APOMORPHINE-INDUCED NEURODEGENERATION IN MONGOLIAN GERBIL HIPPOCAMPUS

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Dopamine is fundamental in the regulation of central motor activity, motivation, emotion and cognition, but also in pathologies such as schizophrenia[1]. Researcher have used pharmacological agents acting on the dopaminergic system, such as apomorphine (APO), as suitable models of schizophrenia according to the dopaminergic hypothesis[1]. To determine whether a dopaminergic hyperactivity may produce neuropathological changes, we have treated young Mongolian gerbils (MG) with a subcutaneous injection (s.c.) of APO 0.45 mg/kg. Under a stereomicroscope, brains were divided in half at level of a coronal plane 2mm behind the optic chiasm. From every bloc obtained, CA1 region was dissected and treated for transmission electron microscopy (TEM) and Scanning electron microscopy (SEM). For TEM and SEM analysis were used respectively a Zeiss TEM 900 and a Zeiss DSM 940 microscope. S.c. administration of APO induced a strong increase of locomotor activity and stereotypy for about 30 min after administration. Ultrastructural characteristics of APO-treated gerbils were pronounced degenerative changes. Swollen dendrites and axons in neuropil and swelling of synaptic endings with an evident decrease in the number of synaptic vescicles were found at TEM study, with the presence of a few dark neurons. SEM confirmed the data about the changes in neuropil with a “pruned” pattern characterized by the presence of swollen neuronal processes instead of the normal picture of cobbled paving. This kind of pruning is interesting in relation to the clinical evidences of impairment in executive and cognitive functions which suppose that schizophrenia is a synaptic disease. Anatomical studies also point to a neurodevelopmental aetiology of abnormal neuronal circuits[2] and decreased density of dendritic spines[3]. The epidemiologic evidence, the abnormalities in cytoarchitecture, and the altered expression of synapse-related proteins provide support for a model of abnormal neurodevelopment in schizophrenia that affects neuronal migration, synaptogenesis, and synaptic pruning[4]. In conclusion we think that this animal model is intriguing, because shows important indications about the presence of a mechanism that via a hyperactivation of dopaminergic systems may produce pathological changes in the hippocampus.

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