Changes in Plasma $\beta$-NGF and Its Receptors Expression on Peripheral Blood Monocytes During Alzheimer's Disease Progression

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**Abstract:** Alzheimer's disease (AD), the most common cause of dementia, is characterized by the deposition of extracellular amyloid-β (Aβ) plaques and intracellular neurofibrillary tangles, and by neuroinflammation. During the pathogenesis of AD, monocyte-macrophage lineage cells become increasingly ineffective in clearing Aβ deposits, less able to differentiate, and shift toward pro-inflammatory processes. Beta-nerve growth factor (β-NGF) and its receptors, TrKA and p75NTR, produce several biological responses, including cell apoptosis and survival, and inflammation. In the central nervous system, the involvement of these receptors in several critical hallmarks of AD is well known, but their role in circulating monocytes during the progression of dementia is unclear. We investigated the relationship between plasma β-NGF concentration and TrkA/p75NTR receptor expression in monocytes of patients with mild cognitive impairment (MCI), mild AD, and severe AD. We observed that plasma β-NGF concentration was increased with a higher expression of TrkA, but not of p75NTR, in monocytes from patients with MCI and mild AD, whereas β-NGF concentration and TrkA expression were decreased and p75NTR expression was increased, associated with caspase 3-mediated apoptosis, in patients with severe AD. In our study, we show evidence of variation in plasmatic β-NGF and monocytes TrkA/p75NTR receptor expression during the progression of dementia. These novel findings add evidence to support the hypothesis for the involvement of β-NGF and its receptors on monocytes during AD progression.

**Keywords:** Alzheimer's disease, β-NGF, mild cognitive impairment, monocytes, p75NTR, TrkA

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