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Presentation Abstract

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Title:	Pro-neurogenesis therapy rescues hippocampal-mediated learning and memory deficits in the ts65dn mouse model of Down syndrome
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Abstract:	Down syndrome (DS) is the most frequent cause of mental retardation in adults and children. It has been proposed that cognitive disabilities associated with DS may be ascribed to neurogenesis impairment during both development and adulthood. This view is supported by findings in relevant genetic animal models of DS. Specifically, it has been shown that the Ts65Dn mouse model recapitulates key cognitive deficits of DS and presents significant impairment of neurogenesis. Adult neurogenesis in the dentate gyrus (DG) of rodents has been associated to memory formation and hippocampus-dependent learning. Thus, the poor performance of Ts65Dn mice in learning and memory tasks may be due to impaired DG adult neurogenesis. We have previously demonstrated that lithium administration restores neurogenesis in the subventricular zone of Ts65Dn mice. We postulated that lithium administration could also restore DG neurogenesis enhancing hippocampus-dependent cognitive functions. To elucidate the effects of lithium-induced neurogenesis on cognition, we thus administrated lithium carbonate (2.4 g/kg of chow) to Ts65Dn mice for 1 month and evaluated its effects on learning and memory tasks, neurogenesis and synaptic plasticity in the DG. Neuronal precursor proliferation and neurogenesis were assessed by BrdU labeling of dividing cells and immunohistochemistry analysis with specific markers of newborn neurons (i.e., doublecortin and calretinin). Long term potentiation was evaluated by field

recordings in the DG of hippocampal slices from lithium-treated and untreated mice. Functional effects of lithium on learning and memory have been evaluated using the novel object recognition task and the contextual fear conditioning test.
We found that chronic lithium administration effectively promoted neurogenesis in the DG of Ts65Dn mice, restoring synaptic plasticity and cognitive functions. This indicates that lithium may be of potential benefit for DS therapy. Further analyses are ongoing to unravel molecular mechanisms underlying lithium effects on neurogenesis and cognition.

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