Noradrenaline Potentiates Conditioned Fear Bradycardia, N170, and Late Positive Potential Amplitudes

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Background

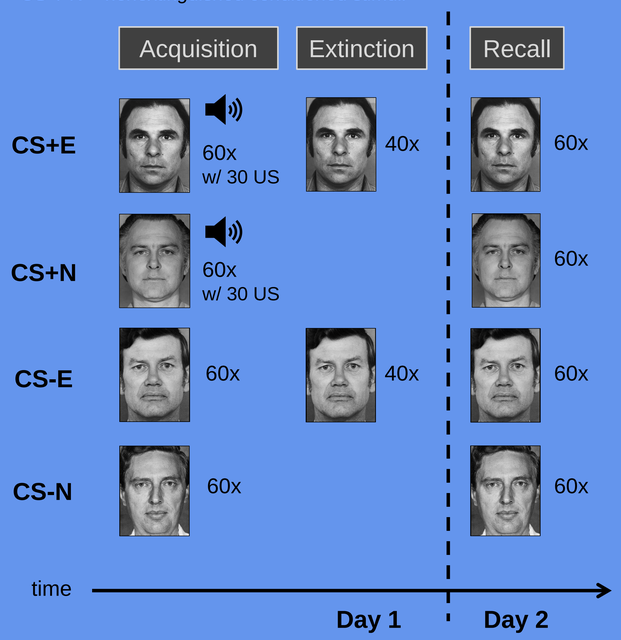
Fear conditioning is an important model for understanding the etiology and maintenance of anxiety disorders, while extinction of fear is considered to reflect the underlying learning process of exposure therapies. Previous research has pointed to a potential role of noradrenaline and dopamine, in acquiring emotional memories (e.g., McGaugh, 2013; Bowers & Ressler, 2015).

Here, we investigated whether the noradrenergic alpha-2 adrenoreceptor antagonist yohimbine and the dopaminergic D2 receptor antagonist sulpiride modulate long-term fear conditioning and extinction in humans.

We showed that yohimbine modulated consolidation and enhanced recall of conditioned (but not extinguished) fear. We did not find dopaminergic effects on fear and extinction consolidation.

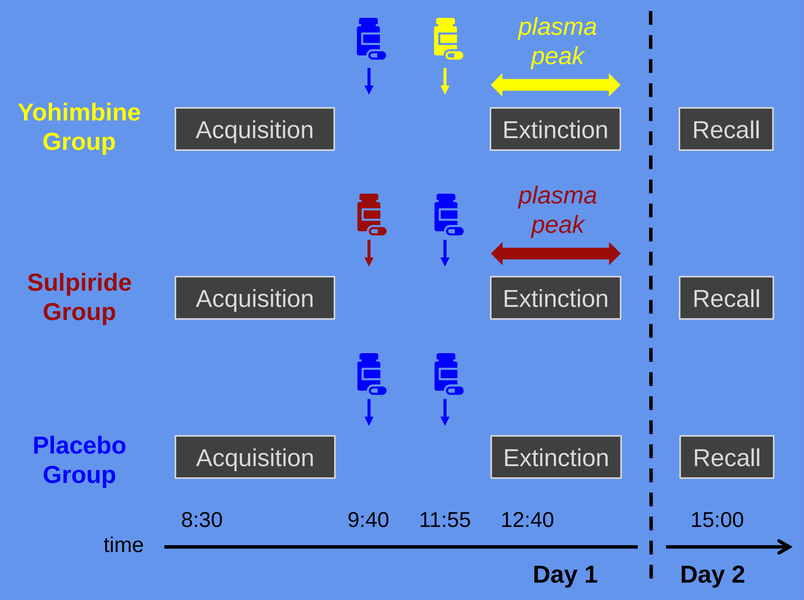
Fear Conditioning and Extinction Paradigm

CS+/-E = extinguished conditioned stimuli
CS+/-N = nonextinguished conditioned stimuli



Fifty-four participants underwent a differential fear conditioning and extinction paradigm (Mueller et al., 2014; face CS: Ekman & Friesen,1976; 95 dB white noise US). Fear and extinction recall was assessed one day later.

Pharmacological Challenge: Yohimbine and Sulpiride

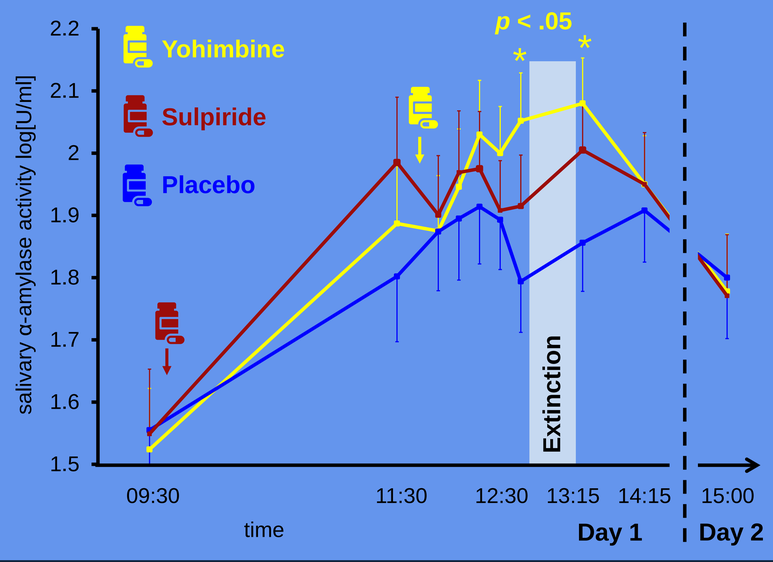


Participants received yohimbine (10 mg, n = 18), sulpiride (200 mg, n = 18), or placebo (n = 18) between acquisition and extinction stages.

Experimental Manipulation Check: α-Amylase

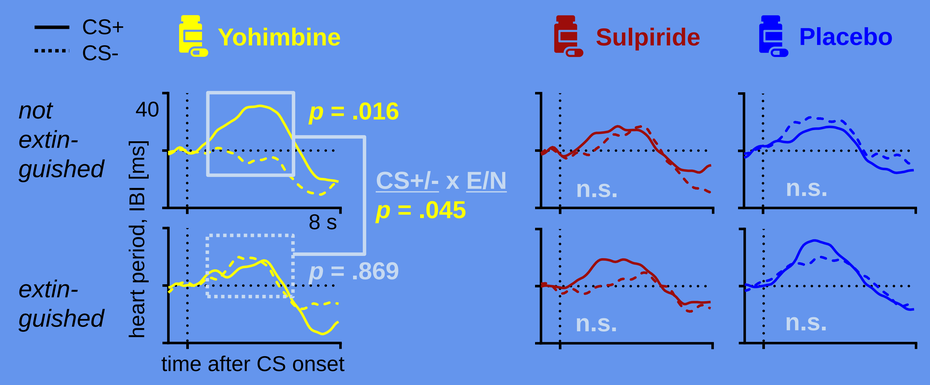
Increased α-amylase activity for yohimbine group

(reflecting central noradrenaline release; Ehlert et al., 2006)



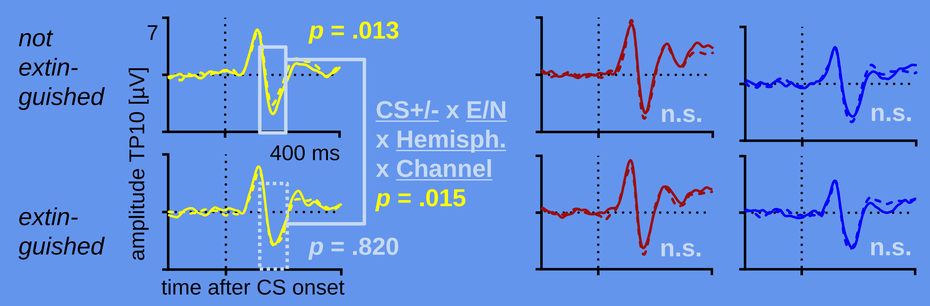
Day 2 Fear and Extinction Recall Only in Yohimbine Group

ECG: Fear bradycardia (cardiac deceleration 2-5 s post-CS)



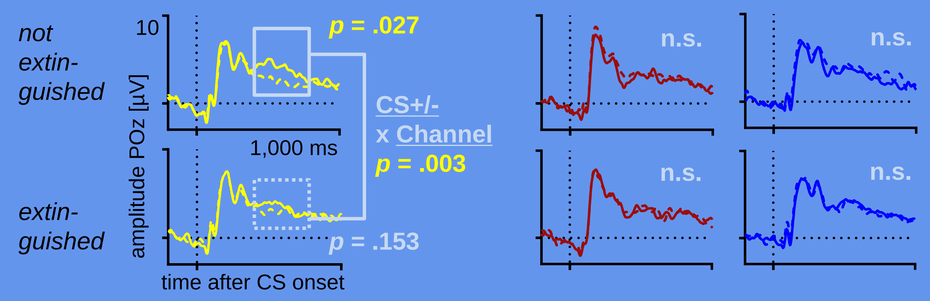
Contingency (CS+/-) x Extinction (E/N) x Substance: $p = .020$ (first 10 trials)

EEG: N170 (145-185 ms post-CS, T7/8, TP7/8, TP9/10, P7/8, PO9/10)



CS+/- x E/N x Hemisphere x Channel x Substance: $p = .019$

EEG: LPP (400-800 ms post-CS, P1/z/2, PO3/z/4, O1/z/2)



CS+/- x Channel x Substance: $p = .003$; CS+/- x E/N x Substance: $p = .069$

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