Memantine improves cognition and reduces Alzheimer's-like neuropathology in transgenic mice.

Abstract:
Memantine is an N-methyl-d-aspartate receptor antagonist that is approved for the treatment of moderate to severe Alzheimer's disease (AD). In this study, three groups of triple-transgenic (3xTg-AD) mice with differing levels of AD-like pathology (6, 9, and 15 months of age) were treated for 3 months with doses of memantine equivalent to those used in humans. After the treatment, memantine-treated mice had restored cognition and significantly reduced the levels of insoluble amyloid-beta (Abeta), Abeta dodecamers (Abeta*56), prefibrillar soluble oligomers, and fibrillar oligomers. The effects on pathology were stronger in older, more impaired animals. Memantine treatment also was associated with a decline in the levels of total tau and hyperphosphorylated tau. Finally, memantine pre-incubation prevented Abeta-induced inhibition of long-term potentiation in hippocampal slices of cognitively normal mice. These results suggest that the effects of memantine treatment on AD brain include disease modification and prevention of synaptic dysfunction.