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Highlights

- PTSD showed altered behavioral responses to potential monetary losses
- When avoiding monetary losses, PTSD depicted increased activation of basal ganglia
- When anticipating monetary gains, PTSD exhibited altered activation of basal ganglia
- During receipt of monetary gains PTSD showed altered activation of basal ganglia

Posttraumatic Stress Disorder is associated with altered reward mechanisms during the anticipation and the outcome of monetary incentive cues

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Abstract

Background: Recent studies suggest that Posttraumatic Stress Disorder (PTSD) might be associated with dysfunctional reward circuitry. However, further research is needed to understand the key role of the reward system in PTSD symptomatology.

Methods: Twenty participants with PTSD and 21 Trauma-Exposed matched Controls (TECs) completed the Monetary Incentive Delay (MID) task during an MRI session. Reaction times (RTs) and hit rates were recorded. Brain activity was investigated during the anticipation and the outcome of monetary gains and losses.

Results: During the anticipation of monetary loss, PTSD participants had higher RTs than TECs. However, the groups did not differ at the neurofunctional level. During successful avoidance of monetary loss, PTSD patients showed higher activation than TECs in the left caudate nucleus. During the anticipation of monetary gains, no differences in RTs were found between groups. PTSD patients had specific activations in the right amygdala, nucleus accumbens, putamen, and middle frontal gyrus ($p < 0.05$ family-wise error (FWE)-corrected), while TECs had specific activation in the anterior cingulate cortex. When obtaining monetary gains, PTSD patients had specific activation in the caudate nucleus, while TECs had specific activations in the right hypothalamus, subthalamic nucleus, and left inferior frontal gyrus.

Conclusion: For the first time, functional brain activation during both the anticipation and the outcome of monetary rewards is reported altered in PTSD patients. These alterations might be associated with the complex symptomatology of PTSD.

Introduction

Posttraumatic stress disorder (PTSD) is a debilitating psychiatric disorder that can develop after experiencing a traumatic event (1). PTSD consists of different dimensions of symptoms: re-experiencing the traumatic event, avoidance/emotional numbing, and hyperarousal emotions so the exploration of the underlying mechanisms is considerably complex (1,2). PTSD has been conceptualized as heightened fear reactivity (3), but recent studies suggest that besides the well-described alterations of the brain fear circuitry (4–6), altered reward circuitry could also contribute to core components of the pathology, such as emotional numbing, characterized by a diminished interest in pleasant activities (7). Preclinical studies also suggested that chronic stress is responsible for striatal dopaminergic alterations, contributing to re-experiencing symptoms (8,9). Thus, altered reward circuitry might be associated with different dimensions of the symptoms.

Two phases or periods can be distinguished in reward processing. The anticipation phase represents the period during which an individual is expecting the reward, and the consummatory phase represents the period during which an individual actually obtains the reward (10-12). In line with this distinction, functional MRI (fMRI) studies have highlighted distinct neural mechanisms underlying the anticipation and the consumption of monetary gains and losses (13,14). In healthy participants, anticipation of a reward has been found to activate foci in the ventral striatum including the nucleus accumbens (NAcc), while reward delivery recruits the medial prefrontal cortex (mPFC), the dorsomedial part of the caudate nucleus, and the posterior cingulate cortex (14, 15).

To date, only few behavioral studies have focused on reward mechanisms in PTSD. In a paradigm during which participants were instructed to rate the attractiveness of female faces, PTSD veterans spent less time viewing the stimuli than did male veterans without PTSD, which revealed their lack of motivation to pursue pleasant experiences (16). Self-reported

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ratings of expectancy and satisfaction evaluated with a wheel-of-fortune gambling task were lower in PTSD veterans than trauma-exposed controls (TECs) (17). In line with this, in a decision-making task during which participants could maximize their total number of points (i.e., reward) by learning a particular response pattern, healthy control participants learned correct responses faster than did PTSD patients (18). In contrast, a study using a probabilistic classification task reported that male veterans with severe PTSD symptoms performed better than male veterans without PTSD symptoms in reward trials, with no difference in punishment trials (19).

Only a few investigated the neural dysfunction of the reward system. Despite no differences observed during the expectation of reward, altered responses have been observed during the expectation of an aversive outcome (20). As compared with healthy controls, PTSD patients showed lower activation in key components of the reward system when obtaining rewards, namely the NAcc, the ventral and dorsal striatum and the mPFC (20,21). Understanding the neural mechanisms underlying the expectation and the outcome periods in PTSD patients and their association with the complex symptomatology may help clinical assessments of the effect of interventions.

To date, studies have focused on a limited number of structures of the reward system, such as the NAcc and orbitofrontal cortex (OFC), and the implication of other brain structures has not been explored in PTSD. Hence, there is a need for whole-brain studies to investigate changes in the reward circuitry globally. Moreover, previous studies mainly compared gain and loss trials, which precluded the exploration of the effect of monetary gain and loss independently.

The aim of the present study was to investigate the neurobiological mechanisms underlying the anticipation and the outcome of both monetary gain and loss in PTSD patients at the whole-brain level. We hypothesized that the reward brain circuitry would be differently

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activated during both the anticipation and the outcome of monetary reward in individuals with

PTSD as compared with TECs.

Methods and Materials

Participants

PTSD patients were recruited from the Psychiatry Pole of three different hospitals in the region of Marseille, France (Hôpital de la Conception, Hôpital d'Instruction des Armées de Sainte-Anne, Hôpital Laveran). TECs were recruited by advertisements/flyers distributed at the "Hôpital de la Conception" hospital. The structured Mini-Internal Neuropsychiatric Interview for DSM-IV (1) was administered by psychiatrists to assess PTSD diagnosis and to rule out any potential comorbidities. Demographic and clinical characteristics of participants are described in Table 1. Participants recruited at the "Hôpital d'Instruction des Armées de Sainte-Anne" and "Hôpital Laveran" hospitals were veterans, and those recruited at the "Hôpital de la Conception" hospital were civilians. In total, 22 PTSD patients met the DSM-IV criteria for PTSD following one traumatic event (1). PTSD patients additionally completed the trauma-related scale, the PTSD Check List Scale (PCL-S) French version (22). Two patients were excluded from the data analysis due to excessive head motion during image acquisition. Subsequent analysis included 20 PTSD patients. Twenty-three TECs without a history of neurologic or psychiatric disorders were included. Two participants were excluded from the data analysis due to excessive head motion during image acquisition. Thus, the final sample included 21 TECs. These participants were exposed to one traumatic event (ascertained by self-report), without PTSD developing according to the DSM-IV criteria. The groups did not differ in age: t(39) = 1.10, $p > 0.1$, education: t(39) = -1.00, $p > 0.1$, or sex: $\chi^2(2, 41) = 0.01$, $p > 0.1$ (Table 1).

Exclusion criteria for all participants included noncompliance with 3T fMRI safety standards, a history of head injury with loss of consciousness, significant untreated medical illness, neurological disorders, pervasive developmental disorders, and pregnancy. Exclusion criteria for PTSD patients included a history of bipolar disorder or schizophrenia, and alcohol

or substance dependence not in sustained full remission within 6 months before the study. The study was carried out in accordance with the Declaration of Helsinki. Participants provided written informed consent in agreement with ethical approval from the committee South Mediterranean 2 (registration no.: 2013-A01016-39).

Experimental paradigm

The Monetary Incentive Delay (MID) task developed by Knutson and colleagues (2008) was used (See Figure 1). The detailed task description is included in the Supplemental material.

MRI acquisition

fMRI data were acquired as described in Supplemental material.

Behavioral Data Analysis

Behavioral data were analyzed with SPSS (v18.0). Reaction times (RTs) and hit rates (HRs) were recorded for each participant. Only the correct trials for which participants responded within the 1-s time window were included. Because we intended to compare neural mechanisms during incentive versus non-incentive trials, we analyzed RT and HR differences between incentive and non-incentive cues. Therefore, we used repeated-measures ANOVA for each condition (positive and negative cues) with *Group* (PTSD and TEC) as the between-subject factor and *Incentive* (10-0€ cents; 50-0€ cents; 200-0€ cents) as the within-subject factor for both RTs and HRs. Bonferroni correction was used for post-hoc comparisons. Main and interaction effects were analyzed separately for negative (i.e., predicting possible loss) and positive (i.e., predicting possible gain) cues.

fMRI data analyses

MRI data were analyzed by using SPM12 (Wellcome Trust Centre for Neuroimaging www.fil.ion.ucl.ac.uk/spm). The first 4 volumes from each session, corresponding to signal stabilization, were excluded from the analysis. We used standard preprocessing procedures, including motion correction, slice timing correction, EPI co-registration to the T1 image, normalization to the Montreal Neurological Institute (MNI) space, and smoothing with an 8-mm full-width-half-maximum (FWHM) Gaussian kernel.

Statistical analysis of fMRI data focused on the blood oxygen level-dependent response that occurred during the anticipation of monetary gain/loss and the outcome of monetary gain/loss, by using a mass-univariate approach based on General Linear Models (GLMs). For each participant, we computed a model with 12 regressors describing events of interest: anticipation of gain (i.e., +10, +50 and +200); anticipation of no gain (+0, still requiring a response); anticipation of loss (i.e., -10, -50 and -200); anticipation of no loss (-0, still requiring a response); hit gain (+10, +50, and +200); failed gain (+0); no gain, as announced (+0); avoided loss (-0); non-avoided loss (-10, -50 and -200); no loss as announced (-0); neutral (triangle); and button press. To investigate the linear relationship between brain activity and the magnitude of the incentive value, parametric regressors modulated the following conditions: anticipation of loss, anticipation of no loss, hit gain and non-avoided loss. These regressors of interest were convolved with the canonical hemodynamic response function.

The 6 realignment parameters were included to correct for signal changes due to head movement. To control for scanner and physiological noise, additional regressors that depicted harmonic changes up to 1/128 Hz were added.

Results from the single-subject level for our contrasts of interest were fed into a flexible factorial design as implemented in SPM, including the *Subject* and *Incentive* values

(±0 versus ±10 ±50 ±200) as within-subjects factors and the *Group* (PTSD and TEC) as a between-subjects factor. The comparisons were as follows: anticipation of gain versus anticipation of no gain; anticipation of loss versus anticipation of no loss; outcome of hit gain versus outcome of failed gain, and outcome of avoided loss versus outcome of loss.

Common group effects were assessed by using conjunction analyses, showing significant activation increase in both PTSD patients and TECs (23). Given the exploratory purpose of this research and the within-subject nature of this study, we used an exclusive masking procedure to compare maps of brain activity between groups. The exclusive masking procedure allows for detecting differences between groups in spatial patterns of significantly activated voxels. With masking, any significant area of change in one group is excluded from the analysis of the other group, leaving only changes exclusive to this other group in the statistical assessment. This statistical technique has been described in functional neuroimaging studies (24–29). A threshold of $p < 0.05$ uncorrected was used for the SPM maps used for the exclusive masking. The more liberal the exclusive mask threshold, the more conservative the masking procedure. The resulting statistical maps were then corrected for multiple comparisons with a $p < 0.05$ Family-Wise Error (FWE) cluster-extent threshold (30) across the whole brain.

For the PTSD group only, the extracted parameter estimates for each significant cluster and the PCL-S scale scores and subscores were investigated using Pearson correlation with Bonferroni correction. The PCL-S scale can be divided into 3 subscores, corresponding to 3 main symptoms of the disorder: reexperiencing (item 1-5), avoidance/numbing (items 6-12) and hyperarousal (items 13-17). These correlation analyses explored the relationship between brain changes activity and PTSD core symptoms.

Results

As expected, for the PTSD patients, PCL-S total scale scores were higher than the cut-off of 44 points ($M_{PCL-S\ total\ score}$ = 61.90, SD = 12.33) (22). Behavioral results are described in Table 2. Mean RTs, total gain, the rating of feeling of motivation and the rating of feeling of fear of losing money did not differ significantly between the PTSD and TEC groups.

During the anticipation of monetary losses, *Group* had a main effect on RTs ($F_{1,39}$ = 5.42; $p < 0.05$), with TECs responding faster during target presentation than PTSD patients (See Figure 2A). We found neither a main effect of *Incentive* ($F_{2,78}$ = 2.02, $p = 0.14$) or *Group* by *Incentive* interaction ($F_{2,78}$ = 0.06, $p = 0.94$) on RTs during the anticipation of monetary losses, but found a main effect of *Incentive* on HRs ($F_{2,78}$ = 12.08, $p < 0.001$) (See Figure 2C); thus, both groups had better performance when anticipating higher potential monetary losses. We found no main effect of *Group* ($F_{1,39}$ = 1.86, $p = 0.18$) during the anticipation of monetary losses.

During the anticipation of monetary gains, we found no main effect of *Group* ($F_{1,39}$ = 0.00, $p = 1.00$) or *Incentive* ($F_{2,78}$ = 2.60, $p = 0.08$) and no *Group* by *Incentive* interaction on RTs ($F_{2,78}$ = 1.61, $p = 0.21$) (See Figure 2B), but found a main effect of *Incentive* on HRs ($F_{2,78}$ = 5.47; $p < 0.001$) (See Figure 2D), demonstrating better performance when anticipating higher monetary rewards. We found no main effect of *Group* on HRs ($F_{1,39}$ = 0.01; $p = 0.95$) during the anticipation of monetary rewards.

fMRI Results

During the anticipation of gain *versus* no gain, both PTSD patients and TECs showed activation in key structures of the reward circuitry including the head of the caudate nucleus, left insula, inferior frontal gyrus, and dorsal anterior cingulate cortex (ACC) (31–33) (Table 3). PTSD patients but not TECs exhibited significant activation in a cluster including the right

NAcc, putamen, and amygdala (see Figure 3A, Table 3). Parameter estimates extracted from each structure within this cluster are depicted in Figure S1 of the Supplemental material. Moreover, PTSD patients but not TECs showed significant activation in the right superior frontal gyrus (SFG; BA 6) (see Figure 3B, Table 3). Conversely, TECs but not PTSD patients showed activation in the bilateral ACC (BA 24, BA 33) (see Figure 3C, Table 3). We found no group differences during the anticipation of loss *versus* anticipation of no loss. For PTSD patients, Pearson correlation coefficients were not significant between extracted parameter estimates and PCL-S scale scores and subscores (all $p_s > 0.1$).

During the outcome of hit *versus* failed gain, both PTSD patients and TECs activated a network of brain region involved in the receipt of reward, including precentral gyrus, precuneus, superior parietal lobule, middle frontal gyrus and subcallosal gyrus (Table 4) (34). PTSD participants showed a unique significant activation in the body of the caudate nucleus bilaterally (see Figure 4A, Table 4). However, TECs but not PTSD patients showed a significant activation in a region including the right hypothalamus and the right subthalamic nucleus (See Figure 4B). Parameter estimates extracted for each structure of this cluster are depicted in the Figure S2 of the Supplemental material. In addition, TECs but not PTSD patients activated a cluster in the left IFG (BA 46, BA 10) (See Figure 4C, Table 4).

Finally, during the outcome of avoided loss *versus* loss, PTSD patients but not TECs showed activation in the body of the left caudate nucleus (Figure 5; Table 5).

Discussion

The present findings identify differences between PTSD patients and matched TECs in behavior and neural activation in the reward circuitry during both the anticipation and the outcome of monetary rewards. During the anticipation of monetary losses, PTSD patients were slower than TECs to respond during target presentation, but the groups did not differ at the neural level. PTSD patients showed higher functional activation in the left caudate nucleus when they successfully avoided monetary losses. In contrast, during the anticipation of monetary rewards, PTSD patients showed higher activation in the putamen, NAcc, amygdala, and SFG, despite no difference in behavioral performance. However, PTSD patients did not show activation in the ACC during the anticipation of monetary rewards. Moreover, when they finally obtained money, PTSD patients showed a unique significant activation in the caudate nucleus but failed to reproduce the TEC activations in the subthalamic nucleus, hypothalamus and left IFG.

Our behavioral results for monetary losses are in agreement with the literature describing PTSD patients having slower behavioral responses toward negative stimuli (35–37). This behavioral pattern has been associated with an attentional bias of PTSD patients toward trauma cues (38-40), which suggests that their behavioral responses to potential monetary losses might relate to some attentional disengagement difficulties from threatening stimuli. This hypothesis fits with the cognitive theory positing that emotional distress and maintenance of anxiety disorder is due to the existence of non-adaptative attentional biases toward information with adverse value (41). However, when participants expected to lose money, the two groups did not differ at the neural level.

Despite no differences in behavioral responses between the groups during the expectation of monetary gains, we found specific activation patterns in PTSD patients. To our knowledge, this is the first study describing specific activation in cortico-striatal circuitry and limbic

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circuitry, including the putamen, NAcc, amygdala, and SFG, during the anticipation of monetary rewards in PSTD patients. Our results differ from studies that previously reported NAcc hypoactivation in PTSD patients when receiving monetary rewards (18,42). NAcc is known to code for expected positive incentive magnitude (15,20), so PTSD patients might show high NAcc activation when anticipating but not when receiving rewards.

Our result of higher amygdala activation in PTSD patients during the anticipation of monetary reward was surprising because exaggerated amygdala activity in PTSD patients has repeatedly been found in paradigms provoking PTSD symptoms (42, 43) but also in response to stimuli provoking the anticipation of anxiety (44), in fear conditioning and extinction paradigms (45-47) or during the processing of faces displaying negative emotion. Nevertheless, the finding of amygdala activation fits well with studies of healthy individuals showing an amygdala response to positive, rewarding stimuli, as well as during appetitive conditioning (48-54). One study showed amygdala reactivity to happy versus neutral faces in a masked facial affect paradigm in patients with anxiety disorders (PTSD, panic disorder and social phobia) (55), which suggests that the amygdala may be involved in processing emotional salience in general, rather than the negative valence (56–59). In this respect, increased amygdala activity may be associated with increased emotional significance of patients expecting money. This situation might reflect a maladaptive strategy of PTSD patients to cope with a stressful situation while trying to achieve goals (60). Moreover, ACC activation was found in TECs but not PTSD patients, which reinforces our interpretation of patients having altered strategies to cope with stressful situations. Indeed, the ACC has long been thought to play a critical role in emotional processing (61), and its hypoactivation is known to be associated with disrupted fear mechanisms (4,5,62). Thus, in line with animal (63) and human studies (64–66), alterations in the fear circuitry could parallel those observed

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in the reward circuitry, which would contribute to PTSD patients unreasonably anticipating the negative consequences of an action.

The putamen, part of the dorsal striatum, is known to be activated during the anticipation of a reward (15, 67), particularly when participants are presented with potential rewards such as the opportunity to obtain money (68, 69). Specific putamen activation in PTSD might be associated with the opportunity to obtain money. Finally, we found increased activation in the SFG in PTSD patients during the anticipation of monetary rewards. The SFG projects to the dorsal striatum and is involved in motor/sensorimotor function and integration (70,71). Given the key role of this structure in the integration of sensorimotor, cognitive, and motivational information, PTSD patients may have recruited motor resources to a greater degree to successfully achieve the task. Given the absence of significant differences in behavioral performances between the groups when attempting to get money, increased activity in those motor structures could reflect enhanced efforts from PTSD patients to obtain equivalent behavioral responses.

When receiving monetary rewards, we found a specific activation in the left caudate nucleus of PTSD patients. The caudate nucleus is part of the dorsal striatum, known to mediate affective properties of outcomes in rewarding conditions (32,35-37). It is particularly important for predicting and evaluating actions based on information about their outcome, consistent with its role in goal-directed behavior (38-40). This structure has been found activated by tasks entailing both a perceived connection between the action and outcome and an uncertainty about whether the action will lead to the desired outcome (41). O'Doherty and colleagues (2004) postulated that dopamine projections to the dorsal striatum might be involved in the modulation of stimulus-response or stimulus-response-reward associations. Thus, when PTSD patients finally received money, the increased activation in the caudate nucleus could result from the cognitive effort developed during the anticipatory period. This

interpretation also fits with the finding of increased activation in patients' left caudate nucleus during successful avoidance of monetary losses. When they obtained money, TECs but not PTSD patients showed activation in the right hypothalamus, STN, and left IFG. The hypothalamus is involved in primary motivational processes that can be related to hedonic responses (72). The STN is known to respond to reward delivery (73,74), but its inactivation can lead to reduced affective responses for positive and negative stimuli (75). A possible explanation for this finding is that structures having a key role in hedonic processes may be less active in PTSD patients when receiving the reward. Reduced activation in these areas could reflect altered processing in the evaluation of hedonic information, which might be related to emotional numbing in PTSD. Moreover, reduced activity in the IFG, a brain region having a key role in cognitive and emotional processing (76) and more specifically in emotional regulation (77,78) could also contribute to emotional numbing.

In summary, PTSD may feature altered brain activity associated with reward mechanisms during both the anticipation and the outcome of reward. On the one hand, these alterations could be described as the association of attentional bias to threatening stimuli together with exaggerated activity of structures involved in goal-directed behaviors during their avoidance. On the other, they could be associated with exaggerated recruitment of structures having a key role in cognitive processes during the anticipation and the outcome of reward, counterbalanced by hypoactivation of structures involved in hedonic and emotional regulation processes.

The present study provides promising results with a few limitations. It includes a sample with high heterogeneous trauma type, including civilians and veterans with PTSD, and controls exposed to civilian trauma. Veterans with PTSD experience different symptoms than do civilians with PTSD (79). The nature of the traumatic event may affect our results, but the size and heterogeneity of our population prevent the exploration of this question. We

encourage future studies to explore the impact of trauma type on brain functioning in PTSD. Although the comorbidity profiles of PTSD patients in this study are similar to those reported in most neuroimaging studies, and patients were on stable medical treatment, the pharmacological caveat needs to be mentioned. Indeed, previous studies showed that pharmacological treatment has an effect on brain structure and function in PTSD patients (80). Moreover, clinical data support the impact of serotoninergic and other medication changes on reward brain mechanisms (81). In the current study, the main effects and between-group differences remained after excluding PTSD patients on medication from the analysis. Future research controlling for medication status might be warranted. Finally, the lack of significant correlations between clinical scale scores and functional brain activity differences precludes the investigation of a causal relation between them.

By describing altered activation of structures involved in fear and reward circuits in PTSD, this study contributes to a better knowledge of the neural mechanisms involved in this psychiatric condition, suggesting new perspectives for the development of therapeutic strategies. Because fear and reward mechanisms are intrinsically linked, therapeutic strategies should benefit addressing symptoms on both fronts. A primary goal of cognitive behavioral therapy is to improve hedonic capacity (82), so changes in reward-related brain activity in response to cognitive behavioral therapy in PTSD should be further explored.

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Figures

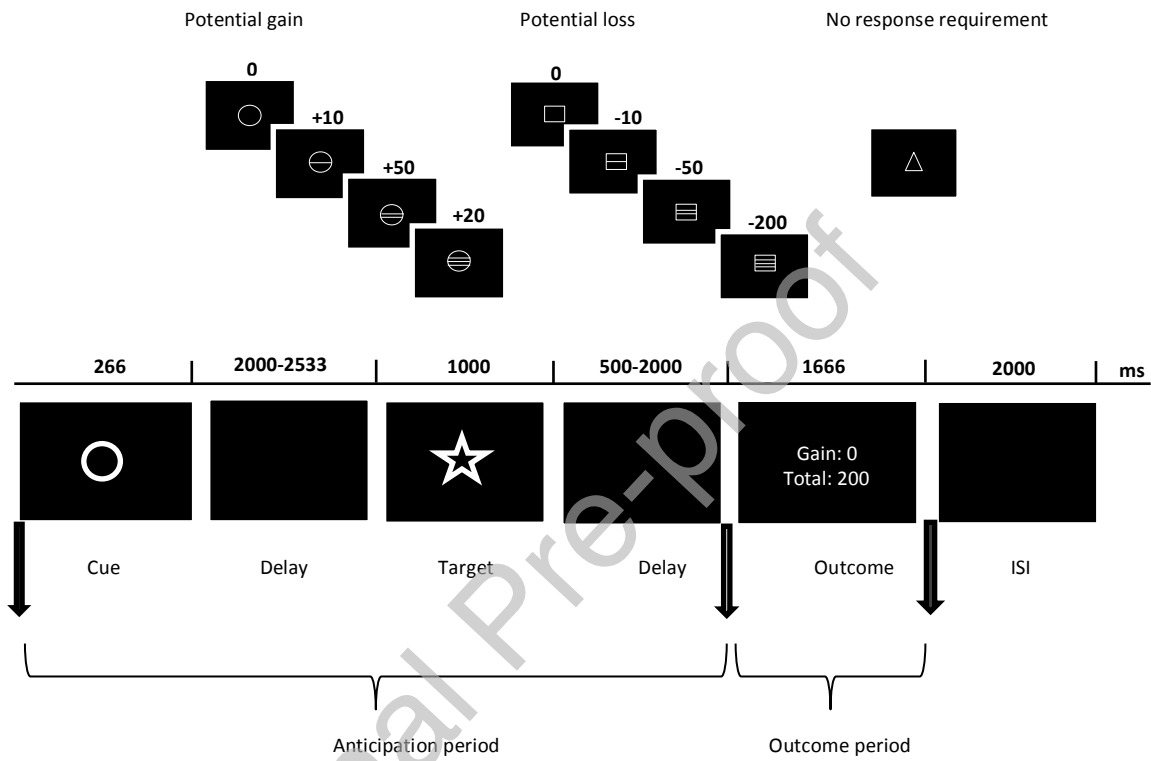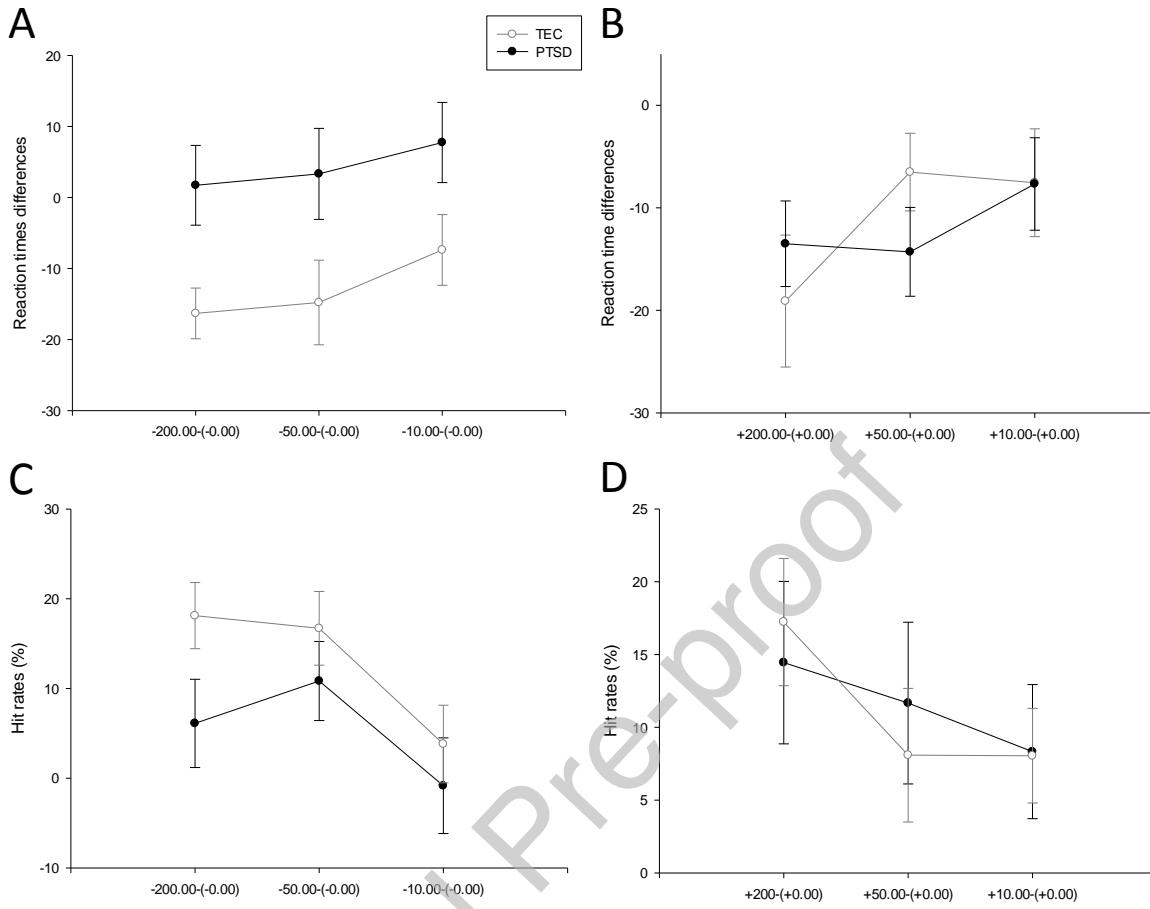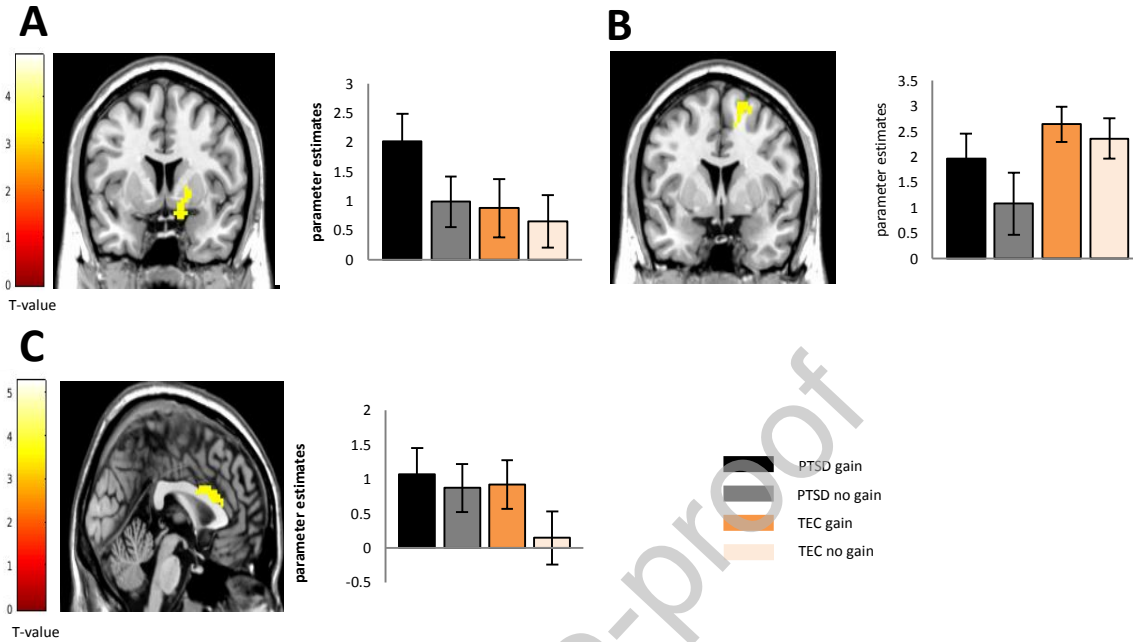**Figure 1. Monetary Incentive Delay (MID) Task Structure**

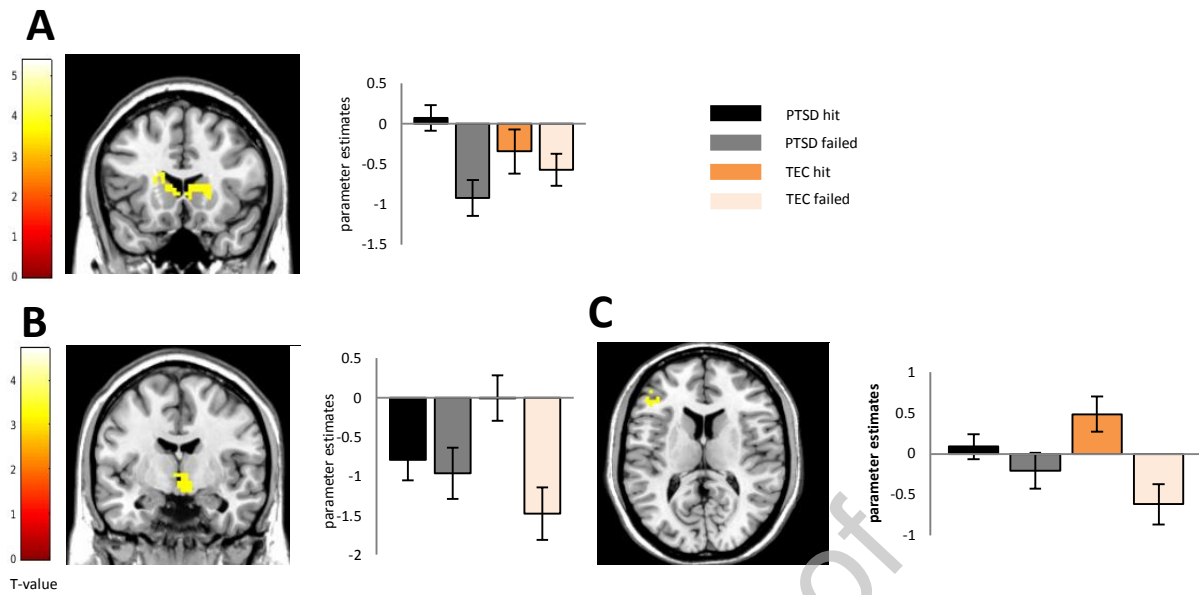**Figure 2. Behavioral responses of participants**

Mean and Standard Error of reaction time differences and hit rate differences; A. Reaction time differences (ms) for negative cues. B. Reaction times differences for positive cues. C. Hit rates differences (%) for negative cues. D. Hit rates differences (%) for positive cues.

Figure 3. Anticipation period - brain response to gain *versus* no gain
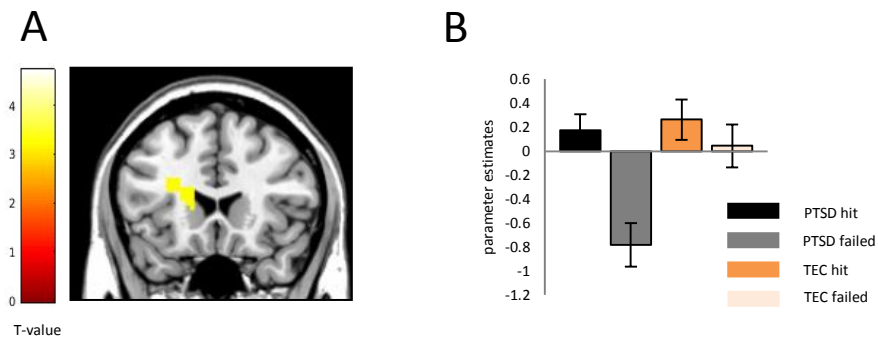

A-B (left): Increased responses to the anticipation of gain *versus* no gain in PTSD exclusively masked by trauma-exposed controls (TEC); **C (left):** Increased responses to the anticipation of gain *versus* no gain in TEC exclusively masked by PTSD; mask threshold *p* < 0.05. **A**: Region including the right amygdala, the right putamen, the right caudate nucleus (head); Parameter estimates extracted from the peak of the cluster depicted in A illustrate a selective activation for anticipation of gain in PTSD but not in TEC; B. Right superior frontal gyrus **C**. Anterior Cingulate Cortex (ACC) (BA 24, 33); **A-B (right)**: Parameter estimates extracted from the peak of the cluster illustrate a selective activation for the anticipation of gain in PTSD but not in TEC; **C:** Parameter estimates extracted from the peak of the cluster illustrate a selective activation for the anticipation of gain in TEC but not in PTSD.

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Figure 4. Outcome period - brain response to monetary gain *vs.* no-gain

Brain response to monetary gain versus no gain **A:** PTSD exclusively masked by trauma-exposed controls (TEC); **B-C:** TEC exclusively masked by PTSD; mask threshold $p < 0.05$. **A**. Cluster including the bilateral body of the caudate nucleus; **B**: Cluster including the right Hypothalamus, and subthalamic nucleus **C**: Cluster including the left inferior frontal gyrus; Parameter estimates extracted from the peak of the cluster illustrate activation for the outcome of successful positively cued trials compared to failed cued trials in the PTSD group but not in the TEC group (A right) and in the TEC group but not in the PTSD group (B,C right).

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Figure 5. Outcome period - brain response to avoided loss *vs.* loss

A: Brain responses to avoided loss *versus* loss in PTSD exclusively masked by trauma-exposed controls (TEC); threshold $p < 0.001$ and mask threshold $p < 0.05$. B. Parameter estimates extracted from the peak of the left caudate (body) illustrate a selective activation for avoided loss in PTSD but not in PTSD.

Tables

Table 1. Demographic and clinical characteristics of participants

	PTSD n=20	TEC n=21	Statistics
Sex	7 F, 13 M	8 F, 13 M	χ^2 (2, 41)=0.01, p>0.1
Age, years (SD)	39.30 (13.39)	34.76 (10.83)	t(39)=1.10, p>0.1
Education, years (SD)	7.80 (3.04)	8.86 (2.83)	t(39)=-1.00, p>0.1
Main Trauma Type			
Natural disaster (earthquake)	1	0	-
Vehicular accidents	4	5	-
Physical assaults	4	3	-
Sexual assaults	0	3	-
Hold-up	4	0	-
Combat exposure	7	1	-
Unexpected death	0	9	-
Duration since trauma, months (SD)	55.45 (73.00)	97.32 (91.08)	t(39)=-1.62, p=0.11
Comorbidity			
Major Depressive Disorder (MDD)	11	0	-
MDD + General Anxiety Disorder	1	0	-
Medication			
Antidepressant	1	0	-
Anxiolytic	3	0	-
Antidepressant + psychoactive medication	6	0	-

Characteristics of participants: Mean and Standard Deviation (SD) for age, education, duration since trauma exposure.

Table 2. Behavioral characteristics of participants

	PTSD *n*=20	TEC *n*=21	*p*-value
Behavioral data			
Mean RT (msec)	230.45 (22.00)	222.05 (19.82)	0.21
Mean RT positive cues (msec)	219.28 (35.17)	217.60 (26.48)	0.86
Mean RT negative cues (msec)	223.66 (27.08)	224.65 (33.37)	0.92
Total gain	10.94 (12.99)	7.35 (19.67)	0.49
Rating of feeling of Motivation	7.73 (2.75)	6.69 (2.25)	0.19
Rating of feeling of fear to lose Money	4.25 (3.78)	3.64 (3.02)	0.57

Behavioral characteristics of participants: Mean and Standard Deviation (SD) for the presentation of target, the total gain, rating of feeling of motivation, rating of feeling of fear to lose money

Table 3. Anticipation period - brain response to gain *versus* no gain

Regions	L/R	MNI Coordinates			BA	k	Z score
PTSD and TEC (conjunction)							
Caudate head	R	9	12	-3	-	317	4.71
Brain stem	L	-6	-15	-12	-	151	4.49
Insula left	L	-42	15	-9	-	149	4.34
Inferior Frontal Gyrus	R	48	3	27	9	285	4.29
Precuneus	L	-21	-69	48	7	66	4.19
Dorsal anterior cingulate cortex	R	3	36	27	32	330	4.03
PTSD exclusively masked by TEC							
Putamen/ NAcc/amygdala	R	18	6	-3	-	69	4.28
Superior frontal gyrus	R	18	3	63	6/8	59	4.27
TEC exclusively masked by PTSD							
Ventral anterior cingulate cortex	L/R	0	9	27	24/33	99	4.49

Stereotactic coordinates correspond to standard MNI brain. Reported regions survived a threshold level of p <0.05 FWE-corrected. Mask threshold for group comparisons was set at a conservative level of p <0.05. L=left; R= right; MNI= Montreal Neurological Institute; BA = Brodmann area

Table 4. Outcome period - brain response to hit gain *vs.* failed gain

Regions	L/R	MNI Coordinates			BA	k	Z score
PTSD and TEC controls (conjunction)							
Precentral gyrus	L	-42	6	30	-	90	5.50
Precuneus	L	-27	-72	42	-	450	5.25
Superior parietal lobule	R	30	-69	48	-	275	4.93
Middle frontal gyrus	R	30	9	60	-	88	4.74
Subcallosal Gyrus	L	-15	9	-12	-	209	4.31
PTSD exclusively masked by TEC							
Caudate nucleus	R	18	18	3	-	220	4.60
TEC exclusively masked by PTSD							
Hypothalamus/STN/	R	6	-6	-9	-	42	3.99
Inferior frontal gyrus	L	-42	42	6	10/46	60	3.97

Stereotactic coordinates correspond to standard MNI brain. Reported regions survived a threshold level of p < 0.05 FWE-corrected cluster. Mask threshold for group comparisons was set at a conservative level of p < 0.05. L=left; R= right; MNI= Montreal Neurological Institute; BA = Brodmann area

Table 5. Outcome period - brain response to avoided loss compared to non-avoided loss

Regions	L/R	MNI Coordinates			BA	k	Z score
PTSD exclusively masked by TEC							
Caudate nucleus (body)	L	-27	21	21	-	65	4.18

Stereotactic coordinates correspond to standard MNI brain. Reported regions survived a threshold level of p <0.05 FWE-corrected. Mask threshold for group comparisons was set at a conservative level of p <0.05. L=left; R=right; MNI=Montreal Neurological Institute; BA=Brodmann Area