

**P025** Specific Amyloid- $\beta$  Assemblies Disrupt Memory without Neurodegeneration in a Mouse Model of Alzheimer's Disease  
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The amyloid- $\beta$  protein (A $\beta$ ) is implicated in the pathogenesis of Alzheimer's disease (AD). Functional imaging and neuropathological data support the fact that brain dysfunction in AD precedes neuron loss, leading to the prediction that specific forms of A $\beta$  could disrupt memory before there is significant structural brain damage. Here we show, in the well-characterized Tg2576 mouse model of early AD, that stable memory deficits occur without synapse or neuron loss as a result of the accumulation of dodecameric assemblies of A $\beta$ . These dodecamers are extremely stable, soluble molecules, located in the extracellular space and are constructed from trimeric oligomers secreted from neurons. Our results demonstrate that the size and configuration of A $\beta$  oligomers, which are potential early causative agents in AD, determine their effects on brain function, and suggest that highly specific targeting of these oligomers will prevent dementia in AD.