SINGLE IMMUNIZATION WITH HUMAN NATURALLY OCCURRING AUTOANTIBODIES AGAINST BETA AMYLOID AFTER 24 H LEADS TO ENHANCED SYNAPTOPHYSIN IMMUNOREACTIVITY AND RESTORES COGNITIVE DEFICITS IN TG2576 MICE

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Alzheimer's disease (AD) is the most prevalent neurodegenerative disorder with a devastating prognosis. As previously reported, passive immunization using monoclonal antibodies against amyloid beta was successful in improving cognitive deficits in transgenic mice models of AD. The detection of antibodies against beta amyloid in human intravenous immunoglobulins offers an alternative approach of passive immunization using natural occurring polyclonal anti-amyloid beta antibodies (nAbs-Abeta). The present study tested if a single treatment with nAbs-Abeta has a beneficial effect on synapse formation and cognition in Tg2576 mice.

Tg2576 mice at 22 and 27 months of age were treated once with either nAbs-Abeta (400 µg) or vehicle 24 h prior to assessing non-spatial and spatial memory, and the number of synapses by immunostaining of the presynaptic marker synaptophysin in the hippocampus and frontal cortex.

Tg2576 mice of both ages showed impaired object location memory, which was indicated by a reduced interaction time with the object moved to a novel position. Immunization with nAbs-Abeta restored spatial memory deficits in the object location memory task, which was indicated by an increased interaction time with the object moved to a novel location. Analysis of synaptophysin immunoreactivity in the frontal cortex and hippocampal region showed greater synaptophysin staining in immunized Tg2576 mice, indicating an increased number of synapses in the hippocampus and frontal region after treatment.

These results suggest that single immunization with nAbs-Abeta improve synaptic formation and rescue spatial memory deficits after 24h. This findings make nAbs-Abeta an eligible candidate as an effective therapeutic for AD.