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 transmission 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.

RESULTS:

Evaluation of glutamatergic terminals distribution

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

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.

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.

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

REFERENCES:

CONCLUSIONS:
Acute Foot-shock stress selectively induced a strong increase in the number of vesicles docked to the presynaptic membrane and ready for release. 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