




AUTISM RESEARCH



RESEARCH ARTICLE

An amygdala-centered hyper-connectivity signature of threatening face processing predicts anxiety in youths with autism spectrum conditions

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Introduction

- **Anxiety** is the most prevalent co-occurring mental illness in individuals with a diagnosis for an autism spectrum disorder (ASD) (Rodgers & Ofield, 2018).
- **The amygdala**, as a key brain structure associated to anxiety, is responsible for salience detection in the environment, including threats (Davis & Whalen, 2001).
- **Attentional avoidance patterns** (Koster et al., 2006; Mogg et al., 2004)
 - This study identifies a dissociation of amygdala reactivity dependent on explicit and implicit threat processing.
 - Implicit anxiety in individuals with an autism spectrum condition (ASC) could outweigh explicitly induced threat.
- **Hypothesis:** When explicitly perceiving socioemotional stimuli, ASC individuals with anxiety might use attentional avoidance patterns to restrict affective hyperarousal.

Materials and Methods-Participants

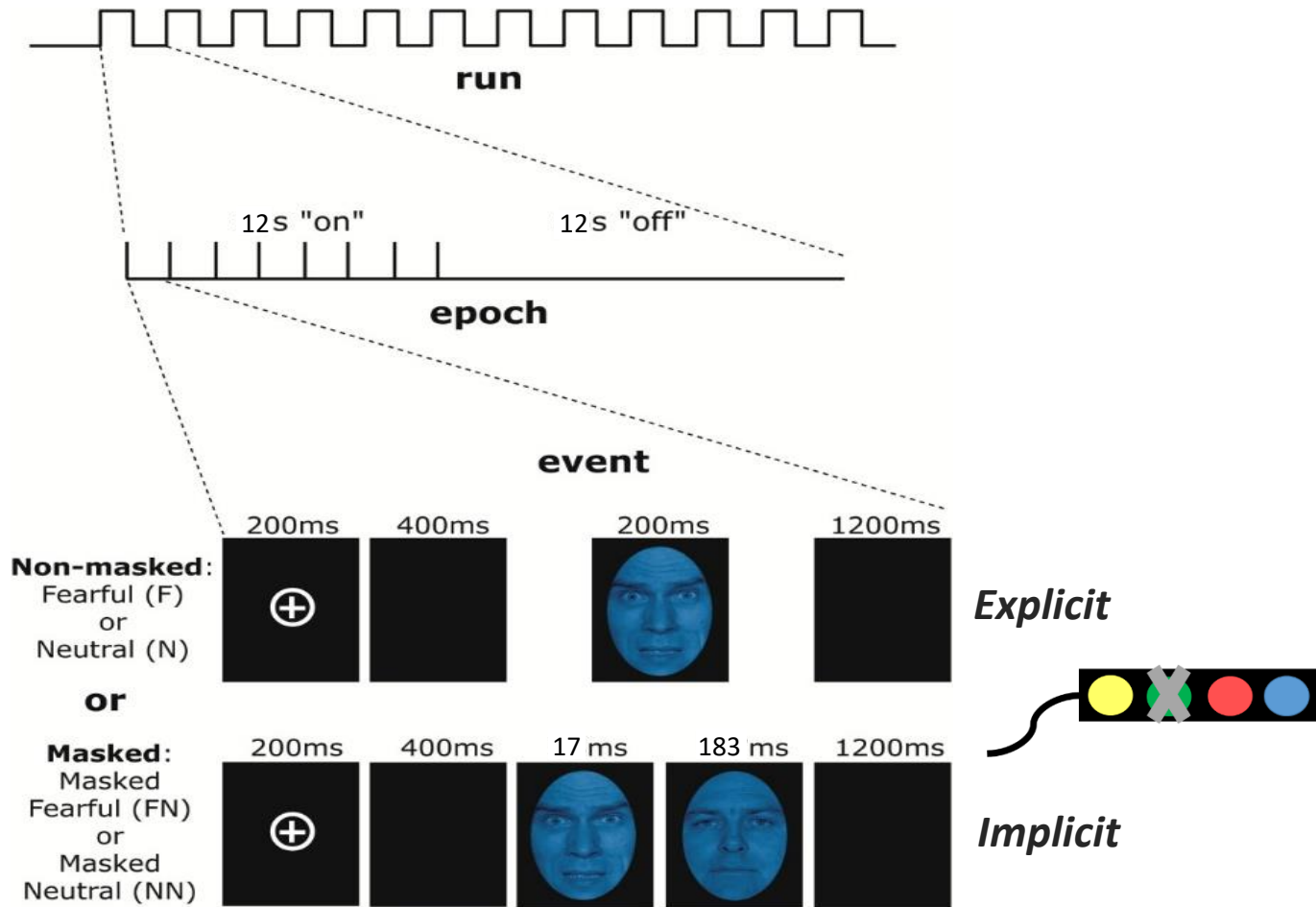
TABLE 1 Demographic and clinical variables of the participants in the study

	<u>ASC</u> (<i>N</i> = 26)	<u>CTL</u> (<i>N</i> = 25)	<i>p</i> value
Age, years	19.5 (1.07)	21.6 (0.61)	0.10
Sex			
Male	26 (100%)	23 (92%)	0.16
AQ	26.12 (1.62)	18.56 (1.38)	0.001
Social skill	5.38 (0.53)	3.52 (0.48)	0.012
Attention switch	6.12 (0.42)	5 (0.42)	0.065
Attention to detail	4.31 (0.42)	2.88 (0.41)	0.018
Communication	5.42 (0.5)	4.64 (0.32)	0.2
Imagination	4.88 (0.47)	252 (0.39)	<0.001
STAI-T	47.92 (2.2)	41.52 (1.69)	0.025
STAI-S	41.46 (2.49)	35 (1.96)	0.047

Note: Data are presented as mean (SE) or number of participants (%).

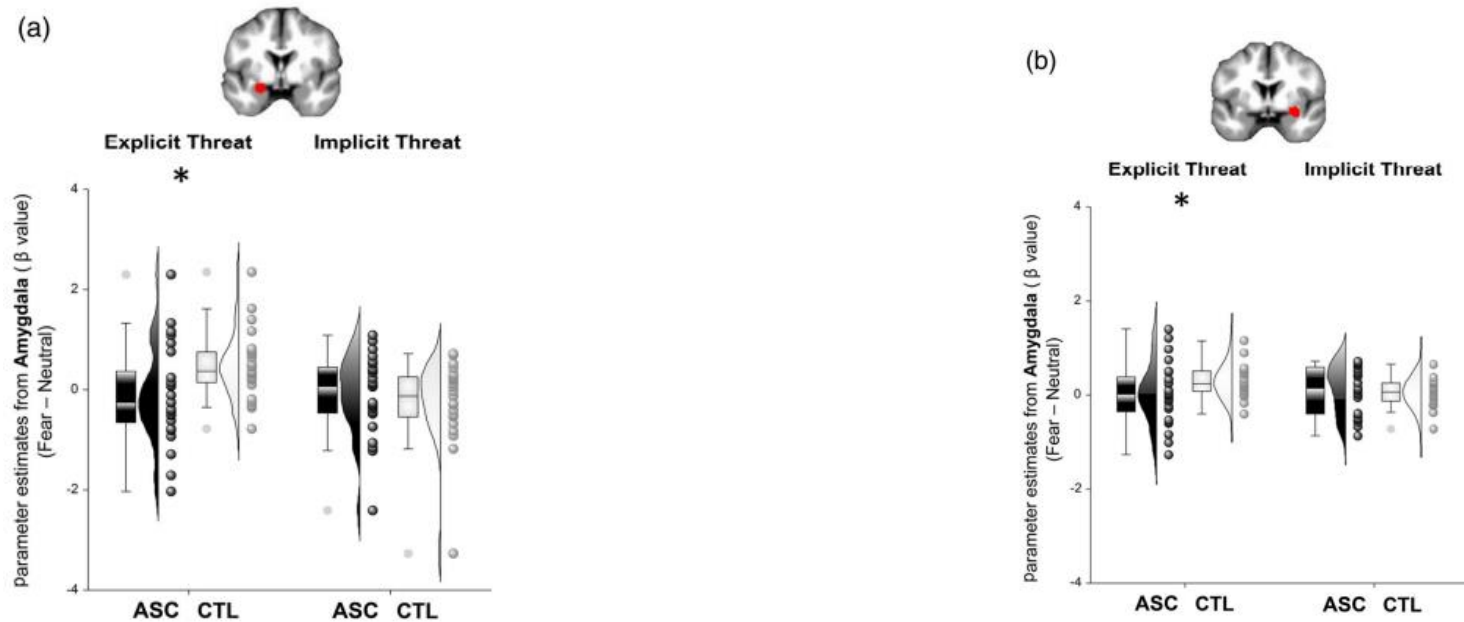
Abbreviations: ASC, autism spectrum condition; STAI, State-Trait Anxiety Inventory.

Materials and Methods-Experimental design



The paradigm for the fMRI scanning was derived from the work by Etkin et al. (2004)

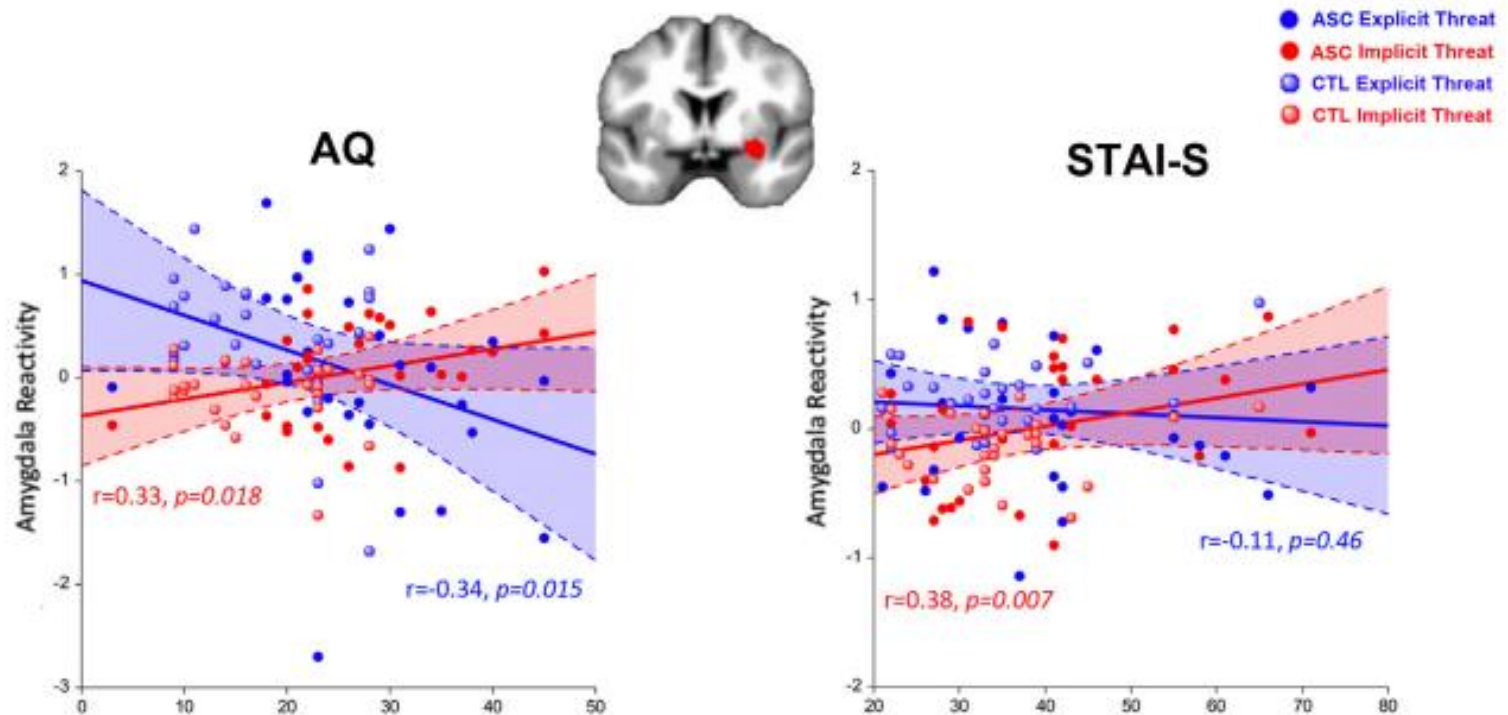
FIGURE 1 Dissociated amygdala reactivity between ASC and controls to explicit and implicit threat.



(a) The left amygdala reactivity reveals an interaction of group (ASC vs. CTL) x attention (explicit vs. implicit) ($F_{1,49} = 4.09$, $p = 0.049$). Post hoc analyses indicated that, as compared to controls, ASC individuals show significantly weaker amygdala reactivity in explicit fear ($p = 0.016$), but comparable in implicit fear ($p = 0.55$).

(b) The right amygdala reactivity reveals an interaction of group (ASC vs. CTL) x attention (explicit vs. implicit) ($F_{1,49} = 6.09$, $p = 0.017$). Post hoc analysis indicate that, as compared to controls, ASC individuals show significantly weaker amygdala reactivity in explicit fear ($p = 0.025$), but comparable in implicit fear ($p = 0.29$).

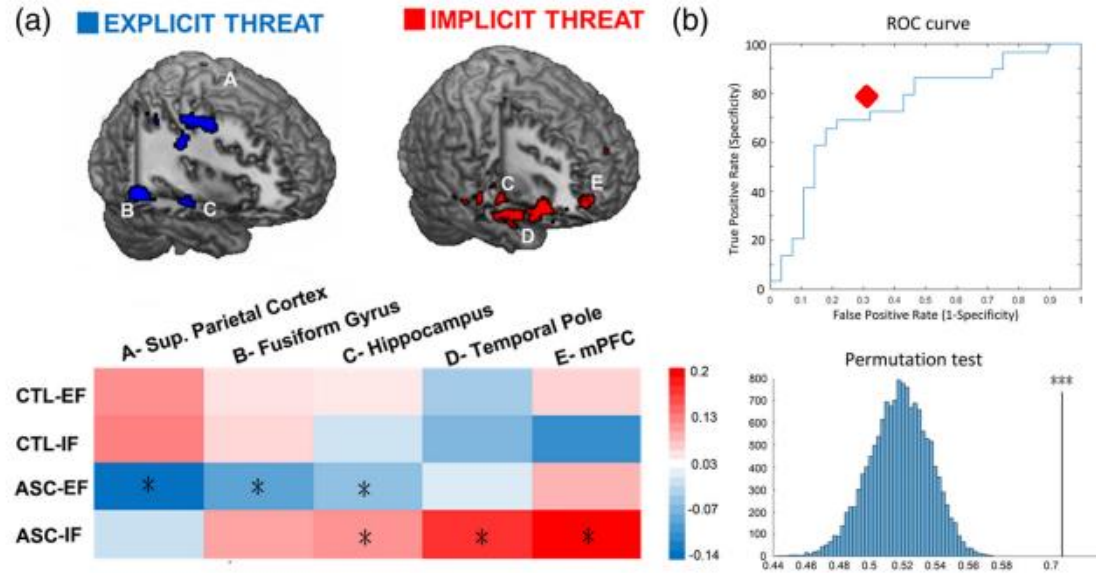
FIGURE 2 Dissociated correlations of autistic traits and anxiety with amygdala reactivity to explicit and implicit threat.



The correlation between the autism quotient (AQ) and amygdala reactivity (30, 0, 26) is negative in explicit fear ($r = 0.34, p = 0.015$), but positive in implicit fear ($r = 0.33, p = 0.018$) when the ASC and control groups are recruited together ($N = 51$). Fisher's z test confirms a significant dissociation ($z = 3.41, p < 0.001$).

The correlation between STAI-S and amygdala reactivity was positive in implicit fear ($r = 0.38, p = 0.007$), but none in explicit fear ($r = 0.11, p = 0.455$). Fisher's z tests confirmed a significant differential correlation ($z = 2.49, p = 0.013$).

FIGURE 3 Dissociated amygdala functional connectivity by explicit and implicit threat in ASC.



- (a) A significance plot of the altered correlation between the seed amygdala activity and superior parietal cortex, hippocampus, and fusiform gyrus in ASC. Compared to the controls, individuals with ASC have a significantly greater negative correlations of the amygdala with the superior parietal cortex, fusiform gyrus, and hippocampus when processing explicit threat, whereas a significantly more positive connectivity of the amygdala with the medial prefrontal cortex (mPFC), temporal pole and hippocampus when processing implicit threat. *, family-wise error rate (FWE-corrected) threshold of $p < 0.05$.
- (b) The LibSVM machine learning model that uses amygdala-centered functional connectivity during explicit and implicit emotional processing predicted the diagnosis of autism (74%, $p < 0.0001$ against the chance level of 50%).

Conclusion

- Our study identifies the dissociation of amygdala reactivity and functional connectivity dependent on **explicit** and **implicit** threat processing.
- Implicit anxiety in individuals with ASC could outweigh explicitly induced threat. When explicitly perceiving socioemotional stimuli, ASC individuals with anxiety might use **attentional avoidance patterns** to restrict affective hyperarousal.
- This gives a sense of urgency for the need to develop a **combined therapy** to include an attention-independent behavioral/neural marker concerning anxiety in ASC.

Thank you for listening!

