# Opposing roles for amygdala and vmPFC in the return of appetitive conditioned responses in humans

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## INTRODUCTION

- Pavlovian reward cues can trigger craving and increase relapse risk in addiction
- Pavlovian relapse phenomena like reinstatement challenge the success of extinction-based treatments
- Translational human models of appetitive Pavlovian relapse are missing

## METHODS

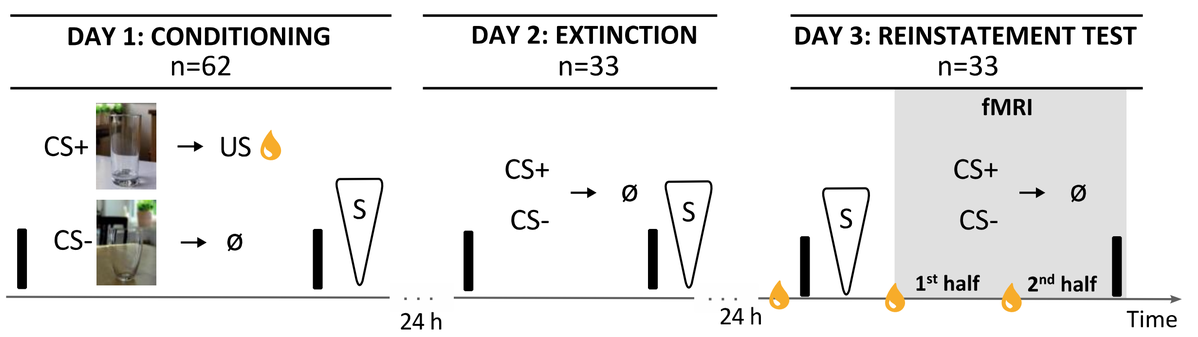


**FIG 1 Three-day design** During conditioning, one of two neutral pictures (CS+) was followed by 1 ml of liquid food (50% reinforcement schedule), delivered directly into the participants' mouth.

- Multimodal assessment of conditioned responses: valence ratings, SCRs, startle reflexes, heart rate, RTs, fMRI
- Imaging analysis within SPM12: flexible factorial design with factors cue (CS+/CS-) and phase (early/late); SVC for a priori defined VOIs (bilateral amygdala, Nacc, and vmPFC) at p<0.05 FWE correction

## RESULTS I

### Conditioning & extinction of conditioned responses

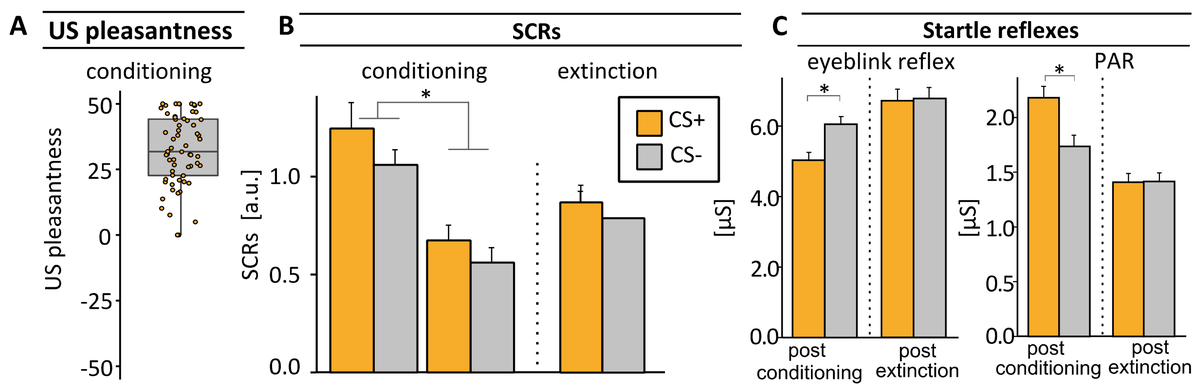


**FIG 2 A** US pleasantness ratings during conditioning (inclusion criterion) **B+C** differential SCRs (main effect cue: $F(1,59)=7.08$, $p=.010$) and startle reflexes ($p\leq.005$) during conditioning vanished during extinction ($p\geq.329$); PAR: postauricular reflex; a.u.: arbitrary units; *$p\leq.05$

## RESULTS II

### Appetitive reinstatement activates amygdala & NAcc

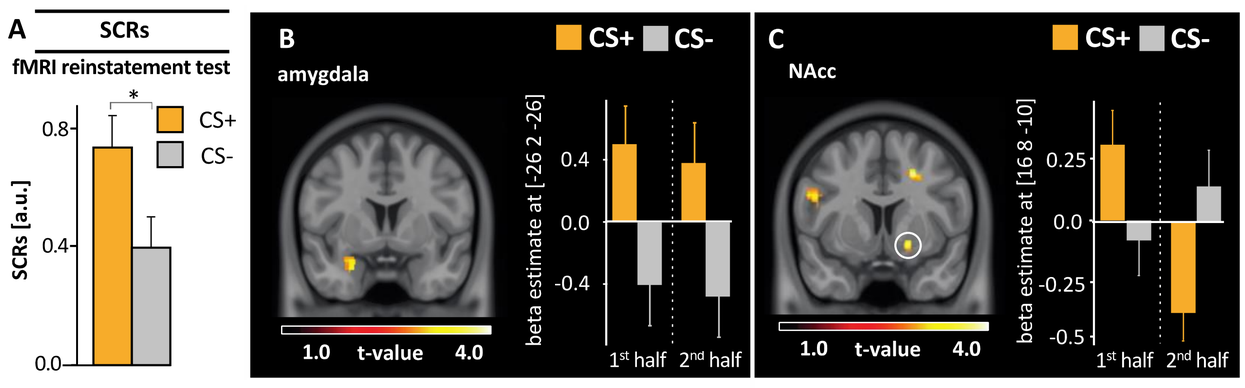


**FIG 3 A** Return of differential SCRs (first 5 trials after reinstatement: $t(32)=2.25$, $p=.031$). **B** Elevated BOLD response in the left amygdala over phases (MNI peak at [-26 2 -26], $p_{FWE\ ROI}=.01$). **C** CS+ related activation declines from early to late recovery test in the right Nacc (cue × phase interaction: MNI peak at [16 8 -10], $p_{FWE\ ROI}=.016$).

### vmPFC activity & amygdala–vmPFC connectivity mediate appetitive Pavlovian relapse

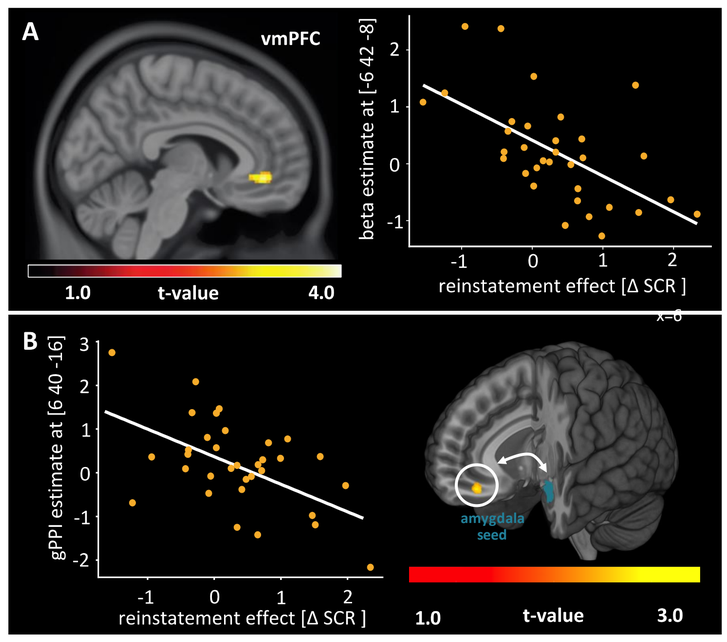


**FIG 4 A** Differential BOLD responses in the vmPFC during reinstatement test were anti-correlated with reinstated SCRs (MNI peak at [-6 42 -8], $p_{FWE\ ROI}=.022$). **B** Cue-dependent functional amygdala-vmPFC connectivity (gPPI) during late reinstatement (MNI peak at [8 44 -16], $p_{FWE\ ROI}=.032$) was marginally anticor-related with reinstated SCRs (MNI peak at [6 40 -16], $p_{FWE\ ROI}=.061$). All t-maps displayed at $p<.005$ uc., k≥20 cluster extend.

## DISCUSSION

- We highlight a role for the vmPFC and its functional connection with the amygdala in regulating appetitive Pavlovian relapse
- the vmPFC might therefore be a promising target for novel interventions to counteract appetitive Pavlovian relapse

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Transl Psychiatry, 2019; 9:148