STRESS-INDUCED ENHANCEMENT OF MOUSE AMYGDALAR SYNAPTIC PLASTICITY DEPENDS ON GLUCOCORTICOID AND ß-ADRENERGIC ACTIVITY

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Background

- **Corticosteroid hormones**, in interaction with **noradrenaline**, enable the consolidation of emotionally arousing and **stressful** experiences
- This is thought to occur mainly in the basolateral nucleus of the amygdala (**BLA**), which is crucially involved in **emotional memory formation**.
- Extensive evidence points to long-term synaptic potentiation (**LTP**) as a mechanism contributing to memory formation.

Aim

To determine the effects of stress on LTP in the LA-BLA pathway and the specific roles of corticosteroid and β-adrenergic receptor activation in this process

Methods

Exp 1: effect of stress on *in vitro* BLA LTP (male C57/Bl6 mice)
20 min restraint stress or left undisturbed

Exp 2: effect of antagonist pretreatment on BLA LTP in controls
In vivo i.p. pretreatment with antagonists 50 min prior to decapitation: 10 mg/kg propranolol (β-adrenoceptor), 10 mg/kg mifepristone (GR), 50 mg/kg spironolactone (MR) or vehicle (Fig. 1A)

Exp 3: effect of antagonist pretreatment on LTP in stressed mice
In vivo pretreatment with antagonists prior to 20 min of restraint stress (Fig. 1A)

- field potential recordings in mouse brain slices (*in vitro*) via stimulation of the LA-BLA pathway (Fig.1B, C)
- 1x100 Hz (1s) tetanization to evoke BLA LTP (Pu *et al.*, 2009)

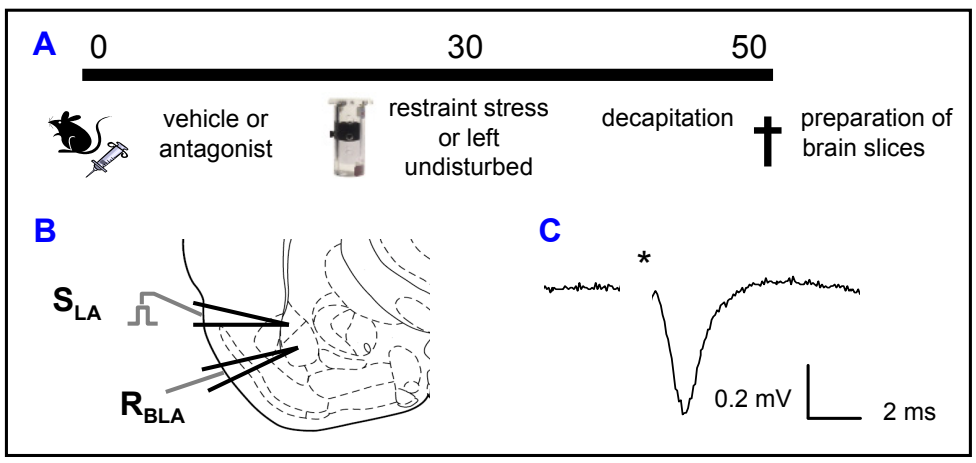

Fig. 1 | A Schematic overview of the experimental design. B Positioning of the stimulation electrode (SLA) and the recording electrode (RBLA) within the lateral and the basolateral amygdala, respectively. C: Representative trace of a mouse BLA field potential (fEPSP), * indicates stimulation artefact.

Results

Exp 1: acute stress enhances BLA LTP

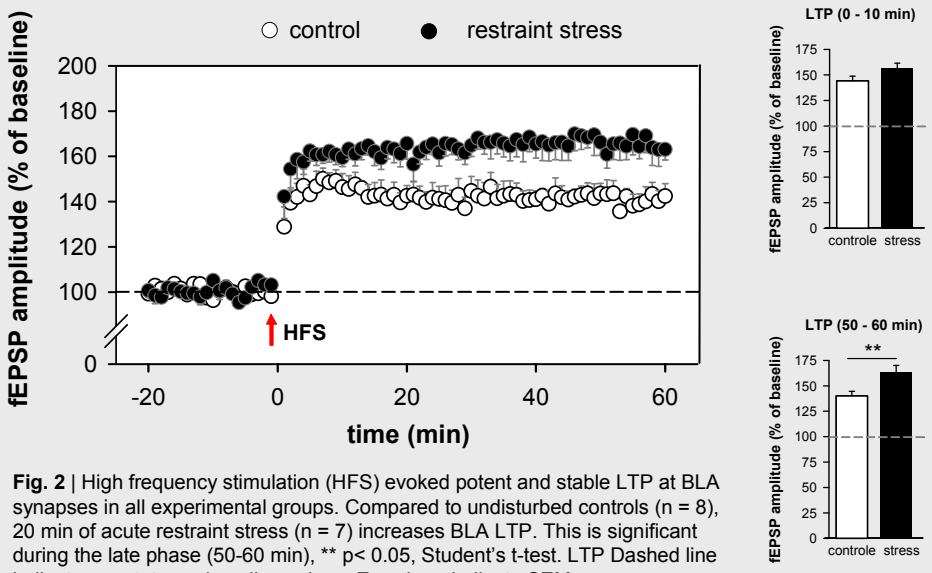

Fig. 2 | High frequency stimulation (HFS) evoked potent and stable LTP at BLA synapses in all experimental groups. Compared to undisturbed controls (n = 8), 20 min of acute restraint stress (n = 7) increases BLA LTP. This is significant during the late phase (50-60 min), ** p< 0.05, Student's t-test. LTP Dashed line indicates pre-tetanus baseline values. Error bars indicate SEM.

Exp 2: BLA LTP is affected by spironolactone

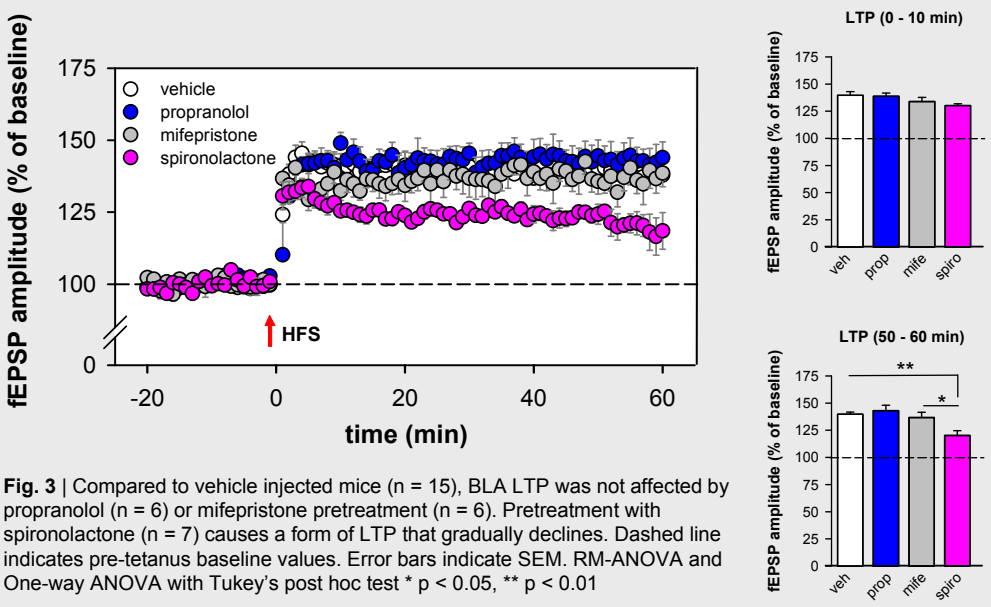

Fig. 3 | Compared to vehicle injected mice (n = 15), BLA LTP was not affected by propranolol (n = 6) or mifepristone pretreatment (n = 6). Pretreatment with spironolactone (n = 7) causes a form of LTP that gradually declines. Dashed line indicates pre-tetanus baseline values. Error bars indicate SEM. RM-ANOVA and One-way ANOVA with Tukey's post hoc test * p < 0.05, ** p < 0.01

Exp 3: β-adrenoceptor and GR necessary for stable LTP after stress

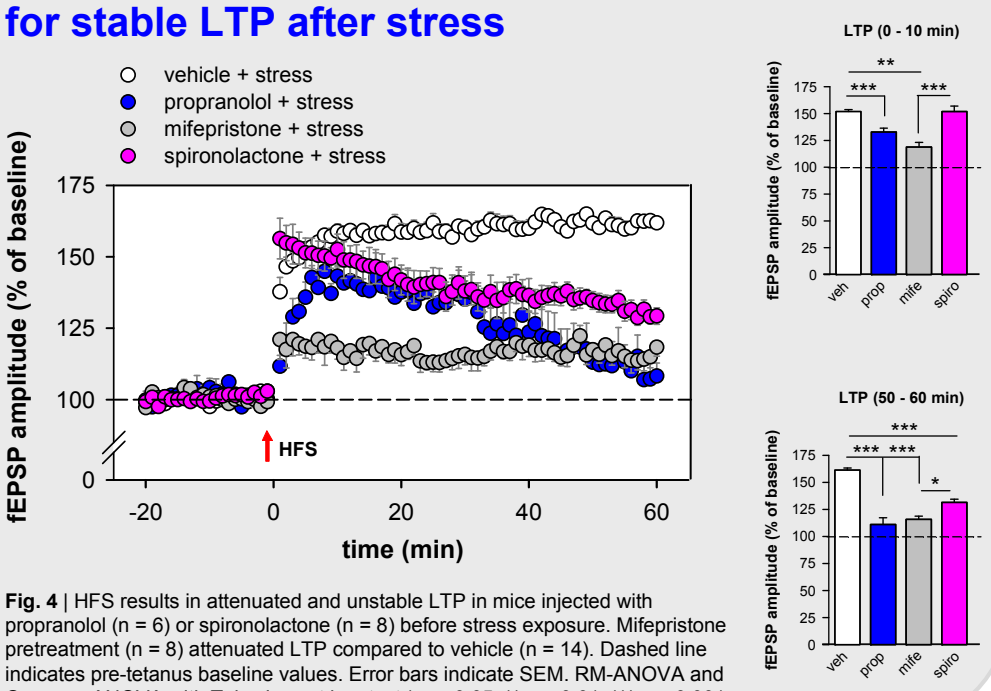

Fig. 4 | HFS results in attenuated and unstable LTP in mice injected with propranolol (n = 6) or spironolactone (n = 8) before stress exposure. Mifepristone pretreatment (n = 8) attenuated LTP compared to vehicle (n = 14). Dashed line indicates pre-tetanus baseline values. Error bars indicate SEM. RM-ANOVA and One-way ANOVA with Tukey's post hoc test * p < 0.05, ** p < 0.01, *** p < 0.001

Conclusions

- **Acute stress changes BLA electrical properties such that subsequent LTP induction is facilitated.**
- **Both β-adrenergic and glucocorticoid receptors are involved in the development of these changes.**
- **MRs are important for the maintenance of LTP in the BLA, irrespective of stress-induced changes in the circuit.**
- **The prolonged changes in BLA network function after stress may contribute to effective memory formation of emotional and stressful events.**