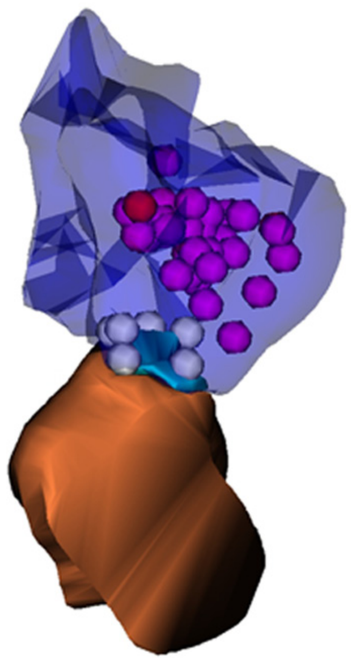

Stress-induced vulnerability of presynaptic glutamatergic terminals and effect of desipramine

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BACKGROUND:

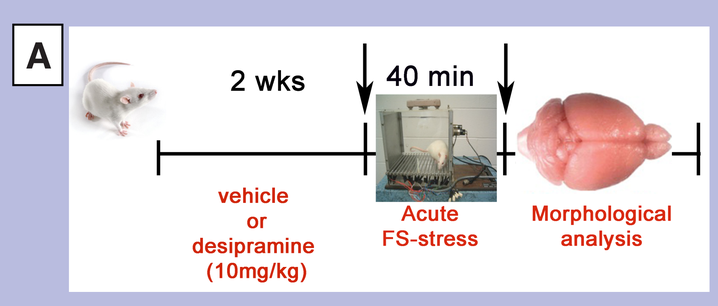
Consistent evidence has documented a primary role for an imbalanced glutamatergic trasmission in stress-related disorders [1]. It is increasingly recognized that stress and its neurochemical mediators induce changes in glutamate synapse morphology, however the mechanisms have not been elucidated yet. We have recently shown that acute foot-shock (FS)-stress increases depolarization-evoked release of glutamate from prefrontal and frontal cortex synaptic terminals, in a corticosterone-dependent way. The increase of glutamate release was completely prevented by chronic pretreatment with antidepressants [2].

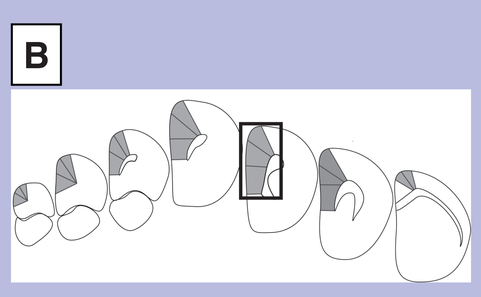
HYPOTHESIS AND OBJECTIVE:

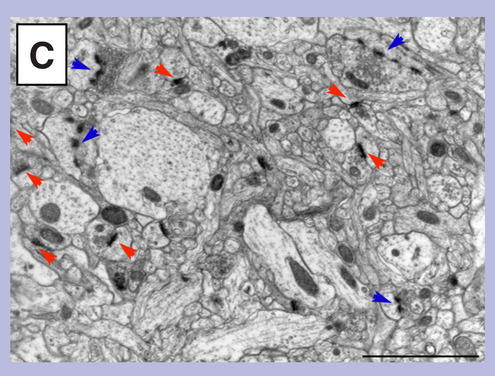
We hypothesize that FS-stress-induced increase in glutamate release is mediated by a mobilization of synaptic vesicles towards the presynaptic membrane; specifically, acute stress would increase the number of vesicles docked to the membrane and ready for release.

METHODS:

Rats were treated for 2 weeks with vehicle or desipramine (DMI) and then subjected to a standard FS-stress protocol (fig.A) [2,3].







Medial prefrontal cortex was identified based on its cytoarchitectural features (fig.B) [4] and sections were sampled and processed for electron microscopy: ultra-thin sections (45 nm) were cut and micrographs taken on a FEI Morgagni TEM with a SIS3 digital camera. Asymmetric synapses were identified based on a prominent post-synaptic density and round shaped vesicles (fig C). Docked and reserve-pool vesicles were counted. Post-synaptic density area was measured and presynaptic terminal volume evaluated with 2D-nucleator and Cavalieri estimator.

REFERENCES:

[1] Popoli et al. (2012) Nat Rev Neurosci 13:22-37
[2] Musazzi et al. (2010) PLoS One 5:e8566
[3] Vollmayr and Henn (2001) Brain Res Brain Res Protoc. 8:17
[4] Van eden and Uylings(1985) J Comp Neurol 241:268-74

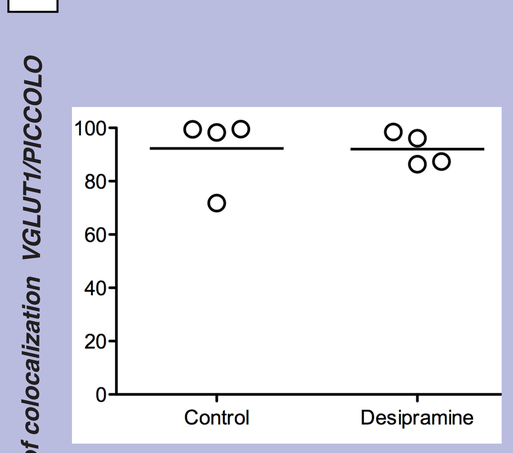
CONCLUSIONS:

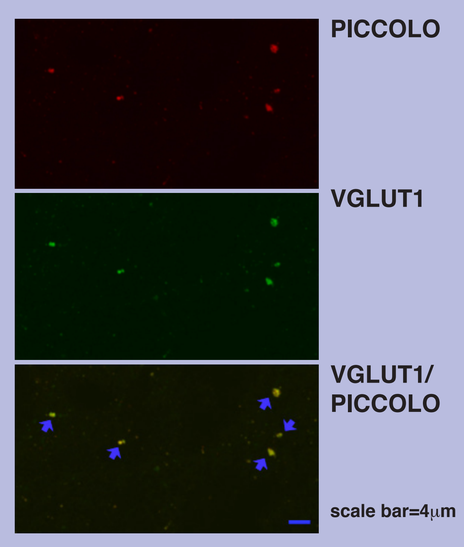
Acute Foot-shock stress selectively induced a strong increase in the number of vesicles docked to the presynaptic membrane and ready for realease. A strong correlation between CORT and *N* of docked vesicles was found. Together, these results suggest a rapid effect of CORT on synaptic vesicles cycle.

No potential conflict of interest

RESULTS:

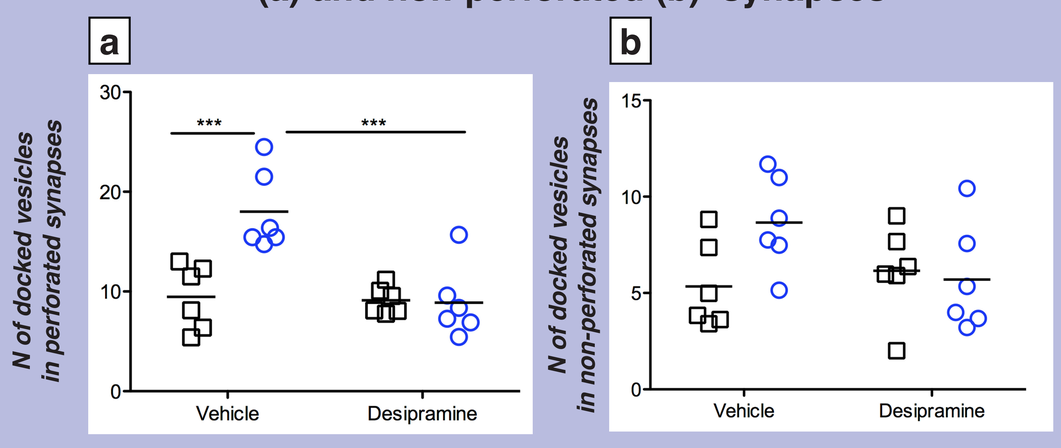
1 Evaluation of glutamatergic terminals distribution





VGLUT1-positive terminals in mPFC of rats subjected to chronic treatment with vehicle (control) or treatment (desipramine).

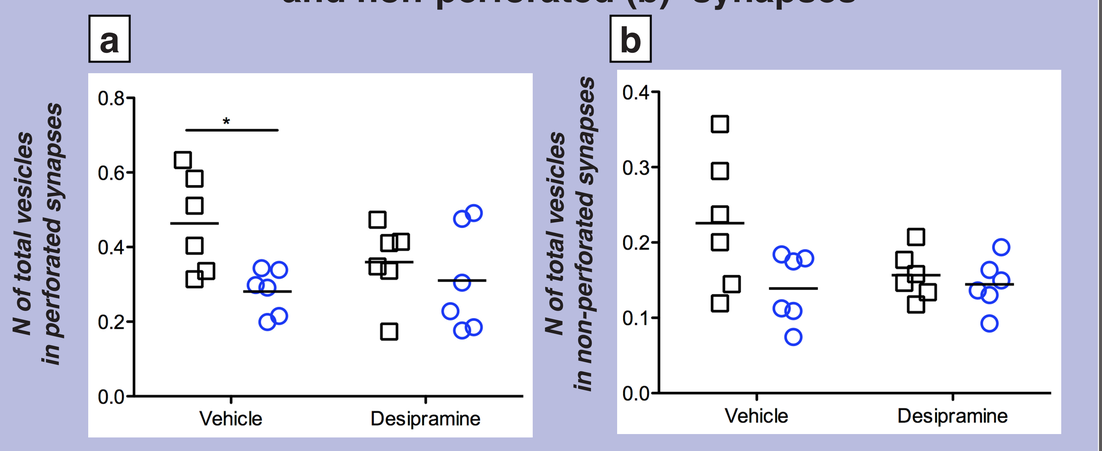
2 Estimation of number of docked vesicles in perforated (a) and non-perforated (b) synapses



N of vesicles docked to the synaptic membrane of rats subjected to chronic treatment with vehicle (control) or treatment (desipramine) and subjected to sham □ or foot-shock stress ○.

***p<0.001, Two-way ANOVA followed by Bonferroni post-hoc test

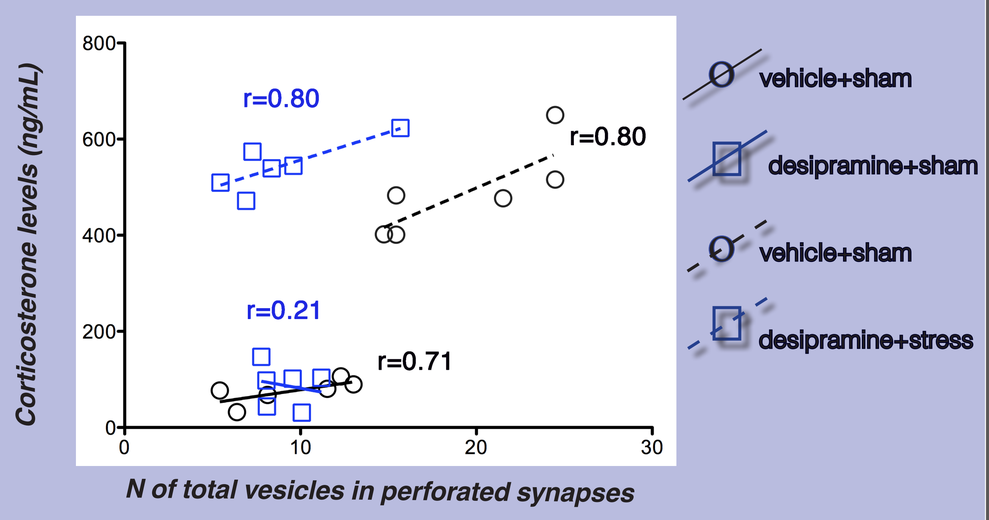
3 Estimation of number of total vesicles in perforated (a) and non-perforated (b) synapses



N of total vesicles of rats subjected to chronic treatment with vehicle (control) or treatment (desipramine) and subjected to sham □ or foot-shock stress ○.

*p<0.05, Two-way ANOVA followed by Bonferroni post-hoc test

4 Correlation between *N* of docked vesicles in perforated synapses and CORT levels



Pearson correlation coefficient