STIMULATION OF NEUROTROPHIC PROCESSES IN APPSWE TRANSGENIC MICE

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Introduction: A challenging question is whether neurogenesis could be induced by drug treatment in Alzheimer’s disease (AD). Different forms of amyloid-β (Aβ) are involved in the pathological mechanisms of AD and induce global changes in the brain, including the reduction of neurotrophic factors. We have earlier shown that treatment of APP23 transgenic mice with the anti-amyloid drug (+)-phenserine augments neuronal differentiation of stem cells transplanted into the brain of these animals (Marutle et al. 2007). Furthermore, long-term treatment of AD patients with the enantiomer (-)-phenserine revealed changes in Aβ levels in the brain and CSF, as well as improved cognition (Kadir et al. 2008).

Aims: To study the effect of (+)-phenserine treatment on neurotrophic processes in young (4-6 months) and old (15-18 months) APPswe transgenic mice.

Methods: APPswe and wild-type mice were administered daily with (+)-phenserine (25mg/kg bodyweight) or saline for 16 days. The effects on Aβ and cell proliferation in the hippocampus were measured.

Results: Following (+)-phenserine treatment, Aβ42 levels were reduced by 33-48% in the younger mice and by 52-53% in the aged mice. Interestingly, treatment reduced the Aβ42/40 ratio in both age groups. A significantly increased number of BrdU+ proliferating cells was observed in the hippocampus of (+)-phenserine treated APPswe mice, and the number of BrdU+ cells was 2.3 times higher in the group of older mice compared to the younger mice.

Conclusions: Drug stimulation of endogenous neuroregeneration in APPswe mice with high Aβ burden may have implications for the possibility of stimulating neurogenesis in AD patients.