Abstract

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Background: The pathogenesis of Alzheimer’s disease (AD) is incompletely understood. Discovery of c-Jun N-terminal kinases (JNKs), involved in regulation of gene expression, inflammation, cell proliferation and apoptosis, may contribute to better understanding of AD pathogenesis. JNK3 is a brain-specific JNK isoform involved in apoptosis of mammalian neurons. Precise localization of JNK3 in the brain still remains unclear. JNK3 silencing achieved by gene knockout had directly decreased beta amyloid (Aβ) levels in previous AD models in mice. We performed an immunohistological study to localize JNK3 gene in the mice brain in order to better focus future gene targeting therapy.

Methods: A transgenic mice model of AD (Tg2576) has been used to study the expression of JNK3 by western blotting compared to the wild type. In the same brains localization of pJNK3 in astroglia (GFAP), microglia (Ox42), neurons (NeuN), senile plaques (Aβ) or pTau, using immunohistochemistry staining has also been checked.

Results: Phosphorylated JNK3 levels (pJNK3), representing the activated form of JNK3 protein, were significantly increased in Tg2576 transgenic mice brains compared to normal controls. By immunohistochemistry we observed, that pJNK3 is associated with amyloid plaques on their periphery. pJNK was also partially associated with hyperphosphorylated tau in these plaques. There was no co-localization of pJNK3 with GFAP or NeuN. Expected association with microglia wasn’t proved, because the stainings with Ox42 antibody didn’t work.
**Conclusions:** The existence of high JNK3 activity together with amyloid plaques as well as increased levels of this protein during AD strongly suggest that JNK3 plays a role in Alzheimer-related neurodegeneration. Due to the lack of co-localization with any specific brain cell type, the question as to which cell type is responsible for the release of this inflammatory kinase still remains open, as does the path to discovering new AD treatment methods which silence the JNK3 gene.