Effect of 3-(4-Fluorophenylselenyl)-2,5-diphenylselenophene on Neurochemical Changes Induced by Long-term Exposure of Corticosterone in Mice

Zborowski, V. A.; Gai, B. M.; Bortolatto, C. F.; Heck. S. O.; Nogueira, C. W.

INTRODUCTION: A long-term exposure to high doses of corticosterone has been used as an experimental model to induce depression-like changes in behavior and neurochemistry. We have shown the antidepressant-like effect of 3-(4-fluorophenylselenyl)-2,5-diphenylselenophene (F-DPS) on corticosterone-induced behavioral changes. Our objective was to investigate the effect of F-DPS on the neurochemical changes induced by administration of corticosterone in mice.

MATERIAL AND METHODS: Mice were randomized into four groups: (I) vehicle; (II) F-DPS 1mg/kg/day (i.g.) for 1 week; (III) corticosterone (20 μg/ml/day, in the drinking water) for 4 weeks; (IV) F-DPS plus corticosterone. Animals were killed 48 h after the last F-DPS administration. Brains were removed; prefrontal cortex and hippocampus were dissected and used for the neurochemical assays.

RESULTS AND DISCUSSION: Our results show a significant inhibition of $[^3]H$glutamate uptake into prefrontal cortex slices from mice exposed to corticosterone for 4 weeks (55.3%). $[^3]H$glutamate uptake into hippocampal slices was not changed. In fact, a number of studies have suggested that corticosterone increases glutamate transmission in areas of the forebrain, which is related to depressant-like behavior in rodents. Interestingly, treatment with F-DPS protected against the inhibition of $[^3]H$glutamate uptake promoted by corticosterone, which can be related to its antidepressant-like action. Corticosterone may also rapidly induce the release of glutamate from presynaptic neuron. However, in this study neither basal nor stimulated $[^3]H$glutamate release was modified. Although our results show that corticosterone did not change the synaptosomal $[^3]H$serotonin uptake from prefrontal cortex and hippocampus, F-DPS promoted a significant inhibition of $[^3]H$serotonin uptake not only in the prefrontal cortex (27.9%) but also in the hippocampus (20.4%). This effect could also explain the positive action of F-DPS on the depressant-like behavior induced by corticosterone. CONCLUSIONS: These results suggest that both glutamatergic and serotonergic systems are involved in the antidepressant-like action of F-DPS.

Keywords: depression, corticosterone, glutamate, serotonine

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