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ABSTRACT

Poster Instructions

Title	**(P037.08) A Role For Adult Neurogenesis In Dentate Synaptic Plasticity Deficits And Memory Impairment In Down Syndrome** **Room: Poster Area - Session: P037 - Abstract Number: 686 - Poster Board Number: C184** **Ref.: FENS Abstr., vol 7, p037.08, 2012**
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Session:	P037: Poster Session - Alzheimer's and Other Dementias III Poster boards: C177-190
Date:	Sunday - July 15, 2012 13:30 - 15:30 (attendance: 7/15/2012 1:30:00 PM)
Location:	Poster Area
Subtopic:	C.1.g Therapeutic strategies
Topic:	C.1 Alzheimer's disease and other dementias
Theme:	C. Disorders of the nervous system

In the mammalian dentate gyrus (DG) neurogenesis continues throughout life. Accumulating evidence suggests a unique contribution of adult-generated neurons in DG synaptic plasticity and hippocampal-mediated learning and memory functions. However, the precise involvement of adult neurogenesis to disease-related cognitive deficits still remains unclear. Intellectual disabilities are the most striking clinical features of Down Syndrome (DS) and are characterized by learning deficits and memory impairment, particularly in hippocampus-related functions. Accordingly, the Ts65Dn mouse model of DS recapitulate many hippocampal cognitive deficits of the human syndrome, and also show decreased adult neurogenesis and impaired DG synaptic plasticity. To elucidate the contribution of faulty adult neurogenesis to DG synaptic plasticity deficits and memory impairment in DS we have treated adult Ts65Dn mice with lithium, a widely used mood stabilizer that also promotes neurogenesis.
Results showed that chronic lithium administration effectively restored adult neurogenesis in the DG of Ts65Dn mice by increasing neural precursor cells (NPCs) proliferation. In vitro experiments on adult dentate NPCs cultures confirmed the reduced proliferation capacity of Ts65Dn cells and also demonstrate that the proliferative action of lithium depended on the stimulation of the Wnt/ß-catenin pathway. As a consequence of increased NPCs proliferation the number of newborn neurons was fully rescued in the DG of Ts65Dn mice. These newborn neurons were also functionally integrated into the DG circuit because neurogenesis-dependent long-term potentiation (LTP) was also totally rescued.
Most importantly, restoring a functional newborn neurons population in Ts65Dn mice rescued cognitive impairment in hippocampal-dependent behavioral tasks. Moreover, lithium-induced rescue of DG synaptic plasticity and memory deficits in Ts65Dn mice was abolished when adult neurogenesis was concomitantly inhibited, highlighting the fundamental role of hippocampal newborn neurons in DS cognitive impairment.
Therefore, promoting adult neurogenesis may represent a new and promising therapeutic target to alleviate cognitive deficits in DS patients.