# Abstract

The findings of recent years have shown that impaired mitophagy is involved in the pathophysiology of Alzheimer's disease (AD) and other neurodegenerative diseases. Studies on brain biopsies of AD patients, cellular and animal models of AD show that age-dependent decline in mitophagy is a significant contributor to AD pathology, and that the levels of mitophagy proteins are altered. However, whether these changes are reflected in the biofluids of individuals with AD, and whether mitophagy proteins could be potential biomarkers of AD, is unknown.The aim of the diploma thesis was to compare the level of mitophagy markers in blood serum and cerebrospinal fluid (CSF) of patients in various stages of AD with cognitively healthy controls (CU) and determine its relationship to the degree of cognitive impairment and standard Alzheimer's biomarkers (amyloid beta (Aβ42), total tau (T-tau) and tau phosphorylated at threonine 181 (P-tau181)). We have shown that mitophagy is impaired in individuals with AD, manifested by increased levels of PINK1 and BNIP3L (activators of mitophagy) and decreased levels of TFEB (master regulator of lysosomal biogenesis) compared to CU. Moreover, these changes were associated with more advanced AD pathology, manifested by increased AD biomarker positivity and cognitive impairment.

These results suggest that in AD, the final step of mitophagy, lysosomal degradation, is impaired, and that disruption of mitophagy is associated with more severe AD pathology. Our findings support the hypothesis of an important role of mitophagy in the pathophysiology of AD.



**Key words:** Alzheimer's disease, autophagy, biomarkers, cognition, blood-based biomarkers, mitophagy