

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- α 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 and 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,

but the result was inconsistent. This study was to investigate the analysis of HRV in PTSD patients according to postural change with head-up tilt testing.

Methods: Seventy-one PTSD patients and seventy normal controls participated. The diagnosis of PTSD was established by the structured clinical interview for diagnostic and statistical manual of mental disorders (SCID)-IV. The posttraumatic stress disorder checklist 5 (PCL5), Beck depression inventory (BDI), Beck anxiety inventory (BAI), psychosocial well-being index short form (PWI-SF) and Pittsburgh sleep quality index (PSQI) were applied to all study subjects. The HRV measurement, including heart rate (HR), standard deviation of the NN interval (SDNN), the square root of the mean squared differences of successive NN intervals (RMSSD), physical stress index (PSI), log total power (LNTP), log low frequency (LNLf), log high frequency (LNHF) and low-frequency/high-frequency ratio (LF/HF ratio), were performed at supine position for the first five minutes, then underwent head-up tilt testing for the last five minutes at an erect position.

Results: The PTSD group showed a significantly higher score than the nonPTSD group in PCL5 ($t=11.625$, $p=0.001$), BDI ($t=5.543$, $p=0.020$) and BAI ($t=9.500$, $p=0.002$). In the PTSD group, SDNN ($t=3.563$, $p=0.039$), RMSSD ($t=3.514$, $p=0.011$) and LNLf ($t=0.902$, $p<0.001$) were significantly lower, but PSI ($t=-3.818$, $p<0.001$) and LF/HF ratio ($t=-1.730$, $p=0.041$) were significantly higher than in the nonPTSD group. After tilting, higher PSI ($t=-2.570$, $p<0.001$), lower LNLf ($t=1.927$, $p=0.011$) and lower LNHF ($t=2.403$, $p=0.025$) were found in the PTSD group, compared to the nonPTSD group. SDNN ($r=-0.209$, $p=0.013$), RMSSD ($r=-0.211$, $p=0.012$) and LNHF ($r=-0.168$, $p=0.046$) were correlated with PCL5 in only supine position.

Conclusion: PTSD patients showed reduced heart rate variability compared to nonPTSD patients, associating PTSD with involvement of autonomic nerve system activity. Although head-up tilt testing might be not more available than supine position testing for measurement of HRV with PTSD patients in this study, HRV might be a usable physiological parameter of assessing and monitoring of autonomic function in PTSD patients.

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Frontal electroencephalographic findings related with psychological symptoms of complicated bereaved familial members of Sewol ferry disaster

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Abstract

Purpose: On April 16th 2014, the Sewol ferry sank off South Korea's southern coast, killing 304 people. Two hundred fifty among the victims were sophomore of a high school on a school trip. This disaster caused over hundreds bereaved families suddenly. Until today, they have been suffered from the death of their children and most of them showed problems related with complicated grief. This study was the first biological investigation for the familial members of the victims of Sewol ferry disaster. The purpose of this study was to investigate whether the neurophysiological change of brain was associated with clinical rating scales in families of the Sewol ferry victims.

Methods: Subjects were 86 family members of the Sewol ferry victims (32 men and 54 women). The mean age was 44.88 (8.51) years (range: 19–60 years). All subjects were recruited through

advertisement of Ansan trauma center. The two-channel EEG device was used to measure of cortical activity in frontal lobe during 5 minutes in resting state with eye-closed condition.

Results: Frontal beta relative power was decreased in the high risk insomnia group ($n=22$) compared to the normal sleep group ($n=18$). There was significant inverse association between frontal beta relative power and insomnia symptom in all subjects ($n=86$). The mean insomnia scores was higher in fathers ($n=27$) than mothers ($n=38$).

Conclusions: Decrease of beta power implies the lack of attention and decreased alertness. The study suggests that decreased frontal beta activity is associated with insomnia symptom severity of bereaved subjects.

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Association between Heart Rate Variability (HRV) and posttraumatic stress symptoms in female victims of sexual violence

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Abstract

Decreased HRV can occur with a variety of physical and psychological disorders including posttraumatic stress disorder (PTSD). However, little is known about the associations between the sexual trauma and HRV measures. The purpose of this present study was to investigate the HRV characteristics associated with PTSD symptoms in victims of sexual trauma.

Data were collected from female victims who had been sexually assaulted ($n = 23$, mean age = 28.2 years). Heart rate variability was measured in resting state. Victims also completed self-report questionnaires including the Korean version of the Impact of Event Scale-Revised (IES-R-K). Chi-square was used for frequency of subject characteristics; independent t-test compared means of HRV measures between victims group and control group ($n = 27$, mean age = 32.6 years); Pearson correlation was used for association between HRV measures and self-report scores.

The results were as follows. First, significantly higher log-transformed very low frequency (VLF) ($p < .0001$), log-transformed low frequency (LF) ($p < .0001$), and log-transformed high frequency (HF) ($p < .0001$) were found in victims group compared to control group. Second, hyperarousal symptom of PTSD symptoms was negatively associated with log-transformed square root of the mean squared differences of successive normal-to-normal intervals (RMSSD) ($r = -0.461$, $p = .03$) and log-transformed standard deviation of normal-to-normal intervals (SDNN) ($r = -0.453$, $p = .03$).

This cross-sectional analysis supports associations between PTSD symptoms, especially hyperarousal, in female victims of sexual violence and reduced HRV measures.

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Children and Adolescent Exposed to Disaster: Delphi Technique Study for the Development of Post-traumatic Assessment and Intervention

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