formation

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Abstract

Both the formation of long-term memory (LTM) and dendritic spine growth that serves as a physical basis for the long-term storage of information require de novo protein synthesis. Memory formation also critically depends on transcription. Adenosine monophosphate-activated protein kinase (AMPK) is a transcriptional regulator that has emerged as a major energy sensor that maintains cellular energy homeostasis. However, still unknown is its role in memory formation. In the present study, we found that AMPK is primarily expressed in neurons in the hippocampus, and then we demonstrated a time-dependent decrease in AMPK activity and increase in mammalian target of rapamycin complex 1 (mTORC1) activity after contextual fear conditioning in the CA1 but not CA3 area of the dorsal hippocampus. Using pharmacological methods and adenovirus gene transfer to bidirectionally regulate AMPK activity, we found that increasing AMPK activity in the CA1 impaired the formation of long-term fear memory, and decreasing AMPK activity enhanced fear memory formation. These findings were associated with changes in the phosphorylation of AMPK and p70s6k and expression of BDNF and membrane GluR1 and GluR2 in the CA1. Furthermore, the prior administration of an mTORC1 inhibitor blocked the enhancing effect of AMPK inhibition on fear memory formation, suggesting that this negative regulation of contextual fear memory by AMPK in the CA1 depends on the mTORC1 signaling pathway. Finally, we found that AMPK activity regulated hippocampal spine growth associated with memory formation. In summary, our results indicate that AMPK is a key negative regulator of plasticity and fear memory formation.

Keywords: AMPK; fear memory; formation; mTORC1

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TNF-a from hippocampal microglia induces working memory deficits by acute stress in mice.

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Abstract

The role of microglia in stress responses has recently been highlighted, yet the underlying mechanisms of action remain unresolved. The present study examined disruption in working memory due to acute stress using the water-immersion resistant stress (WIRS) test in mice. Mice were subjected to acute WIRS, and biochemical, immunohistochemical, and behavioral assessments were conducted. Spontaneous alternations (working memory) significantly decreased after exposure to acute WIRS for 2 h. We employed a 3D morphological analysis and site- and microglia-specific gene analysis techniques to detect microglial activity. Morphological changes in hippocampal microglia were not observed after acute stress, even when assessing ramification ratios and cell somata volumes. Interestingly, hippocampal tumor necrosis factor (TNF)-α levels were significantly elevated after acute stress, and acute stress-induced TNF-α was produced by hippocampal-ramified microglia. Conversely, plasma concentrations of TNF-α were not elevated after acute stress. Etanercept (TNF-α inhibitor) recovered working memory deficits in accordance with hippocampal TNF-α reductions. Overall, results suggest that TNF-α from hippocampal microglia is a key contributor to early-stage stress-to-mental responses.

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A Roadmap to Golden hour intervention for Posttraumatic Stress Disorder

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Abstract

Objective: Currently there are several compounds that are used in preclinical studies to target systems or receptors which are fundamental for consolidation and reconsolidation. While this offers an important opportunity to target these emotional memories and the expression of fear, and there is some validation from clinical studies, there is currently a need for roadmap that will assist in identification and evaluation of these compounds in their efficacy in treatment for PTSD. (This work is part of the Traumatic Stress Network of the European College of Neuropsychopharmacology).

Method: Two windows of opportunity that can be defined as 'golden hours' for treatment of PTSD can be identified: i) event-based golden hours and ii) exposure-based golden hours. The first are defined by the traumatic event, and subsequent consolidation of the traumatic event. The second is determined by the setting in which exposure as a therapeutic tool is introduced and the subsequent reconsolidation phase.

Summary: First we will provide an overview of the current knowledge of compounds – based on preclinical an d clinical work - which are potentially interesting to target emotional memory processing in PTSD. We will discuss applied dosages, population, timing of treatment and exposure. Second, we will use this knowledge to define pertinent questions for future and novel developments to target PTSD. We identified the following potential compounds: Propranolol, Cortisol, D-Cycloserin, Ketamine, Oxytocine and MDMA (XTC).

Conclusions: We conclude that reconsolidation presents an interesting opportunity to modify or alter fear and fear-related memories. Several compounds are being used off label in augmentation of psychotherapy for PTSD. Following a roadmap will assist in moving the field forward in terms of design, dosage as well as effectivity as augmentation strategies for treatment of PTSD.

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Heart Rate Variability of Posttraumatic Stress Disorder in Korean Veterans

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Abstract

Objective: Heart rate variability (HRV) is reported to reflect the autonomic nervous system. Generally, patients with conditions such as posttraumatic stress disorder (PTSD) showed lower HRV,