משרד החינוך
המינהל הפדגוגי
האגף למחוננים ולמצטיינים

מכון הנרייטה סאלד
המכון הארצי למחקר במדעי ההתנהגות

Effects of the "love hormone" oxytocin on fear extinction

ההשפעות של "הורמון האהבה" אוקסיטוצין על הכחדת הפחד

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Introduction

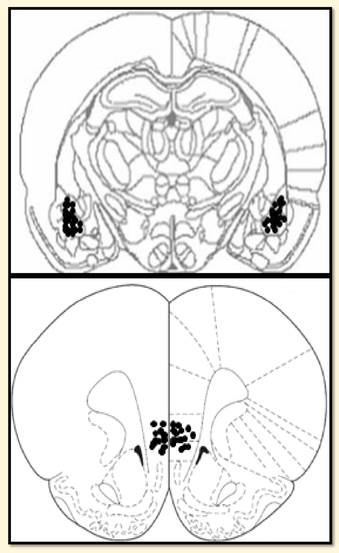
Fear extinction is the learning process where the conditional stimulus no longer predicts the harmful stimulus. This process is an important part of a healthy emotional memory system.
Understanding the interaction between the amygdala - which has a role in expressing emotions like fear- and the pre-frontal cortex – which is important for reducing fear responses- is essential for the extinction of fear.
Oxytocin (OXY) is a neuropeptide hormone that is produced in the hypothalamus. Recent studies show that higher levels of oxytocin are associated with reductions in fear levels and result in relaxation.
Surprisingly, sparse studies addressed the effects of direct manipulations of oxytocin in the amygdala or the pre-frontal cortex on subsequent reduction of fear responses.
To that end, in the present study, we focused on two questions: Changes in the rate of fear extinction following microinjections of oxytocin in the infralimbic pre-frontal cortex (IL), the basolateral amygdala (BLA).
Differences in the effects of oxytocin on extinction in young (post-weanling) and adult animals.

Methods

Animals: Male rats were bilaterally implanted with stainless steel guide cannulas into the IL, the BLA or the CeA.
Contextual fear conditioning and extinction: The rat was placed in a conditioning chamber and received 3 foot shocks (0.8mA for adult rat, and 0.4mA for PW rat for 0.5 sec) with 2 min intervals between them.
Extinction: training took place over the next 3 days: The subject was placed in the context of the conditioning chamber for 10 min, and the duration of freezing was measured.
The behavioral results are presented as percentage of time the animal spent freezing

Microinjections of Oxytocin: Animals were microinjected with either synthetic OXY or its selective agonist TGOT in the BLA and the IL. The control group (vehicle; VH) received saline or ACSF only.

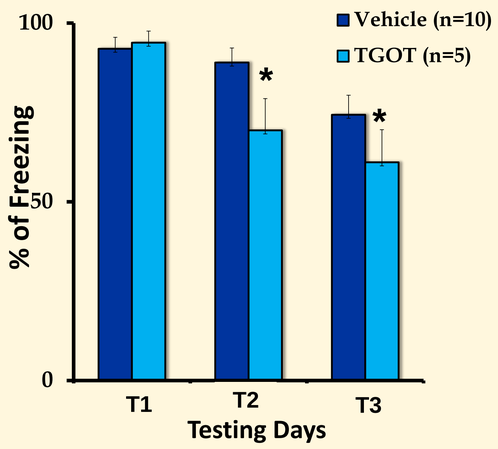
Microinjection Sites



Results

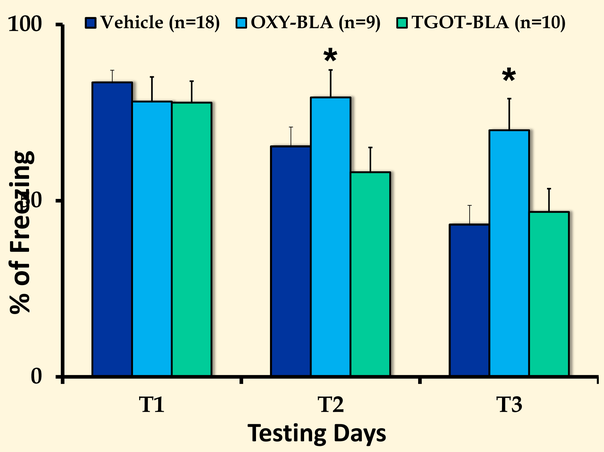
Conditioning —24hr→ Retrieval of fear memory (T1) + drug infusion —24hr→ T2 —24hr→ T3

Figure 1- Adult Rats: Facilitatory effects of TGOT into the IL on fear extinction



The microinfusion of the TGOT into the IL following T1 is associated with facilitation of extinction (* p<0.05).

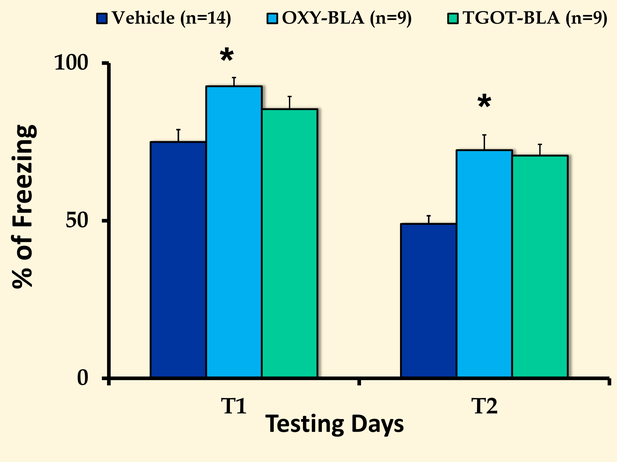
Figure 2- Adult Rats: Inhibitory effects of OXY into the BLA on fear extinction



The microinfusion of OXY into the BLA following T1, enhanced freezing levels (* p<0.05), whereas, the TGOT group was not different from the vehicle-treated group.

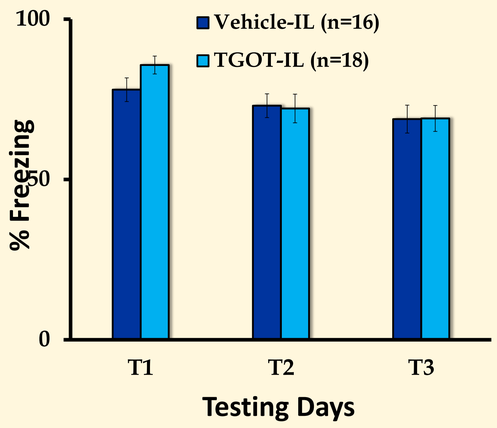
Drug infusion —20min→ Conditioning —24hr→ T1 —24hr→ T2

Figure 3- Adult Rats: The effects of oxytocinergic manipulations in the BLA on fear acquisition



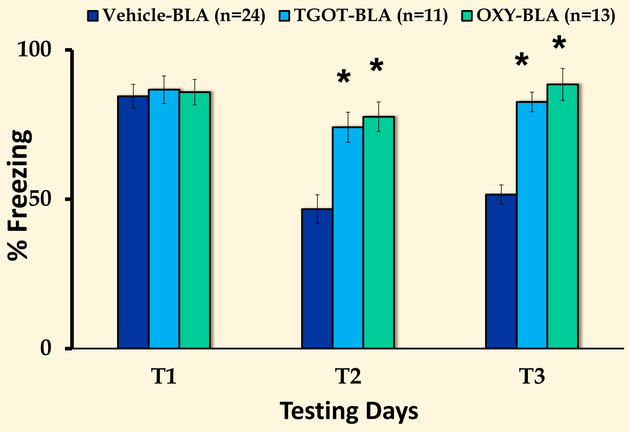
The oxytocinergic manipulations into the BLA before conditioning resulted in high freezing levels (* p<0.05).

Figure 4- PW Rats: The microinfusion of TGOT into the IL did not affect fear extinction.



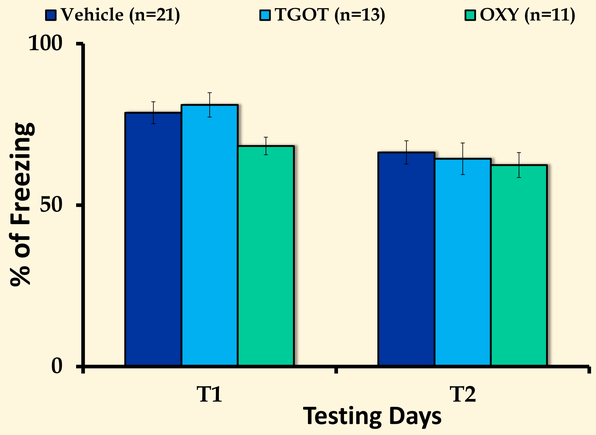
The microinfusion of TGOT into the IL following T1 had no significant effect from the vehicle-treated group.

Figure 5- PW Rats: Inhibitory effects of the oxytocinergic manipulations into the BLA on fear extinction



TGOT and OXY-treated groups were significantly different from the vehicle group and showed high freezing levels (* p<0.05).

Figure 6 - PW Rats: The effects of oxytocinergic manipulations in the BLA on fear acquisition



The microinfusion of TGOT and OXY into the BLA before conditioning did not affect fear acquisition.

Summary

The present study was predominantly designed to understand the effects of the manipulations of the OXY system in the corticolimbic structures on extinction of fear during development.
The results show that manipulating the OXY system is associated with complex effects on fear acquisition and extinction consolidation, depending on the site of injection and the drug used.

- **The microinfusion of TGOT into the IL of the mPFC facilitates extinction in adult rats, while in the PW the microinfusion had no effect.**
- **In the adult BLA, only OXY infusion resulted in impaired extinction (TGOT had no effect). In PW rats both OXY and TGOT resulted in impaired extinction.**
- **In the BLA manipulating the OXY system before the acquisition of conditioning resulted in enhanced freezing and impaired extinction in adult rats, while in the PW rats the OXY manipulations did not affect the acquisition of conditioned fear or subsequent extinction.**