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PRESENILIN-2 MUTATION ALTERS NEURITE EXTENTION, APOPTOSIS AND TRANSCRIPTION FACTOR(NF-KB) ACTIVATION.

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Alzheimer's disease (AD) is characterized by β-amyloid deposition and associated with loss of neuron cells in brain regions involved in learning and memory process. Many cases of early onset autosomal dominant inherited forms of AD are caused by mutation in the genes encoding presenilin-2 (PS-2). However, its pathogenic mechanism in AD are not known. Here we report that expression of an AD-liked human PS-2 mutation (N141I) in PC12 cells resulted in aberrant differentiation responses to nerve growth factor (NGF) and β-amyloid. NGF-induce neurite extension was significantly reduced in cell lines stably expressing mutant PS-2. Induction of apoptosis and apoptosis-associated gene expression by β-amyloid was markedly increased in cells carrying mutant PS-2. The DNA binding activity of the transcription factor NF-kB by β-amyloid was decreased in the cells carrying mutant PS-2. These findings show that altered responsibility to neurotrophic (or neurotoxic) factors could a role in the pathogenesis of AD carrying PS-2 mutations.

keyword : Alzheimer's disease(AD), β-Amyloid, Presenilin-2(PS2), NF-κB