Stress and Memory

—how stress influences memory consolidation

TANG ZIXUAN 3035449645 WANG KE 3035449592

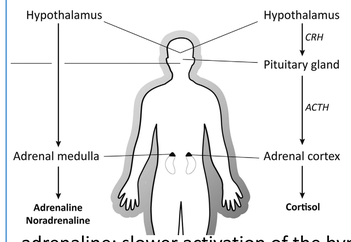
Introduction

The process of memory in our brain can be summarized into three stages. Encoding, which is like listening to a piece of music, consolidation, which is like recording the music, and retrieval, similar to playing the music again.

You may well remember the scene where in a stressful examination, you suddenly found yourself unable to recall anything that you had earlier learned, but the "embarrassing" situation remains vivid even after a long period of time. This is an example of how stress influences our memory retrieval and memory consolidation.

So how can stress influence the consolidation of emotion arousal memory? It has something to do with the interaction between nervous system and endocrine system.

Nervous-endocrine Interaction



When a psychological stressor is perceived by our sensory organs, it will activate two stress systems. Rapid activation of the sympathetic branch of autonomic nervous system (ANS) leads to the secretion of adrenaline; slower activation of the hypothalamus-pituitary-adrenal (HPA) axis lead to cortisol released from adrenal cortex. These hormones will then affect several brain regions critical for memory, such as hippocampus, amygdala and prefrontal cortex.

Stress and Amygdala

The amygdala, especially the basolateral region (BLA) is related to the emotional arousal memory. However, the BLA does not work alone. It projects to many brain regions, including the hippocampus, basal forebrain, the nucleus accumbens (NAc). The stria terminalis (ST) is a major pathway connecting the amygdala to other brain regions. The BLA–ST pathway provides a major efferent projection enabling BLA influences on other brain regions involved in memory consolidation under noradrenergic stimulation.

Adrenaline

Adrenaline does not cross the blood-brain barrier. It enhances memory consolidation by activating β-adrenoceptors located on vagal afferents, which increases the noradrenergic inputs to BLA.

Noradrenergic stimulation in amygdala plays an important role in regulating acute stress effect on memory consolidation.

Cortisol

Cortisol enters the brain directly and bind to glucocorticoid receptors (GRs) and facilitates memory consolidation through a rapid potentiation of the noradrenaline signaling cascade.

Experiment of Amygdala

Basolateral amygdala noradrenergic influence enables enhancement of memory consolidation induced by hippocampal glucocorticoid receptor activation

(cognition/emotional arousal/memory consolidation/norepinephrine/RU 28362)

BENNO ROOZENDAAL*, BICHNGOC T. NGUYEN, ANN E. POWER, AND JAMES L. MCGAUGH

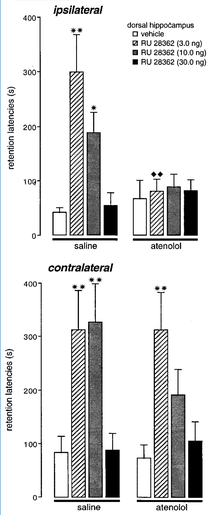
Center for the Neurobiology of Learning and Memory, and Department of Neurobiology and Behavior, University of California, Irvine, CA 92697

Contributed by James L. McGaugh, August 5, 1999

Procedure:

1. Surgery: implanted the guide cannulae unilaterally to 1.5 mm above the left dorsal hippocampus and 2 mm above either the ipsilateral or contralateral BLA.
2. Infuse the specific β-adrenoceptor antagonist atenolol or saline into either the left or right BLA 10 min prior to training.
3. Training: place the rat in the starting compartment (bright) and allowed to enter the shock compartment (dark). When rat entered the shock compartment, close the door and deliver a single footshock for 15s through the floor.
4. Infuse the specific GR agonist RU 28362 dissolved in 2% ethanol or 2% ethanol to left hippocampus and return the rat to its home cage. On the retention test, record the latency to reenter the shock compartment. Longer latencies were interpreted as indicating better retention. Shock was not administered during the retention test trial.

Result

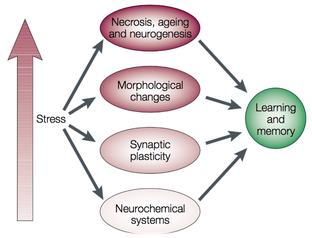


Infusions of atenolol into the ipsilateral BLA did not impair retention latencies, but blocked the memory-enhancing effects induced by post-training infusions of a GR agonist into the hippocampus. Thus, this finding provided strong evidence that activation of β-adrenoceptors in the BLA is essential in enabling glucocorticoid memory-modulatory influences in the hippocampus.

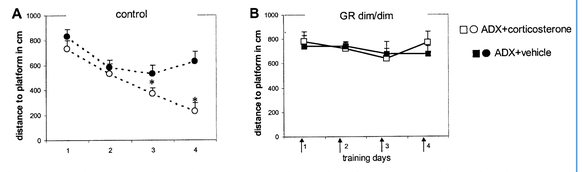
This experiment was to examine whether BLA-hippocampus interactions in memory consolidation involve unilateral projections between these brain regions. If the influence of the BLA on glucocorticoid-induced effects on hippocampal memory processes is mediated through neural connections between the BLA and hippocampus, only inactivation of the ipsilateral BLA should block the GR effects. On the other hand, if the effects are mediated by peripheral stress responses resulting from BLA activation, then inactivation of either the ipsilateral or contralateral BLA should have similar effects. According to the result, inactivation of the contralateral BLA did not block the GR effect so it indicated that BLA influence hippocampal through neural connection.

Stress and Hippocampus

Hippocampus is a sea-horse-shaped structure which is necessary for the formation of explicit memory. The mineralocorticoid receptor(MR) and the glucocorticoid receptor(GR) are two types of receptors that cortisol can bind to in brain, and they are expressed with highest levels in the hippocampus. Therefore, it is highly sensitive to cortisol and different magnitude of stress would lead to various effects on memory in transient and permanent ways.



Experiment of hippocampus



GR dim/dim: rats in which homodimerization and DNA binding of the glucocorticoid receptor were prevented;

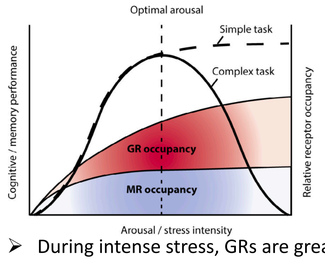
Rats were adrenalectomized bilaterally (cut adrenal) and supplemented with corticosterone before the daily training;

Rats were tested in the water maze to find the hidden platform. The distances for finding the platform were recorded as the measure of the spatial memory;

The results show that corticosterone improved the performance of control but not of GR dim/dim mice. This indicating that effects of corticosterone in hippocampal depend on DNA binding of the GR and the relatively greater importance of GRs compared with MRs in mediating effects of corticosterone on the hippocampus.

Stress and hippocampal plasticity

Long-term potentiation (LTP) is a persistent strengthening of synapses based on recent patterns of activity. And it is generally considered to be the best synaptic model to explain the memory formation. studied have shown that there is an inverted-U-shaped relationship between cortisol and LTP.



- High affinity MRs are almost fully occupied by cortisol when in a relaxed condition. Fully activation of MRs and partially activation of GRs under the low-to-intermediate level of cortisol has been shown to enhance LTP.
- During intense stress, GRs are greatly activated by the high level of cortisol and results in the impairment of hippocampal plasticity. Beside the impairment of LTP, it has been found that long-term depression (LTD, the opposite of LTP) is enhanced at the same time.
- It has also been proved that BLA-hippocampus interactions involving projections between these brain regions plays an important role in memory consolidation. The inputs from the normally functioning amygdala is a crucial component in the modulation of hippocampal synaptic plasticity.

Stress and dendritic morphology

When under chronic stress, dendritic atrophy in the CA1, CA3, and dentate gyrus is found. And deficits in hippocampus-dependent memory and hippocampal atrophy are symptoms usually exist in patients with Cushing's disease, which is caused by an excess secretion of cortisol, indicating cortisol's impact on neuronal morphology.

Stress and adult neurogenesis

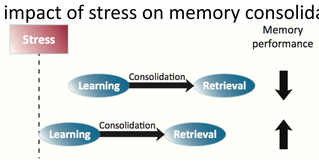
It has also been found that when hippocampus-dependent learning occurs, there will be an increase in adult-generated granule cells. Chronic stress has been shown to decrease the proliferation of adult-generated granule cells and influence memory.

The Time-dependent Impact

On binding to MR and GR receptors, cortisol operates mainly via two different modes of action.

- MR-mediated **non-genetic action** develops rapidly and usually takes place during the initial phase of the stress response when the cortisol level is high. It enhances memory consolidation together with the effect of noradrenaline and corticotrophin releasing hormone.
- **GR-dependent action** develops slowly. it involves DNA transcription and translation and impairs memory consolidation in the later phases.

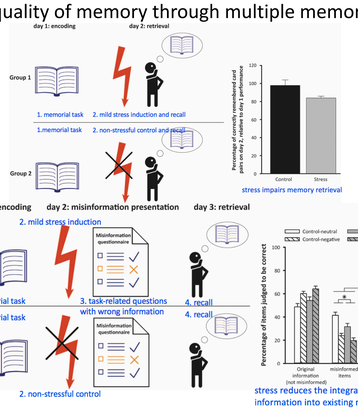
These two kinds of opposite effects lead to the time-dependent impact of stress on memory consolidation.



Stress within the context of a learning situation leads to the release of NA, CRH and CORT, all of which are active in the brain at the time that the initial phases of learning take place. At this stage, the neurotransmitters and hormones facilitate the ongoing process.
If an organism has been exposed to a stressor some time before the learning process takes place, the gene-mediated suppression of activity will have developed by the time that acquisition occurs. Under these conditions corticosterone will impair learning processes.

Broader Application

Besides influencing memory consolidation, stress can impair memory retrieval through the activation of cortisol and noradrenergic pathways in the hippocampus and amygdala and affect the quality of memory through multiple memory systems.



A comprehensive understanding of various effects of stress on memory and the mechanism behind it provide us with new ways to make improvement in our daily life. Here's an example of achieving better learning outcomes for students in the classroom.

Problem	Solution	Classification	Explanation
Bad grades in exams	1. Avoid strong stressors before exams 2. Develop effective coping strategies	Stress & memory retrieval	1.High levels of stress before exams hinders memory retrieval 2.Individual coping strategies affect the activation of stress system
Rigid memories, lack flexible application	Repeatedly practice of useful routines	Stress & the balance of memory systems	1.The training of correct actions during stressful emergency situations 2.Recall automatically, translated to behavior
Poor memory of teaching material	1. Challenge students frequently in class, give positive verbal feedbacks 2. Use related video clips with an emotional context	Stress & memory consolidation	1.mild stress within the context of learning enhances memory consolidation 2.emotional material is usually better remembered than neutral material

Reference

Basolateral amygdala noradrenergic influence enables enhancement of memory consolidation induced by hippocampal glucocorticoid receptor activation

Point mutation in the mouse glucocorticoid receptor preventing DNA binding impairs spatial memory

Learning and memory under stress: implications for the classroom

Stress and Memory: Opposing Effects of Glucocorticoids on Memory Consolidation and Memory Retrieval;

Neurobiology of Learning and Memory

Stress and glucocorticoid receptor-dependent mechanisms in long-term memory: From adaptive responses to psychopathologies

Stress and multiple memory systems: from 'thinking' to 'doing'

Learning under stress: how does it work?

The stressed hippocampus, synaptic plasticity and lost memories

Stress, memory and the amygdala