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Tyrosine kinase receptor B isoforms alter APP and BACE1 endogenous levels independently of BDNF

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ABSTRACT

Brain derived neurotrophic factor (BDNF) levels and signaling via the tyrosine receptor kinase B (TrkB) have been shown to be altered in Alzheimer's Disease. In addition, it has been reported that the isoforms of TrkB can differentially affect metabolism of amyloid precursor protein (APP). Conversely, Aβ, a neurotoxic cleavage product of APP, has been shown to impair TrkB/ BDNF signaling. Therefore, we investigated whether the changes observed in APP metabolism were due to the isoform-specific effects of TrkB on either APP expression, and/or on the expression and activity of ADAM10 and BACE1. Since BDNF levels are decreased in AD, we focused on BDNF independent effects of the TrkB isoforms. We found that TrkB FL increases endogenous APP levels in both HEK293 and SH-SY5Y na?ve cells. We did not find an increase in ADAM10 activity in HEK293 cells, but an increase in BACE1 levels. Additionally, we have found that TrkB FL is able to increase NFAT3 mediated transcriptional activity and we suggest that this causes transcriptional activation of the BACE1 promoter.

KEYWORDS

TrkB; Alzheimer; BACE1; SHC; NFAT

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