Intrainfralimbic administration of the glucocorticoid receptor antagonist RU38486 facilitates fear memory extinction in rats

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Introduction :Presentation of a conditioned stimulus in the absence of unconditioned stimulus during the extinction of fear memories cause to decreasing fear response. Previous study indicated that many regions of brain especially infralimbic of prefrontal cortex (ILPFC) play an essential role in the extinction of fear-based memory. Moreover, we found no studies that assessed the role of glucocorticoid receptors (GRs) in IL in fear memory extinction. Here, we investigated the effect of GRs blocking on auditory fear memory (AFM) extinction in rats.

Methods :Male Wistar rats (250 – 300 g) with surgically implanted bilaterally cannula aimed at the ILPFC were trained and tested in an auditory fear condition task. After fear conditioning on day 1, rats were divided in 3 groups (n = 10): vehicle – vehicle (control), vehicle - RU38486 20ng and vehicle - RU38486 10ng. For investigate the role of GRs in IL, infusion of RU38486 (10 or 20ng /0.5µl/side) was injected into ILPFC prior to extinction training on day 2(test 1), and the freezing behavior measured during 3 days, in 24 intervals.

Results: Results indicated that Intra-IL administration of the glucocorticoid receptor antagonist RU38486 before extinction training facilitate extinction of AFM dose dependently. ANOVA for repeated measures revealed significant difference between vehicle - vehicle and vehicle - RU38486 10ng ($P \leq 0$), suggesting block of GRs facilitate fear extinction.

Conclusion: Glucocorticoids facilitate fear extinction in a dose response manner. One possibility for such effect is related to activation of optimal levels of GR receptors. Blocked of these receptors with RU38486 3ng, leads to facilitation of extinction. Generally the effect of glucocorticoids depend on receptor subtype and the percent of receptor saturation.

Keywords: Extinction, RU38486, Auditory Fear Conditioning, Rat