STRESS AT THE SYNAPSE. THE SYNAPTIC ACTION OF ACUTE BEHAVIOURAL STRESS AND THE PROTECTIVE EFFECT OF PSYCHIATRIC DRUGS.

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INTRODUCTION

Accumulating evidence suggests that repeated exposure to different stressful events represents a risk factor for neuropsychiatric diseases. Acute and chronic stressors can have lasting consequences on the brain; indeed, stress has been shown to cause structural changes, such as dendritic atrophy and loss of dendritic spines in neuronal populations. Although different neurotransmitter and neuromodulatory systems in various brain regions have been shown to contribute to the stress response, several studies suggest a critical role of glutamatergic neurotransmission, in particular in the prefrontal cortex, in mediating some of the major effects of stress on psychopathology and cognition [1]. Indeed, in previous studies we found that Footshock (FS)-stress induced a marked increase of circulating corticosterone (CORT) and a rapid (non genomic) increase of glutamate release from synaptosomes of prefrontal/cortical (PFC) via selective activation of glucocorticoid receptor and rapid accumulation of SNAP complexes in synaptic membranes. The increase of glutamate release was prevented by chronic antidepressant (AD) treatments [2]. Therefore, aim of the present work was to study if FS-stress induces a change in glutamate release by increasing the number of vesicles anchored to the presynaptic membrane and modifying the distribution of vesicles among the presynaptic population, in particular if the readily releasable pool (RRP) is increased by stress or CORT.

METHODS

Rats were chronically (2 weeks) treated with vehicle or desipramine (DMI) 10 mg/Kg and then subjected to a standard Footshock (FS)-stress protocol [3]. Immediately after FS-stress, PFC was dissected and synaptosomes were purified on Percoll gradients. Glutamate release was measured in freshly purified synaptosomes by using superfusion technique [4]. The number of docked vesicles in PFC synaptosomes was measured using electron microscopy [5]. Changes in vesicles mobilization were measured in P/F/C synaptosomes from control rats loaded with 4 μM FM1-43 and incubated or not with corticosterone (10 μM, 10 min) by Total Internal Reflection Fluorescence Microscopy (TIRFM) [6, 7].

RESULTS

Glutamate release induced by hypertonic sucrose is a measure of RRP [8]. In FS-stressed animals the RRP was significantly higher. Chronic desipramine prevented the increase of glutamate release evoked by depolarization but not by hypertonic sucrose.

CONCLUSIONS

- Acute FS-stress increased depolarization-evoked glutamate release from PFC synaptosomes. Previous chronic treatment with antidepressants prevented this effect [2].
- Glutamate release evoked by hypertonic sucrose (which mobilizes exclusively the RRP) was increased by FS-stress. Desipramine did not block the increase of glutamate release induced by hypertonic sucrose, most likely because this is not a "physiological" mechanism of vesicle fusion.
- Both EM and TIRFM studies showed that acute stress/corticosterone induced an increase of the number of docked vesicles. EM showed that DMI only partly prevented this change.

Together, these results suggest that acute stress upregulates glutamate release by increasing the size of RRP and that the dampening effect of antidepressants involves downstream mechanisms (probably affecting the priming of vesicles and the probability of release).

REFERENCES


No potential conflict of interest.