

Bilateral amygdalae show differential activation for correct vs. erroneous antisaccade performance

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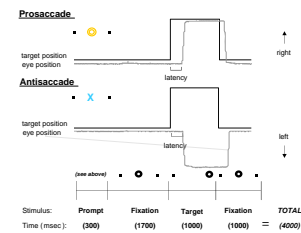
BACKGROUND

- The amygdala (AMY) responds to salient, novel, and/or aversive stimuli
- The rostral anterior cingulate (rACC) may modulate this response
- AMY activation to such stimuli may occur in order to influence behavior
- Errors are both salient (unexpected) and aversive (failure to achieve a goal)
- They are associated with rACC activation
- Errors represent opportunities for behavior change thus AMY response to errors may influence performance
- Hypotheses:**
 - Errors will be associated with increased AMY activation
 - AMY and rACC activation will be correlated during errors
 - AMY activation will correlate with performance (i.e., accuracy), and this relationship may be modulated by rACC

METHODS

Task

- A pseudorandomized sequence of antisaccade and prosaccade trials
- Prosaccade:** automatic response of looking towards a suddenly appearing visual target
- Antisaccade:** inhibition of prosaccade generation of the novel behavior of looking away from a target



Participants

- 19 healthy individuals: 7 female, 12 male
- Mean age: 33 ± 11 years

Behavioral Variables

- Latency of correct saccades
- Directional accuracy of saccades. Antisaccade accuracy = 91%

MRI Data Acquisition

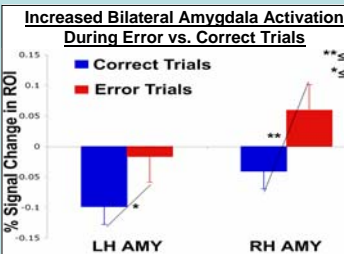
- 2 MP-RAGE, T1-weighted sequences (TR/TE/Flip = 7.25ms/3ms/7°) used for FreeSurfer cortical surface reconstruction/inflation to visualize activation inside sulci and to allow inter-subject registration based on sulcal-gyral pattern
- 20 5mm axial slices parallel to the AC-PC plane (3.13 X 3.13 X 5)
- Gradient echo, T2* weighted sequence (TR/TE/flip = 2000ms/30ms/90°)

Image Analysis

- Preprocessing: motion correction, intensity normalization, spatial smoothing
- Finite impulse response (FIR) model (FS-FAST) estimated hemodynamic responses (HDRs) for 4 event types - correct and error prosaccades and antisaccades
- Regions of interest (ROIs): AMY and rACC
- Hypothesis 1:** Errors will be associated with increased AMY activation.
 - Paired t-tests of error vs. correct antisaccades in AMY ROI at 6 s
 - Paired t-tests of correct and error antisaccades vs. fixation
- Hypothesis 2:** AMY and rACC activation will be correlated during error commission
 - % signal change in AMY ROIs was regressed onto raw BOLD estimates for each vertex on cortical surface
 - Both % signal change and BOLD were from the error vs. correct contrast at 6 s
- Hypothesis 3:** AMY activation will correlate with accuracy, and this relationship may be modulated by rACC activation
 - Standard linear regression of % signal change and # active voxels (defined above) in left and right AMY ROIs onto accuracy
 - Same as above with rACC ROIs included

RESULTS

Hypothesis 1: Errors will be associated with increased AMY activation



Comparisons vs. fixation:

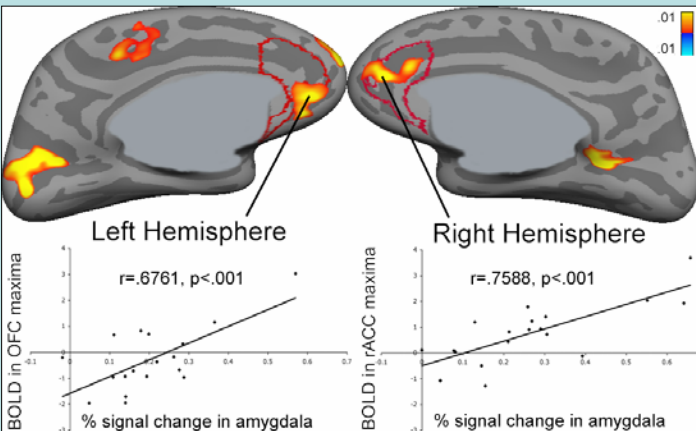
Left Hemisphere

Correct vs. fixation
(t(18)=-3.93, p=.001)
Error vs. fixation
(t(18)=.10, p=.75)

Right Hemisphere

Correct vs. fixation
(t(18)=-1.55, p=.14)
Error vs. fixation
(t(18)=1.66, p=.11)

Hypothesis 2: AMY and rACC activation will correlate during errors



Hypothesis 3: AMY activation will correlate with performance

- Right AMY: Positive correlation of % signal change with accuracy (R²=.23, p=.04)
- Left AMY: Negative correlation of % signal change (trend: R²=.16, p=0.10) and # activated voxels with accuracy (R²=.27, p=0.03).

Does adding rACC to the model improve prediction of performance?

Region	Parameter Estimate	Parameter p-value	Model R ²	Model p-value
LH AMY	- 65.10	.02	.50	.03
RH AMY	12.91	.56		
LH rACC	88.23	.16		
RH rACC	52.35	.40		

How do rACC and AMY correlate with performance?

To explore relationships between AMY and rACC to performance, we compared parameter estimates from the model using t-tests

- F-test between LH AMY & rACC parameter estimates is significant (F(1,18)=5.28, p=.04), suggesting that in the LH, these structures influence performance in a different manner
- F-test between RH AMY & rACC parameter estimates is not significant (F(1,18)<1, p=.60), suggesting that in the RH, these structures do not differ in their relationship to performance

SUMMARY OF FINDINGS & DISCUSSION

Errors were associated with differential AMY activation, the pattern of which differed by hemisphere

- RH AMY activation increased from baseline with errors, and decreased from baseline during correct trials
- LH AMY activation showed no increase from baseline during errors but rather a decrease from baseline during correct trials

AMY activation correlated with rACC activation

- RH AMY activation correlated with activation in perigenual ACC, a region involved in emotional expression
- LH AMY correlated with activation in subgenual ACC, a region thought to be involved in inhibiting amygdala responses

AMY activation was related to performance; this relation differed by hemisphere

- RH AMY activation correlated positively with accuracy
- LH AMY activation correlated negatively with accuracy

Parameter estimates of full model suggest that the contribution of AMY and rACC activation to performance differs by hemisphere

- In LH, there appears to be a different contribution of rACC and AMY to performance
- In RH, there appears to be a non-different contribution of rACC and AMY to performance
- However, given that only the LH AMY parameter is significant in this model, this suggests other models may be more appropriate (i.e. SEM)

SUMMARY:

- We hypothesize the right amygdala responds to the salience/aversiveness of errors, and signals them as events to be avoided in future. Thus, the amygdala may make a unique contribution to error-based optimization of performance.
- In contrast, we hypothesize that activation in the left amygdala represents a negative appraisal of behavior that may interfere with performance

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