

Overlapping neural systems mediating extinction, reversal and regulation of fear



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Introduction

- Fear learning is rapid and resistant to modification. These characteristics are evolutionary beneficial in preventing the need to relearn about danger, and in promoting ways to avoid threats. However, it is also advantageous to flexibly readjust fear behavior, and a failure to do so might cause anxiety disorders.
- We investigated 3 ways to modify fear learning:
 - 1) Extinction** - a process by which learned fear responses are no longer expressed after repeated exposure to the conditioned stimuli with no aversive consequences.
 - 2) Regulation** - fear responses are diminished using a cognitive strategy of re-evaluation of the conditioned stimuli.
 - 3) Reversal** - fear responses are switched between two stimuli following a reversal of reinforcement contingencies.

Our aim was to identify brain mechanisms underlying modulation of fear through examination of similarities and differences in neural responses in these three different tasks.

Three fear modulation paradigms

- Simple visual or auditory discrimination paradigm with partial reinforcement
- Galvanic skin response (GSR) served as an index of FEAR

Extinction



Regulation



Reversal



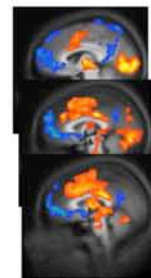
fMRI data acquisition and analysis

- 45 participants (Extinction task - 16, Regulation task - 12, Reversal task - 17)
- The data were initially corrected for motion, spatially smoothed using a 3-D Gaussian filter (6-mm FWHM), temporally processed to remove scanner drift, slice scan time was corrected, and functional data was transformed into Talairach space to allow for group analyses.
- A random-effects General Linear Model was used to construct group maps.

- 3 T Siemens head-only scanner
- 39 slices were obtained parallel to the AC-PC plane
- 3 mm isotropic voxels
- TR = 2000 ms; TE = 25 ms
- Event-related design

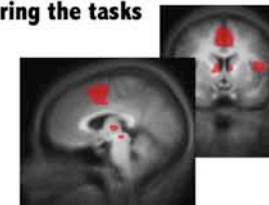
Acknowledgements

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All events > ITI
P (FDR corrected) < 0.05

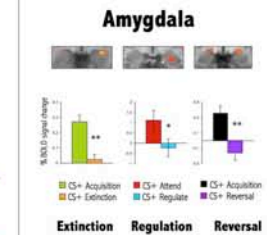
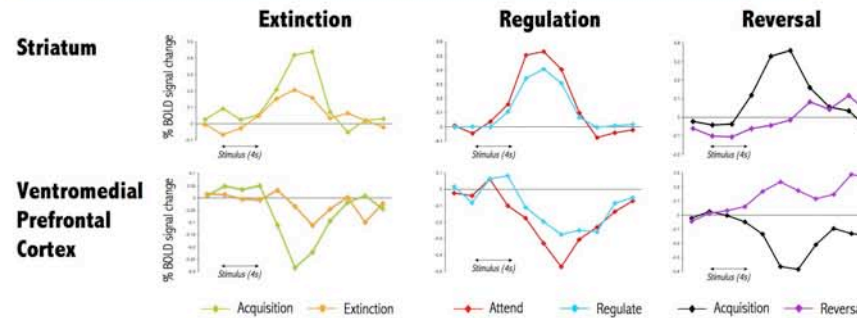
Overlapping regions showing **increased** activity during the tasks



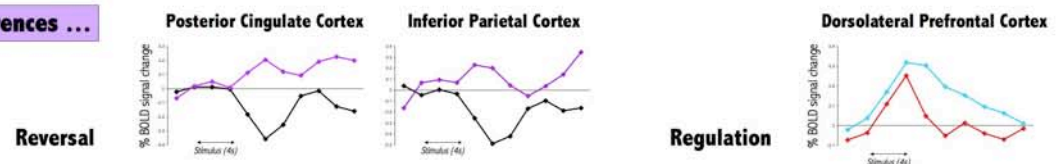
Overlapping regions showing **decreased** activity during the tasks



Overlapping brain responses tracking the modulation in fear predictive cues



Differences ...



Discussion

Similarities Fear acquisition was consistent across studies engaging the same brain regions (amygdala, striatum, thalamus, insula, dorsal anterior cingulate and midbrain) showing increased activation to the fear predictive stimulus, which diminished following regulation, extinction or reversal.

Differences vmPFC activation was greater in reversal compared to the other tasks, and additional regions (posterior cingulate cortex and inferior parietal cortex) were recruited, suggesting more resources were required for a switch in response as opposed to mere reduction.

The ventromedial prefrontal cortex (vmPFC) showed mirror activation, with **decreased** (below baseline) activation to CS+, that **increased** when the CS+ became less predictive of danger due to regulation, extinction or reversal.

The regulation task elicited dlPFC activation which did not overlap with reversal and extinction, this might be due to the more cognitive nature of the task.

These results point to a two-system interaction in the control of fear. A system learning responses to external stimuli that are predictive of aversive consequences, while another system readjusts these learned responses when environmental circumstances change.