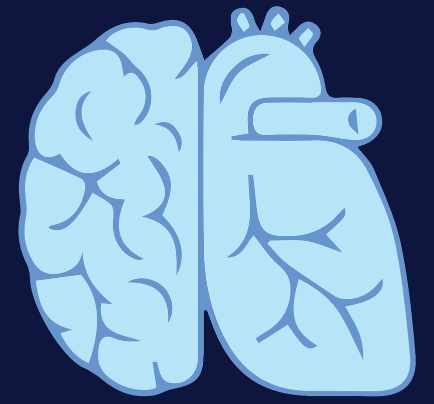

A meta-analytic reevaluation of the primate amygdala's role in affective processing

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Background

Beliefs about the amygdala and its role as a "fear center" are pervasive in neuroscience and are held by both scientists and the general public (Davis 1992, LeDoux 2014). Yet, accumulating evidence suggests that the amygdala may play a more limited role in threat processing and a broader role in affective processing (e.g., Fullana et al. 2016, Fullana et al. 2018, Chavanne & Robinson, 2020, Visser et al., 2021). For decades, non-human primates have been used to causally test hypotheses about amygdala function, including the famous work by Klüver and Bucy describing *Klüver-Bucy Syndrome* (Klüver & Bucy, 1937, 1939). Quantitative meta-analytic synthesis of decades of experiments provides the opportunity to generate a clearer picture of the amygdala's role in threat processing and general affective behavior.

Methods

We extracted effect sizes (*k*=421) from 15 articles detailing studies in which monkey sustained amygdala damage published between 1975–2021 (see Extended Poster for study references). Effect sizes represent behavioral responses to threatening or neutral conditions in tests of responsivity to unfamiliar humans ("Human Intruder Test") or novel objects/animals by monkeys with amygdala lesions or intact controls. We fit four multi-level meta-analytic models with effect sizes nested within studies, allowing for variance between studies, variance within studies, and sampling variance. 408 effect sizes remained after sensitivity analyses for outlier detection were performed. Moderators including the type of behavior measured (categorized according to author descriptions or generally accepted function) and the type of threatening stimulus (among others variables not shown here) were coded for all papers and moderator analyses were performed to explain effect size variance.

Model 1: Amygdala Lx vs. Control Responding to Threatening Stimuli (*k*=131)
Model 2: Amygdala Lx vs. Control Responding to Neutral Stimuli (*k*=68)
Model 3: Amygdala Lx Responses to Threatening vs. Neutral Stimuli (*k*=98)
Model 4: Control Responses to Threatening vs. Neutral Stimuli (*k*=111)

Conclusions

We assess the necessary contributions of the primate amygdala to threat responding with unprecedented statistical power. Our findings suggest that the amygdala is not *necessary* for threat responding, but amygdala damage selectively alters some behavioral responses to threat. In particular, our findings highlight a potential confound in the threat-processing literature where reward retrieval is used to index the magnitude of threat response—a variable which produces the most apparent difference following lesions. Finally, we uncover a potentially domain-general function for the amygdala in promoting behavioral variability that may be compatible with existing theories of amygdala function.

Results

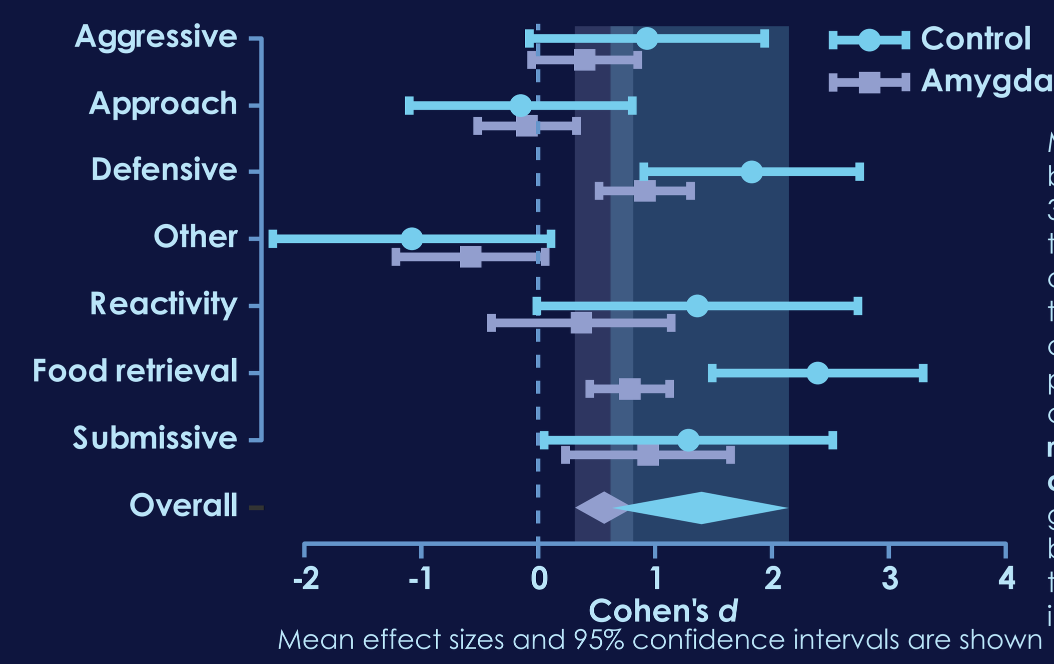
Monkey demographics (N=195 total)

N=167 males, **N=15** females, **N=16** no sex reported
N=173 *Macaca mulatta*, **N=25** *Macaca fascicularis*

N=103 amygdala-lesioned
N=64 complete lesions, **N=39** partial lesions
N=90 bilateral lesions, **N=13** unilateral lesions
N=75 neurotoxic, **N=20** cautery, **N=8** aspiration

N=95 controls
N=70 unoperated, **N=25** sham-operated

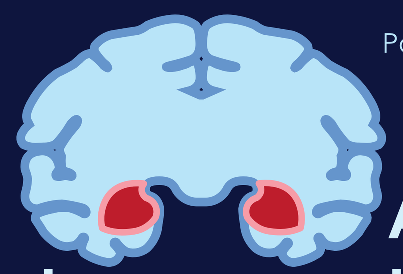
Amygdala lesions reduce behavioral variability without eliminating threat responding



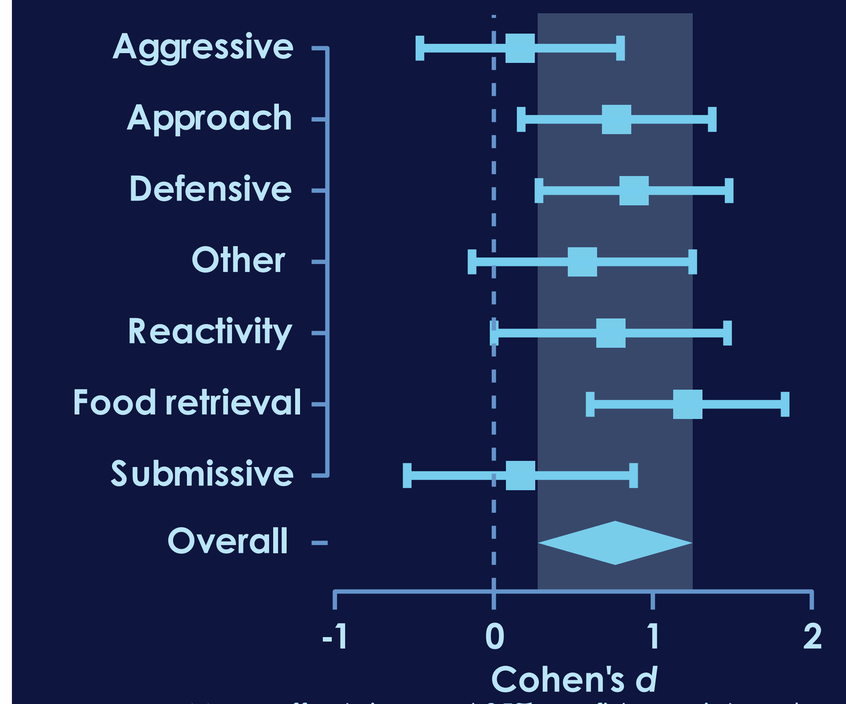
Mean effect sizes and 95% confidence intervals are shown

Moderator analyses of behavioral category for Models 3 and 4 (contrasting responses to threatening and neutral conditions across groups) show that amygdala-lesioned and control monkeys exhibit similiar patterns of behavior across categories, with **dramatically reduced variance in the amygdala-lesioned group**. Both groups significantly modulated behavior in the presence of threat, with greater modulation in the control group.

Positive effect sizes represent ↑aggressive ↓approach ↑defensive ↑other ↑reactivity ↓food retreival frequency ↑food retrieval latency ↑submissive in threatening vs. neutral conditions



Amygdala lesions are most influential to food retreival behaviors in the face of threat



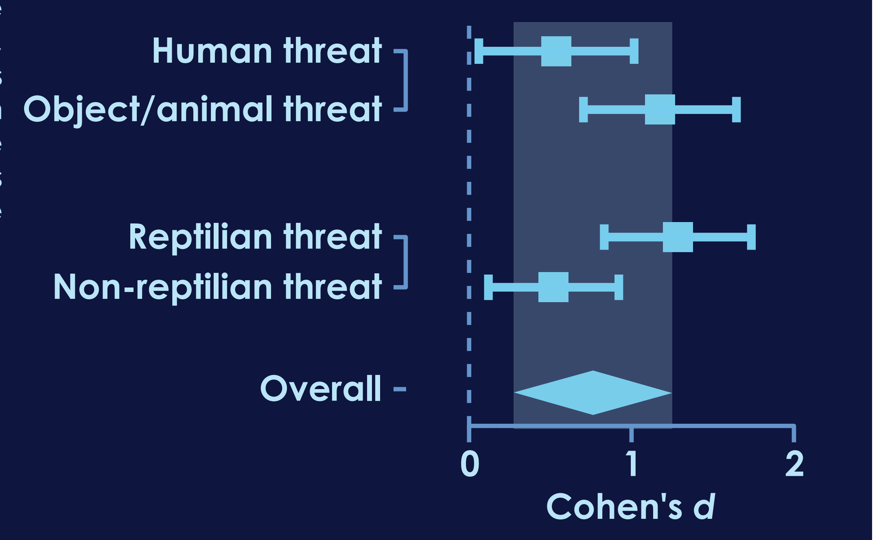
Mean effect sizes and 95% confidence intervals are shown

Moderator analyses of behavioral category for Model 1 (contrasting responses to threat in amygdala-lesioned vs. controls) show that **amygdala-lesioned and control monkeys differ most robustly in their food retrieval behaviors (*d*=1.22).** Groups did not differ in aggressive, other, or submissive behaviors and showed smaller differences in defensive behaviors, approach behaviors, and reactivity scores. While food retrieval has historically been used as an index of threat response magnitude, this result suggests the potential presence of a confound given the amygdala's established role in reward processing.

Positive effect sizes represent ↓aggressive ↑approach ↓defensive ↑other ↓reactivity ↑food retreival frequency ↓food retrieval latency ↑submissive in amygdala-lesioned vs. control monkeys

Amygdala lesions do not alter responding to all threatening stimuli equally

Moderator analyses of the type of stimuli used for Model 1 (contrasting responses to threat in amygdala-lesioned vs. controls) show that **amygdala-lesioned and control monkeys differ more in their responses to threatening animals and objects than threatening humans**. When we classified stimuli as either reptilian (i.e., objects intended to resemble reptiles or live reptiles) or non-reptilian, **amygdala-lesioned and control monkeys differed more in their responses to reptilian threats than non-reptilian threats**. These findings suggest a more specific, perhaps evolutionarily conserved, role for the amygdala in responding to reptilian threat.



Mean effect sizes and 95% confidence intervals are shown

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