NITRATION OF AMYLOID B AT TYROSINE 10 PROMOTES AGGREGATION AND PLAQUE FORMATION

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In Alzheimer’s disease (AD) the inducible nitric oxide synthase (NOS2) is upregulated resulting in increased production of NO. We identified Aβ nitrat ed at tyrosine 10 (3NTyr¹⁰-Aβ) as a new NO target. Nitration of Aβ promoted its aggregation and was detected in the core of Aβ plaques of APP/PS1 mice and AD brains. In vivo, we found that NOS2 deficiency and the NOS2 inhibitor L-NIL were able to revert cognitive impairment, increased amyloid β (Aβ) plaque deposition and deficits in synaptic plasticity in an AD mouse model (APP/PS1). Further, injection of 3NTyr¹⁰-Aβ into the brain of young APP/PS1 mice induced the formation of plaques. This suggests a disease modifying role for NOS2 in AD and represents a potential therapeutic target.