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The possible link between corticotropin releasing factor and post-traumatic stress disorder

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Introduction:

Post-traumatic stress disorder (PTSD) is an anxiety disorder which has become a global health issue with prevalence rates of up to 37%¹. PTSD is triggered by traumatizing events. In the case of PTSD, the reminder of such a traumatizing event can lead the individual into a prolonged state of stress. This can produce avoidance of situations that would not normally be stressful. It's understood that the amygdala is involved in fear and anxiety but the substances that produce this emotional state are not well understood. Neuropeptides located in the amygdala called corticotropin releasing factor (CRF) are believed to be activated during stress and therefore a crucial part of the neural circuitry of stress².

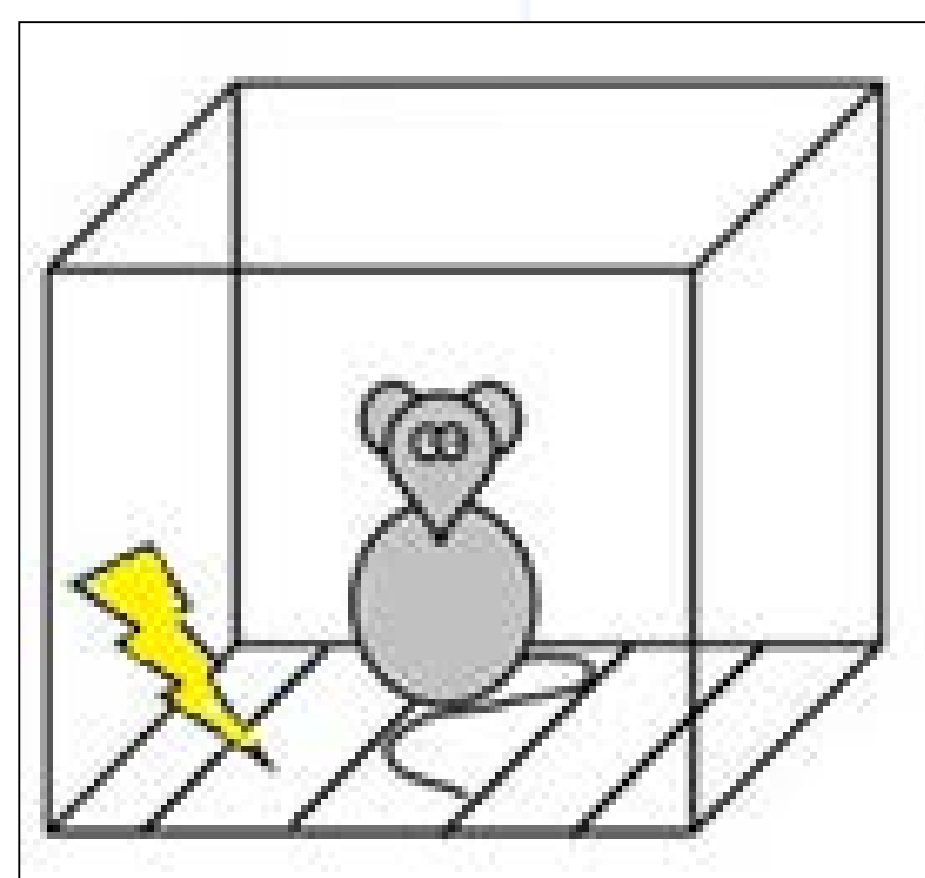
The purpose of this study was to determine if CRF expression levels were increased in rats that have experienced a traumatizing event (footshocks).

The hypothesis is that footshocks (trauma) will induce anxiety and an increased level of the CRF mRNA will be observed in the amygdala of rats.

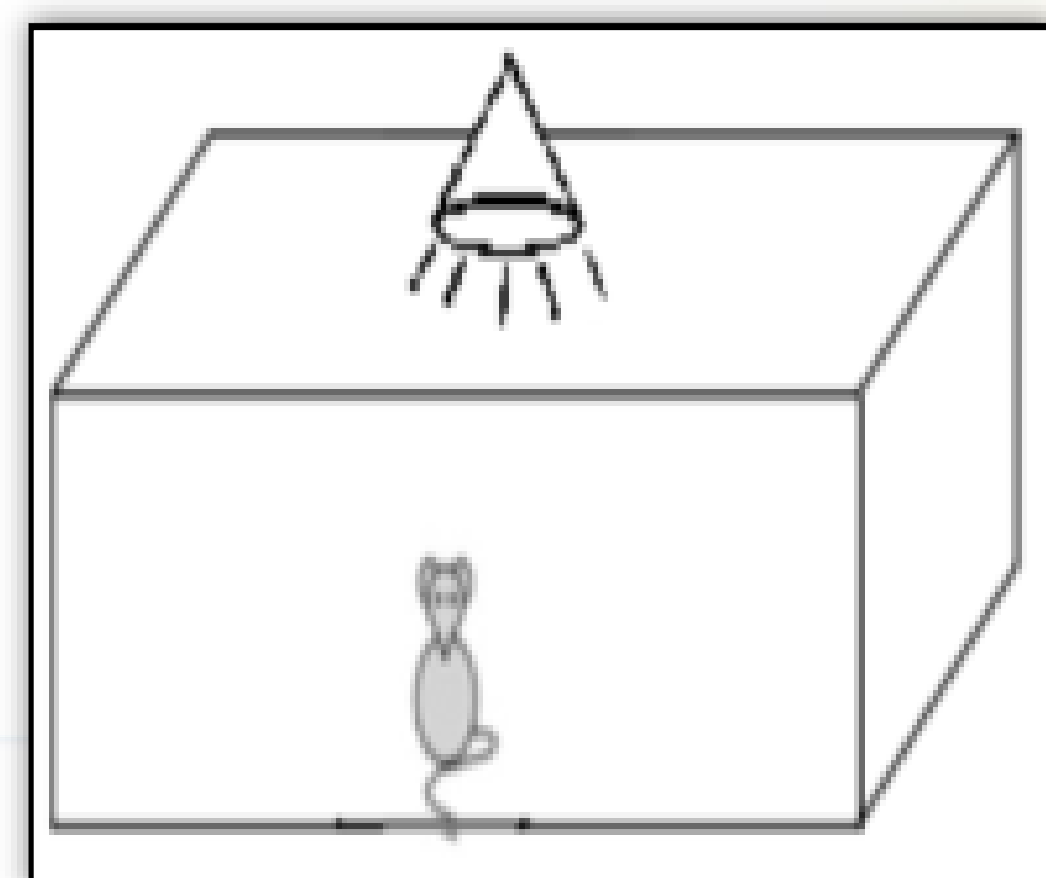
Research Approach:

Rats (n = 30) were exposed to a series of footshocks presented randomly over the course of 3 minutes (5 x 2s episodes of 1.5mA) while a group of non-shock rats were used as the control group (n = 10).

After shock exposure, rats were placed into a novel chamber and introduced to a novel tone. The duration of freezing (immobility), induced by the novel tone, was used to measure anxiety and the results were used to separate rats into low responders (LR) and high responders (HR).



(5 x 2s episodes of 1.5mA)



(Novel Tone and Novel Chamber)

HR

LR

(LR, Immobility < 40%)

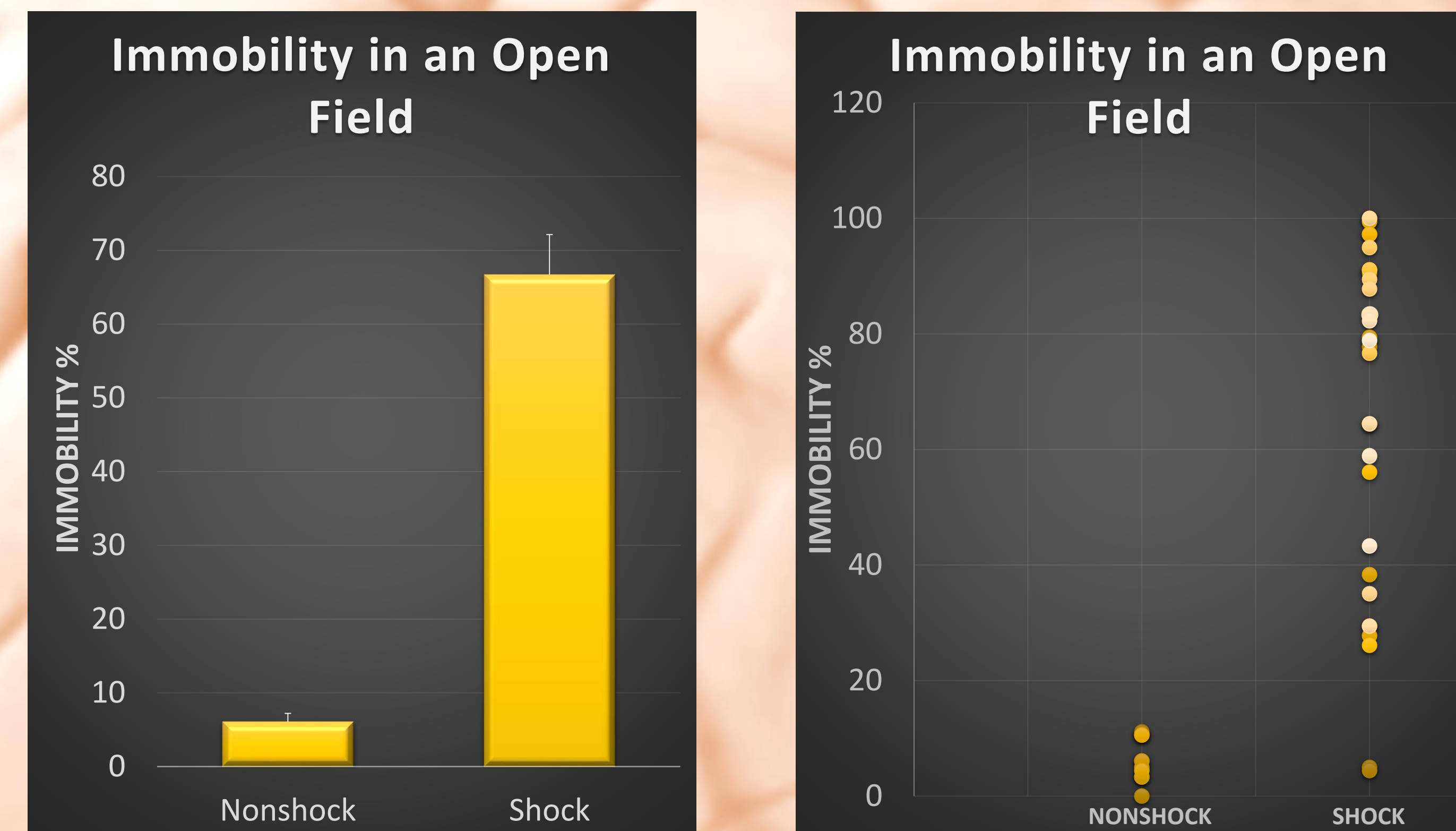
(HR, Immobility > 60%)

Rats were sacrificed 14 days after exposure to footshocks and the amygdala was dissected out and frozen in RNAlater solution for analysis. The collected RNA from the brain were then reverse transcribed into complementary DNA (cDNA) and put through quantitative polymerase chain reaction (qPCR) to analyze the relative concentration of the CRF mRNA in the amygdala.

Results:

Grouping of LR and HR within the Shocked Group

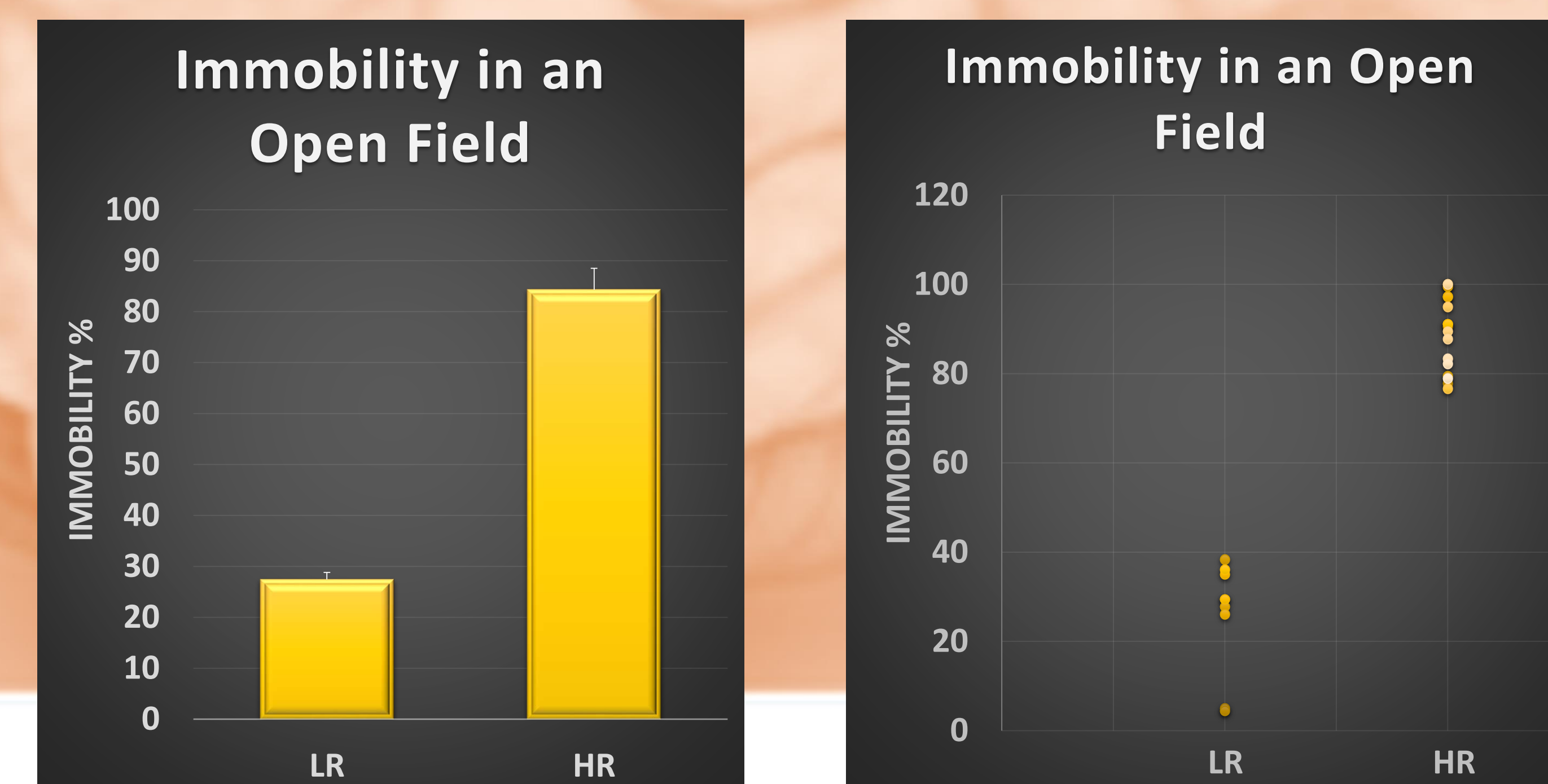
Figure 1 and Figure 2: Non-shock and shock rats in an open field



Generally, the shocked rats displayed more immobility in an open field. Shock rats displaying immobility of <40% were grouped as Low Responders (LR). Rats displaying immobility of >60% were grouped as High Responders (HR).

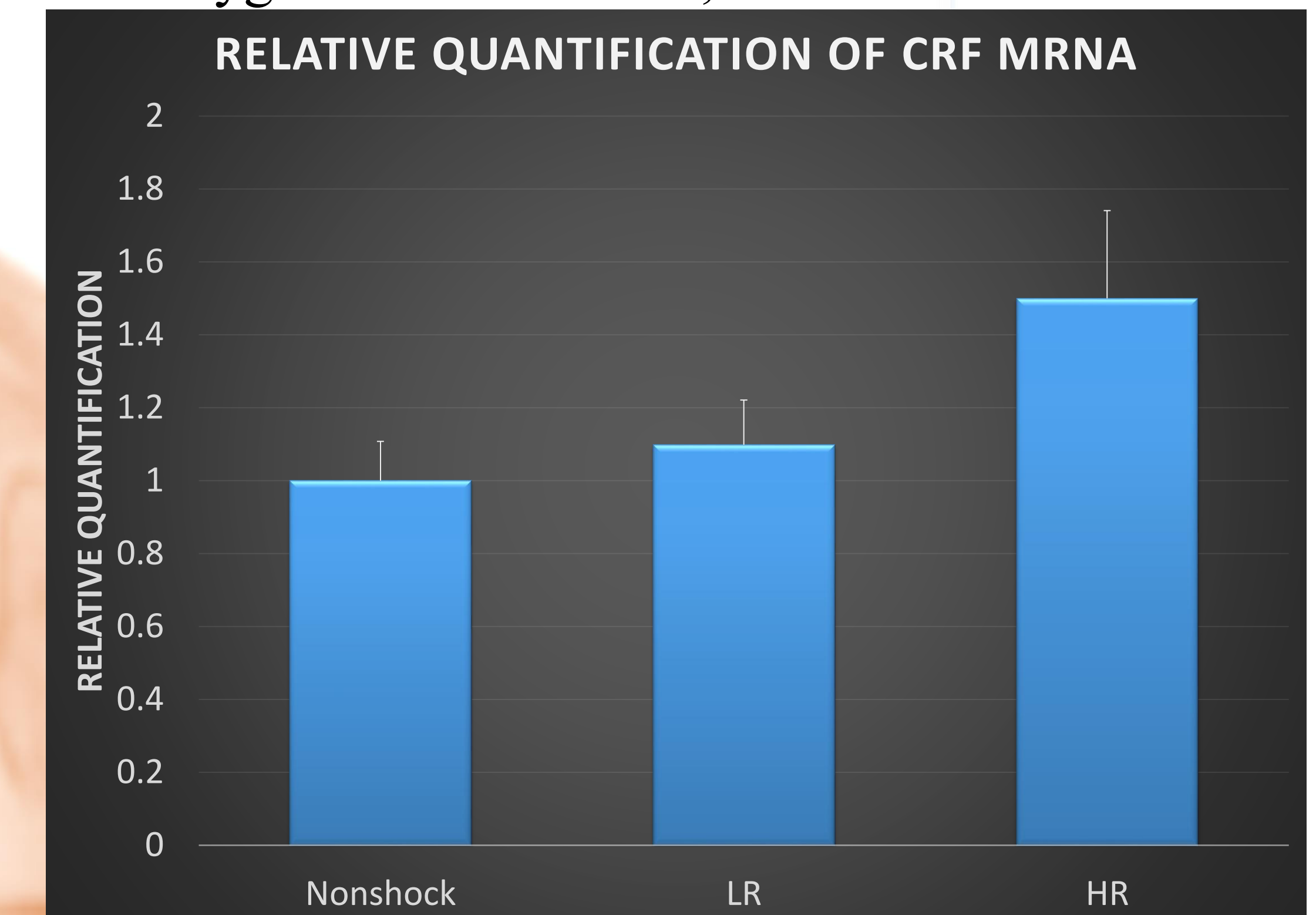
Behavioural Testing and qPCR Analysis

Figure 3 and Figure 4: LR and HR rats' reactions to an open field



Shock rats, which displayed a high level of immobility to a novel tone the day after the footshock (called high responders; HR), showed more avoidance to an open space compared to rats which displayed a lower level of immobility to a novel tone (low responders; LR).

Figure 5: The relative mRNA levels of CRF in the amygdala of non-shock, LR and HR rats



Here qPCR showed that the concentration of CRF in the amygdala of HR rats was significantly higher ($p < 0.05$) than that of the non-shock control rats at about 1.5 times more concentration, and that of LR rats (about 1.2 times greater).

Conclusion:

The results from this study show that the HR rats expressed a generally higher level of CRF in the amygdala than both the LR and non-shock control groups. This suggests that the avoidance which results from relatively intense shock exposure may be related to activity in CRF neurons in the amygdala.

References:

- (1) Van Ameringen, Michael, Mancini, Catherine, Patterson, Beth, Boyle M, H. Post-Traumatic Stress Disorder in Canada.
- (2) Koob GF, Heinrichs SC. A role for corticotropin releasing factor and urocortin in behavioral responses to stressors. Brain Res 1999 Nov 27;848(1-2):141-152.

Acknowledgments:

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