Stress and Cognitive Function

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How does stress affect behavior and cognition?
Acute Stress

Learning & Memory

\[
\downarrow \uparrow \text{Stress}
\]

Memory Retrieval

\[
\uparrow \text{Stress}
\]

(Sandi, 2013, WIRES)

30 min

Acute Stress

\[
\text{Stress} \rightarrow 30 \text{ min} \rightarrow \times
\]

Memory Retrieval

(Sandi, 2013, WIRES)
Acute Stress

Stress 4 h = Stress 5 min

Memory Retrieval

(Sandi, 2013, WIRES)

Acute Stress

Learning & Memory

Stress

(Sandi, 2013, WIRES)
Impact of Acute Stress on Learning

Pavlovian Conditioning

Relational Learning

Stress / Corticosterone

Learning/Memory

Learning under Stress

(Sandi and Pinelo-Nava, 2007)
Radial Arm Water Maze (RAWM)

Water:
16 °C
19 °C
25 °C

Box 2 | Neuroendocrinology of the stress response: glucocorticoids

(Sandi, 2004, Nat. Rev. Neurosci.)
Corticosterone levels after training in the visual-cue RAWM

A) Corticosterone levels at different temperatures.

B) Correlation between temperature and corticosterone levels.

(Salehi et al., Learn Mem 2010)

Learning under Stress

(Salehi et al., Learn Mem 2010)
Principal Component Analysis for ‘Personality’ Traits

<table>
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<tr>
<th>Test</th>
<th>Variance</th>
<th>KMO</th>
<th>Variance</th>
<th>KMO</th>
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<td></td>
<td></td>
<td>Factor 1/3</td>
<td></td>
<td>Anxiety</td>
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<td>52.55 %</td>
<td>Factor 2/3</td>
<td>20.29 %</td>
<td></td>
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<td>19.04 %</td>
<td>Factor 3/3</td>
<td>12.51 %</td>
<td>Activity</td>
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<td>20.29 %</td>
<td>Factor 1/3</td>
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<td>Exploration</td>
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<td>12.51 %</td>
<td>Factor 2/3</td>
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<td>0.69 **</td>
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<td>Factor 3/3</td>
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<td>46.34 %</td>
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<td>46.20 %</td>
<td>Factor 1/3</td>
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<td>8.81 %</td>
<td>Factor 3/3</td>
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<td>0.69 **</td>
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</table>

Note: ** indicates statistical significance.
Learning under Stress

*A: Anxiety*  
*E: Exploration*  
*H: High*  
*L: Low*

Individual differences in performance under high/low stress conditions

(Salehi et al., Learn Mem 2010)

“Acute stress”

- Stress impairs **retrieval** of information when given uncoupled to the cognitive task

- Stress modulates relational **learning** and memory according to an inverted-U shape

- Important role for **individual differences** in the impact of stress on learning
Impact of *Acute Stress on Learning*

**Relational Learning**

- **Learning/Memory**
  - 0
  - 100
  - 200

- **Stress / Corticosterone**
  - low
  - medium
  - high
  - very high

**Glucocorticoids facilitate memory formation**

**Fear Conditioning**
- **US**: electric foot-shock
- Strong Training
  - i.p. metirapone
  - central GR antagonist
  - Impaired retrieval

**Water Maze**
- **US**: water (temperature)
- Weak Training
  - i.p. corticosterone
  - Enhanced retrieval
Glucocorticoids act on glutamatergic pathways to affect memory processes

- Corticosterone
- Glutamatergic vesicle
- Glutamate
- GluR1-containing AMPAR
- GluR2-containing AMPAR
- NR2A-containing NMDAR
- NR2B-containing NMDAR
- Glutamate transporter
- GR
- MR
- Neural transmission

(Sandi, Trends Neurosci, 2011)
Glucocorticoids act on glutamatergic pathways to affect memory processes

**Learning & Memory**

- **Stress**
  - Facilitated learning

**Via Rustica**
- Increasing excitatory transmission by inducing AMPAR synaptic delivery

(Sandi, Trends Neurosci, 2011)

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Glucocorticoids act on glutamatergic pathways to affect memory processes

**Via Vicinale**
- Increasing extracellular glutamate levels and activating extrasynaptic NR2B-containing NMDAR

**Memory Retrieval**
- **Stress**
  - Impaired learning/retrieval

(Sandi, Trends Neurosci, 2011)
“Acute stress”

- Stress impairs **retrieval** of information when given uncoupled to the cognitive task

- Stress modulates **relational learning** and memory according to an inverted-U shape

- Important role for **individual differences** in the impact of stress on learning

- **Glutamatergic mechanisms** are involved in glucocorticoid actions on memory processes
Stress, genotype and norepinephrine in the prediction of mouse behavior using reinforcement learning

Two mouse strains:
CS7 – ‘calm’
DBA – ‘anxious’

(Luksys et al., Nat Neurosci. 2009)

Computational Model based on Reinforcement learning

Doya 2002

Learning rate $\alpha$
Exploitation factor $\beta$
Reward discount factor $\gamma$

$$Q(s, a) = \alpha r(t) + \gamma Q(s_{t+1}, a_{t+1}) - \exp(\beta Q(s, a_t)) / \sum \exp(\beta)$$

(Luksys et al., Nat Neurosci. 2009)
Stress, and its inverted U-shape effects in cognition

adapted from Aston-Jones & Cohen, 2005

Luksys et al., Nat Neurosci. 2009

Stress, and its inverted U-shape effects in cognition

adapted from Aston-Jones & Cohen, 2005

(Luksys and Sandi, Curr Op Neurobiol 2011)
Thank you for your attention
Overview

Stress and cognition
Carmen Sandi

Stress can affect cognition in many ways, with the outcome (i.e., facilitating or impairing) depending on a combination of factors related to both stress and the cognitive function under study. Among the factors identified as particularly relevant to define the cognitive effects of stress are the intensity or magnitude of stress, its origin (i.e., whether triggered by the task or externally), and its duration (i.e., whether acute or chronically delivered). At the cognitive end, the specific cognitive operation (e.g., implicit or explicit memory, long-term or working memory, goal-directed or habit learning) and information processing phases (e.g., learning, consolidation, and retrieval) are essential as well to define stress effects. The emerging view is that mild stress tends to facilitate cognitive function, particularly in implicit memory or simple declarative tasks or when the cognitive load is not excessive. Exposure to high or very high stress acutely (whether elicited by the cognitive task or experienced before being trained or tested in the task) or chronically impairs the formation of explicit memories and, more generally, of those that require complex, flexible reasoning (as typically observed for hippocampus- and prefrontal cortex-related functions) while improving performance of implicit memory and well-rehearsed tasks (as reported for amygdala-dependent conditioning tasks and for striatum-related processed). In addition to these general principles, there are important individual differences in the cognitive impact of stress, with gender and age being particularly influencing factors. © 2013 John Wiley & Sons, Ltd.