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OBXマウスでの中隔野-海馬コリン神経変性は記憶障害を引き起こす

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Degeneration of cholinergic neurons in the medial septum plays a critical role in the memory deficits associated with several neurodegenerative disorders. In this study, we have performed neurochemical and histochemical analyses of the septo-hippocampal cholinergic neurons after bilateral olfactory bulbectomy (OBX). OBX mice revealed severe deficit in working memory as tested in the Y-maze and novel object recognition tests. Western blotting analyses did confirm that expression of vesicular acetylcholine transporter (VACHT) and choline acetyltransferase (ChAT), which are cholinergic neuron markers, decreased in the hippocampus following OBX. Notably, the immunoreactivity in VACHT-positive cholinergic nerve terminal in the CA3 region more largely reduced, compared to that in the CA1 region 14 days after OBX. Moreover, the OBX mice exhibit decreased number of cholinergic neurons in the medial septum with concomitant cognitive dysfunction. Taken together, we conclude that OBX induced neurodegeneration of the septo-hippocampal cholinergic neurons, which accounts for impairment of memory-related behaviors in mice.