

**Stress and its impact on behaviour and cognition in primates**

- Neuropsychological processes
- Acute stress and neuropsychology
- Neuropsychological testing
- Chronic stress and neuropsychology

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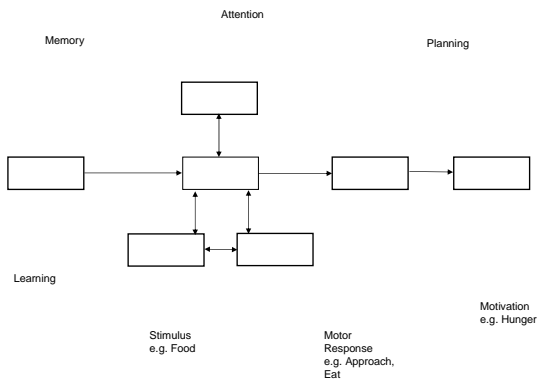
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**Neuropsychology or rewarding stimuli**



Neuropsychological processes

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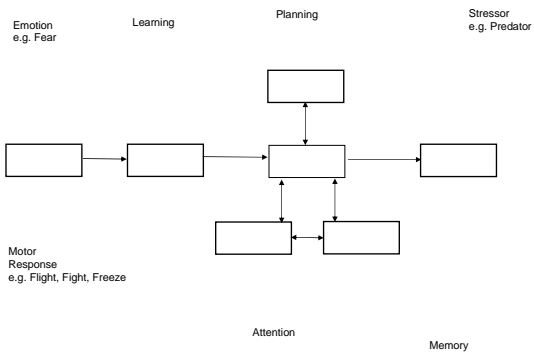
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**Neuropsychology or aversive stimuli/stressors**



Neuropsychological processes

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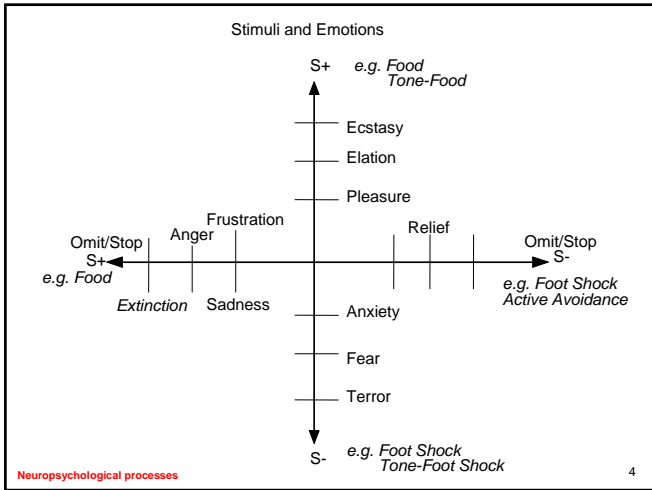
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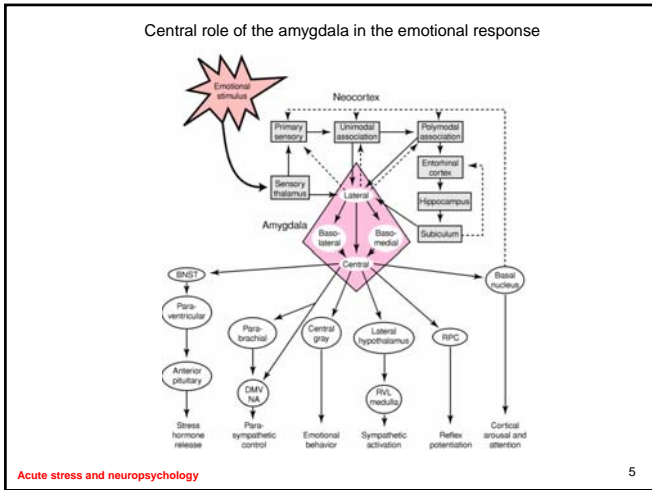
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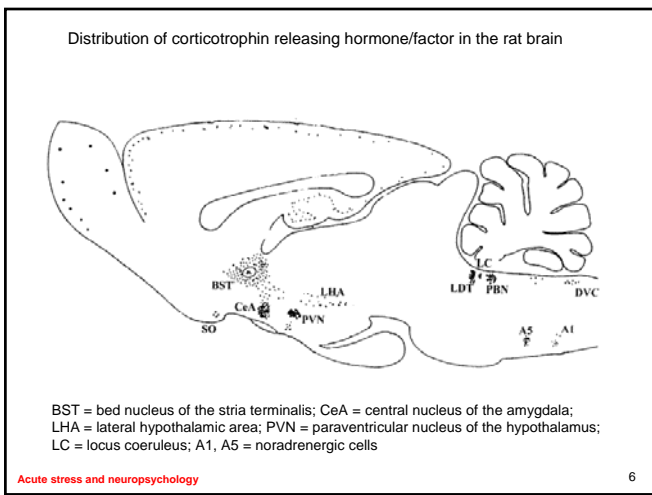
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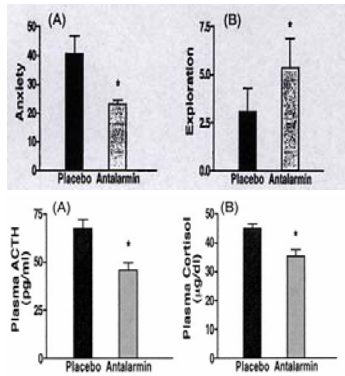
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Reduction of social anxiety and HPA activity in rhesus macaques by CRF receptor antagonist



Acute stress and neuropsychology

Habib et al., PNAS 97 (2000) 7

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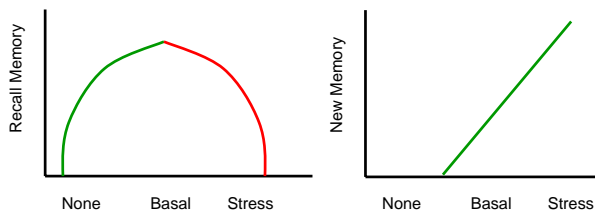
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Relationships between stress, learning and memory



Acute stress and neuropsychology

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CANTAB  
Translational study potential

Comparable human and monkey neuropsychological testing, in order to further understanding of the causation and therefore treatment of human cognitive function and disorders



Neuropsychological testing

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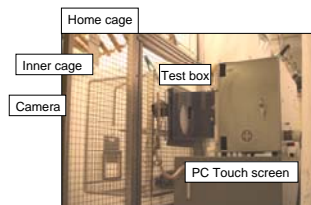
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### Experimental Facilities and CANTAB Study Design

- Male-female pairs of marmosets + offspring
- Large cages, controlled breeding
- Trained marmosets maintained in male-female pairs or family groups
- Home cage training and testing
- One neuropsychological task per study



Neuropsychological testing

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### Cognitive neuropsychological processes

**Attention:** The cognitive neural processes via which the most important stimulus in the environment becomes the focus of behaviour and stimulus processing, including:

- maintenance of alert state to detect rare stimuli (sustained attention, vigilance)
- simultaneous monitoring of two or more important stimuli (divided attention)
- maintaining focus in the presence of distracting stimuli (selective attention)

**Working memory:** The short-term retention of visual and spatial information over periods of seconds, in contrast to long-term retention and then recall across time periods of minutes, weeks, years. Working memory is used to hold information on-line in the service of cognitive activities such as comprehending, reasoning, and problem solving

Neuropsychological testing

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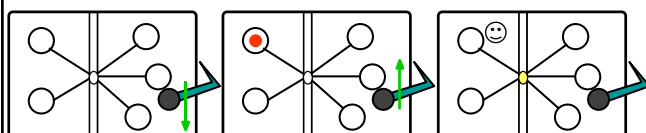
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### Attention: 5-choice serial reaction time task



**Independent parameters:**

- 45-60 trials/session (20 min)
- Lever press duration: 0.1-1.0s
- Stimulus duration: 0.1-1.0s
- Reward: 8s banana milkshake
- Punishment: 4s time out
- Inter-trial interval: 4s

**Dependent measures:**

- %Correct/Total trials
- %Accuracy (Correct/Correct+Incorrect)
- Response omissions
- Release lever too soon
- Lever release latency
- Screen response latency

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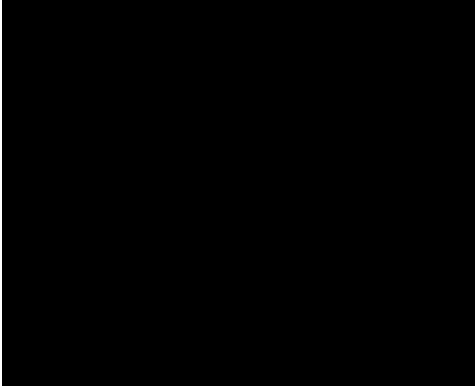
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Attention: 5-choice serial reaction time task



Neuropsychological testing 13

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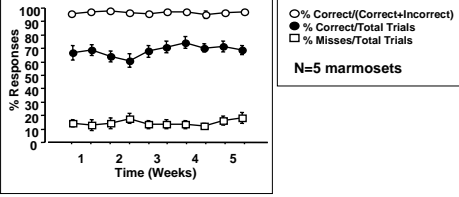
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Attention: 5-choice serial reaction time task



	Stimulus Duration		
	0.1 s	0.5 s	1.0 s
% Correct/Total Trials	54.1 ± 8.7	77.0 ± 2.0	78.5 ± 5.2
% Correct/Total Responses	67.6 ± 9.1 a	93.6 ± 4.1 b	96.0 ± 0.8 b
% Misses	11.1 ± 5.9	7.4 ± 0.7	6.7 ± 1.3
% Release Lever to soon	9.6 ± 2.7	9.6 ± 5.8	11.8 ± 5.8
Lever Release Latency ms	524.1 ± 77.9	458.7 ± 61.5	505.1 ± 41.9
Screen Response Latency ms	1743.8 ± 207.2	1808.9 ± 99.7	1817.8 ± 93.7

Neuropsychological testing 14

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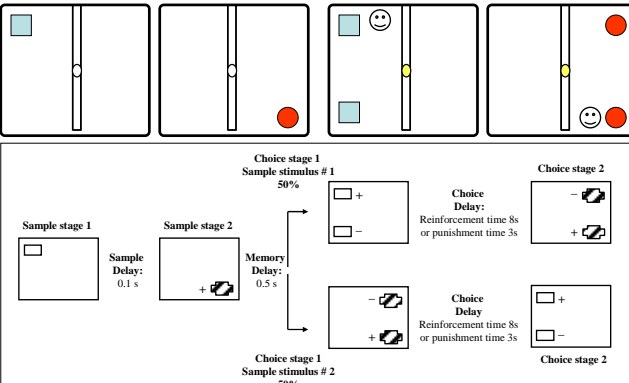
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Working memory: Concurrent delayed matching to position task  
„Marmoset Paired Associates Learning“



Neuropsychological testing

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Working memory: Concurrent delayed matching to position task



Neuropsychological testing

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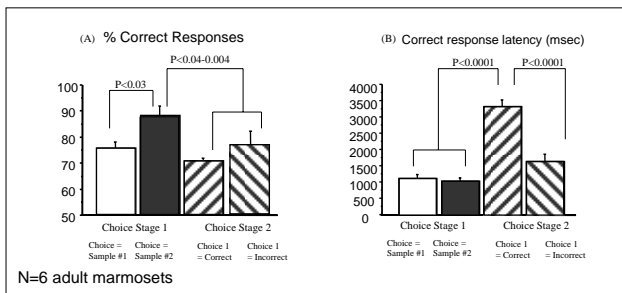
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Working memory: Concurrent delayed matching to position task



Neuropsychological testing

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Neuropsychology of chronic stress/depression

- **Sadness or emptiness**
- **Reduced interest or pleasure**
- **Weight loss**
- **Insomnia**
- **Psychomotor agitation**
- **Fatigue or loss of energy**
- **Worthlessness**
- **Diminished concentration**
- **Suicidal ideation or plan**

\* **Hyper-sensitivity to negative/aversive stimuli:**  
Quantifiable as increased learned helplessness or learned irrelevance?

\* **Hypo-sensitivity to positive/rewarding stimuli:**  
Quantifiable as decreased motivation to obtain or consume reward?

Chronic stress and neuropsychology

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**Learned Helplessness**

Unconditioned stimulus (US) = Aversive stimulus / Stressor  
 Contingency = Occurrence of US is independent of response, i.e. uncontrollable  
 Outcome = generally impaired Stimulus-Response learning, e.g. active avoidance  
 Relevance to depression = emotional state in depression, but how to test?  
 Primate model potential = how to induce? How to test?

**Learned Irrelevance, General Learned Irrelevance**

Unconditioned stimulus (US) = Reward  
 Contingency = Occurrence of US is independent of response  
 Outcome = impaired irrelevant-Stimulus or any-Stimulus -Response learning  
 Relevance to depression = evidence for increased learned irrelevance in depression  
 Primate model potential = how to induce? Translational test possible

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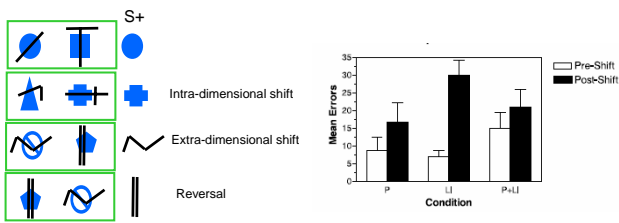
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Extra-Dimensional Shift: Task to assess Learned Irrelevance




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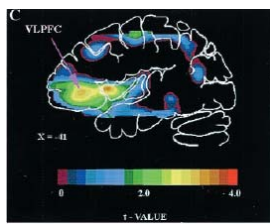
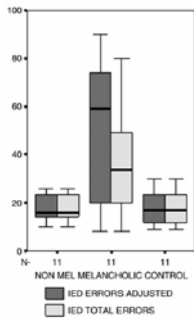
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Extra-Dimensional Shift and Depression:

Deficit in Depression  
 Dependent on intact lateral prefrontal cortex, including areas 9, 10, 46  
 Lateral prefrontal cortex exhibits altered activity in depression




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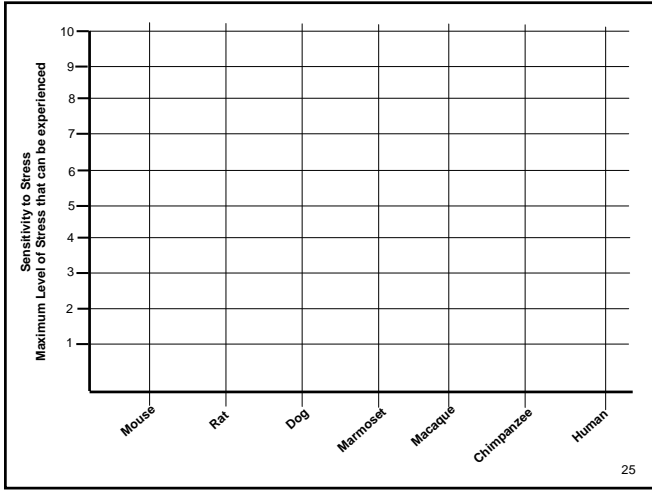
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