

Processing of contextual information during fear extinction in PTSD

INTRODUCTION

- Fear extinction results in the formation of a new memory that exists along with the initial conditioning memory (Rescorla 2001, Quirk 2002).

- Neuronal signaling of contextual information is critically involved in the expression or inhibition of conditioned fear responses (Bouton 1983; Harris 2000). Specifically, contextual information gates the expression of the potentially conflicting conditioning and extinction memories

- Deficient contextual signaling facilitates the development and maintenance of exaggerated fear responses in anxiety disorders. (Mineka 2008, Liberzon 2008)

- *The present study addresses whether patients with PTSD show an altered pattern of brain activation to contexts that have been associated with fear extinction.*

METHODS

- Eighteen PTSD patients and 16 trauma exposed normal controls (TENC) underwent a two-day fear conditioning and extinction procedure.

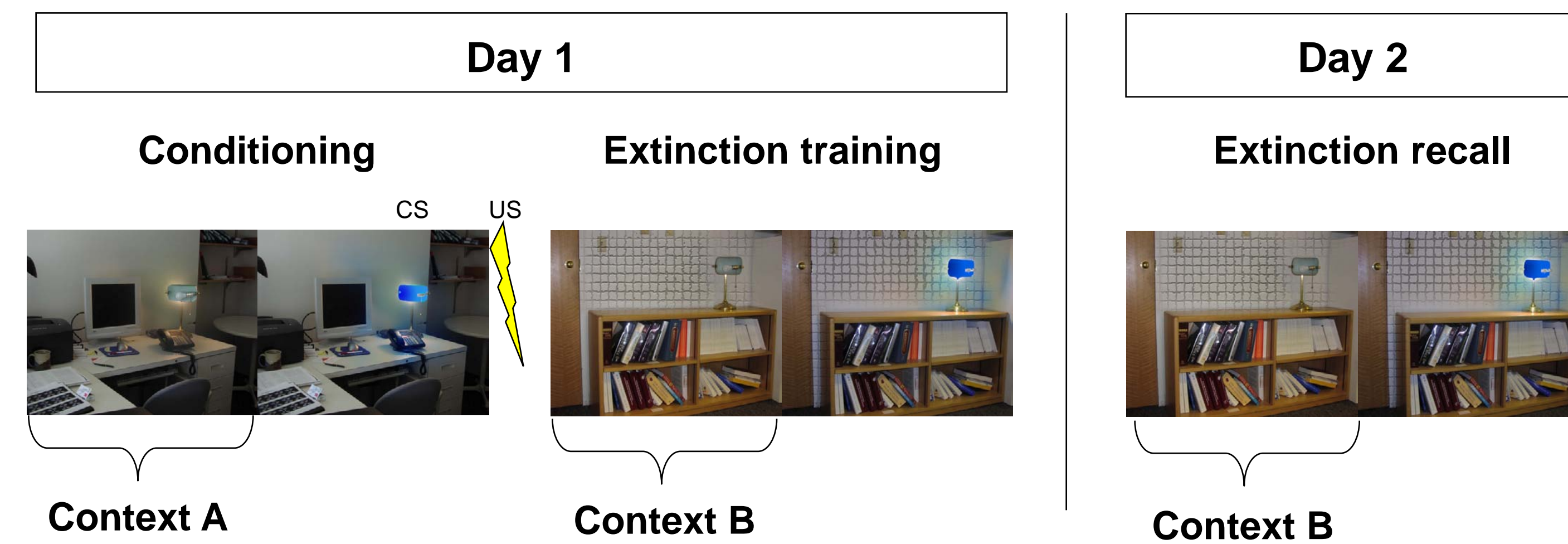
- Participants underwent a two-day fear conditioning and extinction protocol, as previously described (Milad et al., in press). The paradigm entailed fear conditioning in context A and fear extinction in context B on Day 1, and fear extinction recall in context B on Day 2

- All experimental phases were conducted in a 3T fMRI scanner.

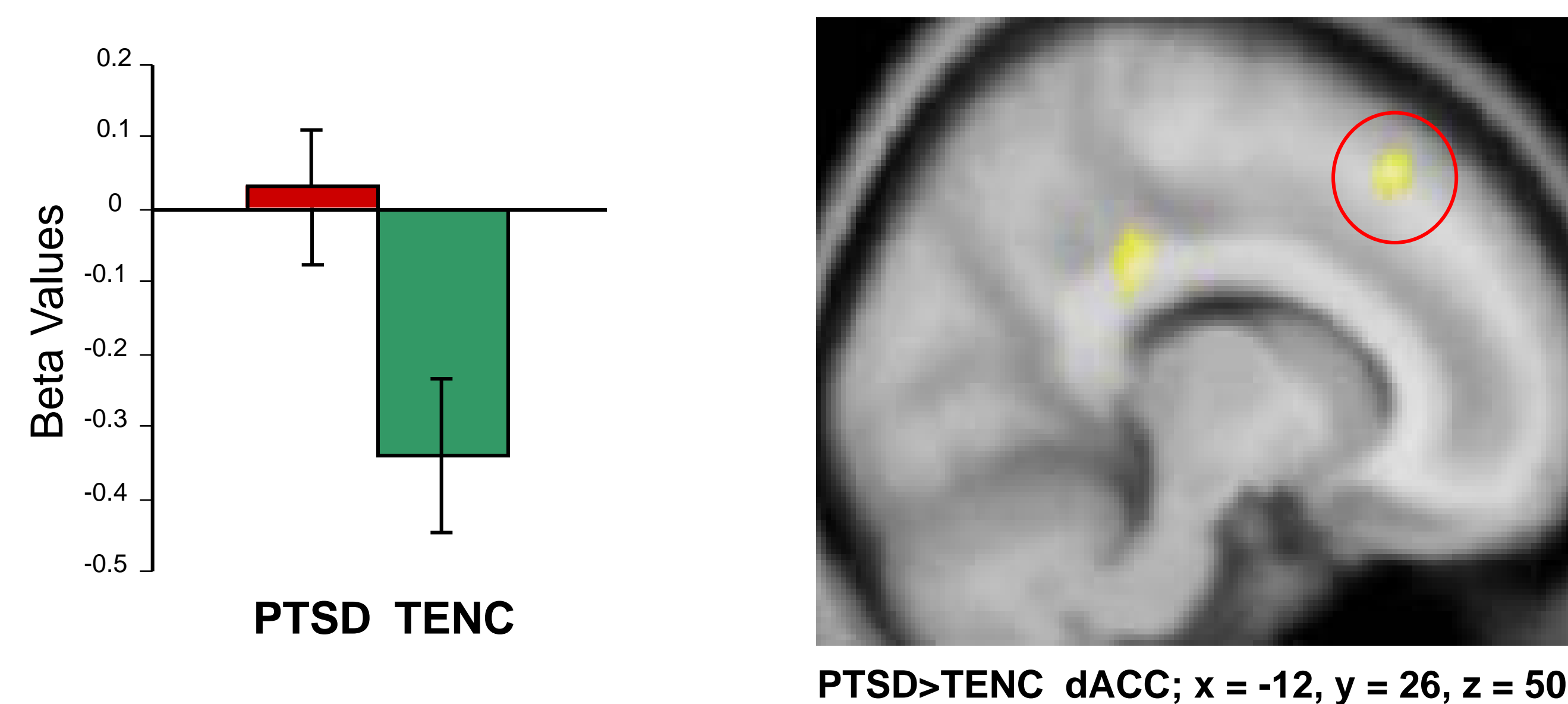
- Data was analyzed in SPM8 modeling context activations with a 3 second epoch convolved with a canonical HRF function. Conditioning, extinction and extinction recall phases were split in an early and late phase.

- The present results all refer to BOLD signal during the context presentation, prior to the conditioned stimulus.

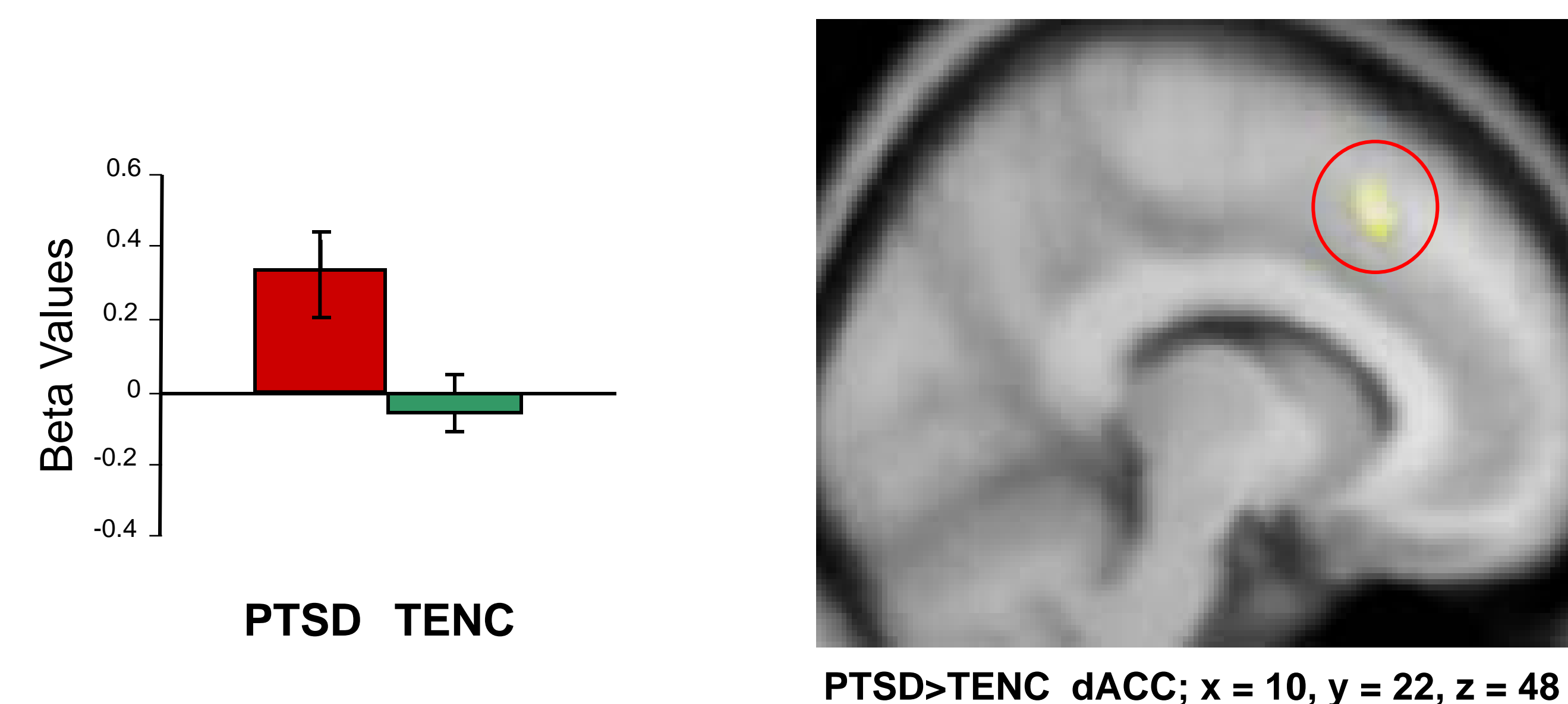
Fear conditioning and extinction protocol



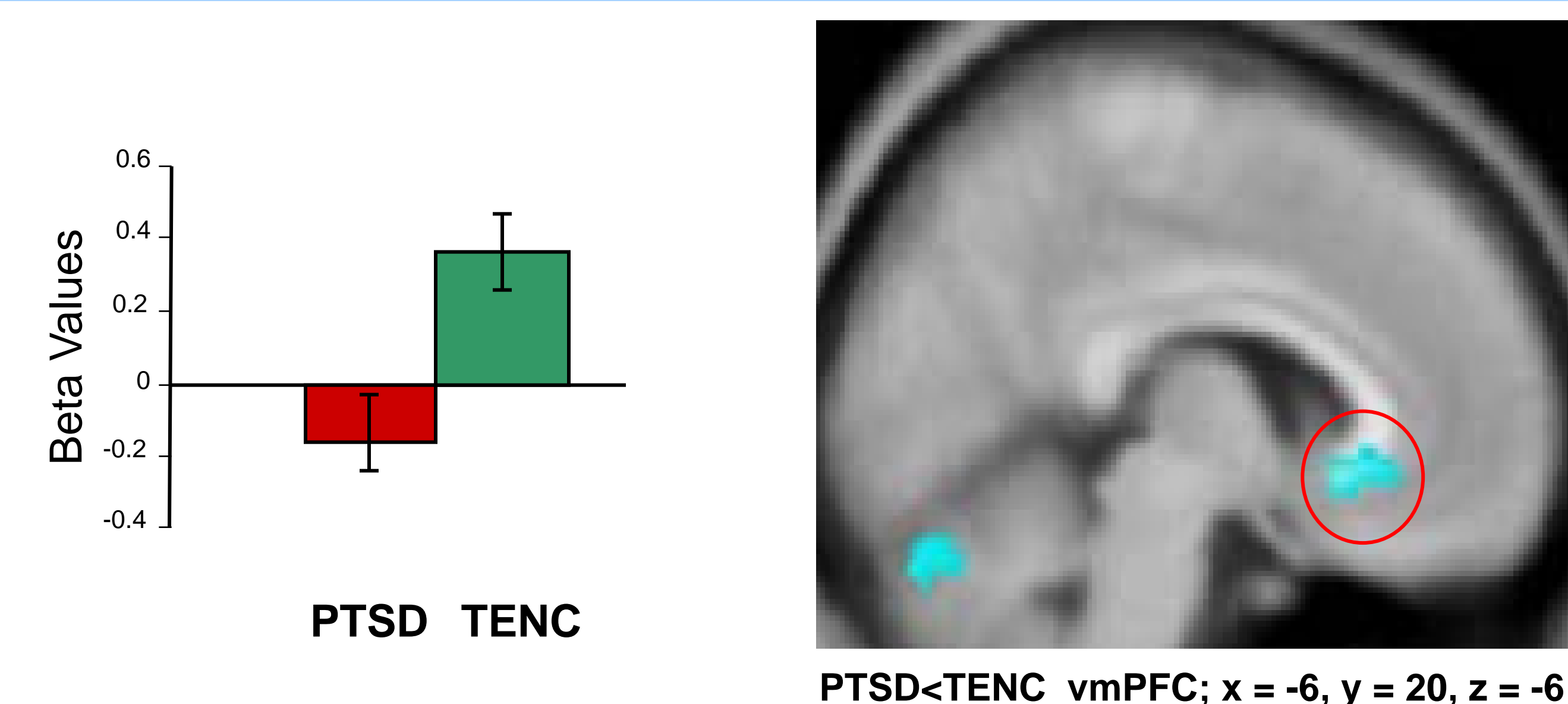
Context activation differences during LATE conditioning



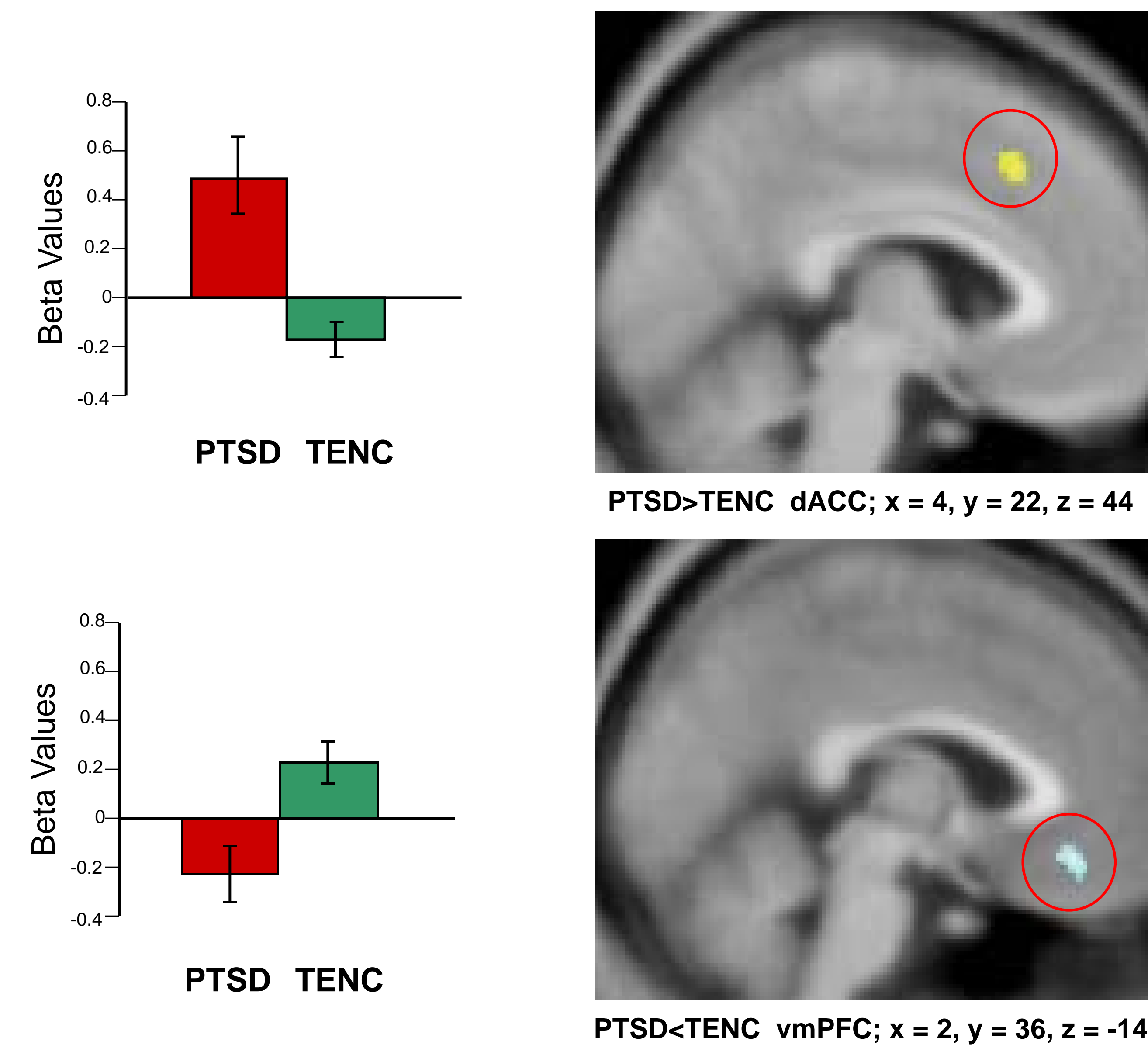
Context activation differences during EARLY extinction



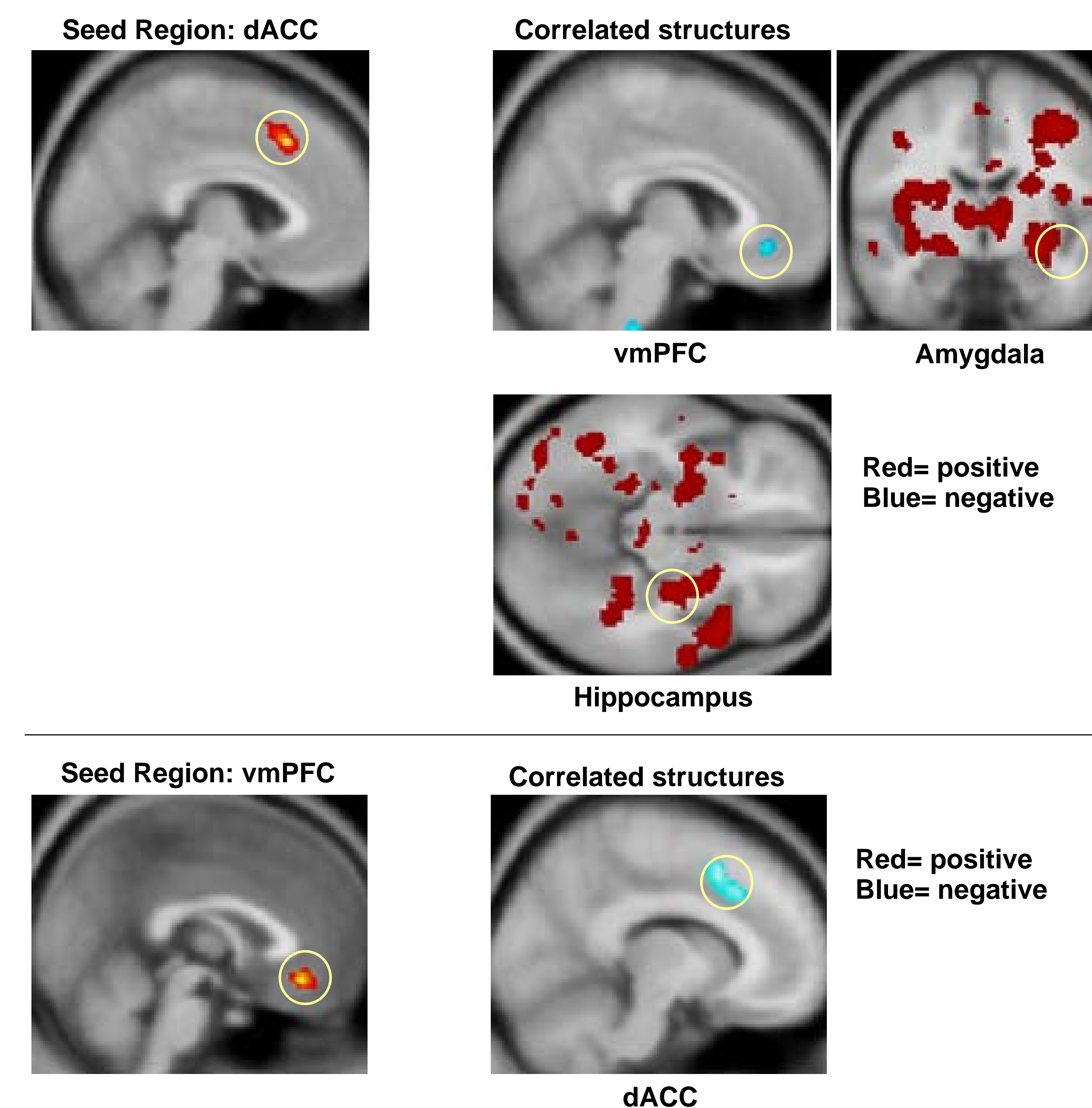
Context activation differences during LATE extinction



Context activation differences during EARLY extinction recall



Covariation of structures during extinction recall context



CONCLUSIONS

- PTSD subjects showed deactivation of the vmPFC and increased activation in the dACC, most evident in the early extinction recall phase, which occurs after both conditioning and extinction learning have been completed, and contextual information is needed to guide the choice of a response to the now-ambiguous CS.

- In addition to finding dysfunctional responses to extinguished cues in PTSD subjects (Milad, in press), our analysis shows that the function of these structures is also impaired during the processing of contextual information.

- The ability to attribute "safety" to safety-related contextual cues seems impaired in PTSD subjects. The contextual information may remain dangerous, or at least ambiguous to patients with PTSD.

- Experiencing trauma-related memories and affects outside the traumatic context might be understood as an inability to express distinctive affective states in accordance with their relevant contexts.

REFERENCES

- Rescorla RA (2001) Retraining of extinguished Pavlovian stimuli. *J Exp Psychol Anim Behav Process* 27: 115-124.
- Quirk GJ (2002) Memory for extinction of conditioned fear is long-lasting and persists following spontaneous recovery. *Learn Mem* 9: 402-407.
- Bouton ME, King DA. Contextual control of the extinction of conditioned fear: tests for the associative value of the context. *J Exp Psychol Anim Behav Process* 1983; 9:248-265.
- Harris JA, Jones ML, Bailey GK, Westbrook RF. Contextual control over conditioned responding in an extinction paradigm. *J Exp Psychol Anim Behav Process* 2000; 26:174-185.
- Mineka S, Oehlberg K. The relevance of recent developments in classical conditioning to understanding the etiology and maintenance of anxiety disorders. *Acta Psychol (Amst)* 2008; 127:567-580.
- Liberzon I, Sripada CS. The functional neuroanatomy of PTSD: a critical review. *Prog Brain Res* 2008; 167:151-169.
- Milad MR, Pitman RK, Ellis CB, Gold AB, Shin LM, Lasko NB et al. Neurobiological basis for failure to recall extinction memory in Posttraumatic Stress Disorder. *Biological Psychiatry*. In press

ACKNOWLEDGMENTS

This work was supported by the NIMH, NRSAD, the CHUV and the Société Académique Vaudoise (Switzerland), LANTERN and MGH. JRR would like to thank Sfn-NSP and APA-DPN for travel support.