Mesencephalic astrocytic derived neurotrophic factor (MANF) and the Conserved dopaminergic neurotrophic factor (CDNF) are members of a family of neurotrophic factors. Both have a saposin-like domain in the N-terminus with which they bind to lipids or membranes. The neurotrophic activity resides presumably in the C-terminal domain. Both proteins are considered to be potential therapeutic agents for the treatment of Parkinson’s Disease (PD): MANF was shown to support the survival of dopamine (DA) neurons in culture and to be protective against endoplasmic-reticulum stress. CDNF has been shown to protect midbrain DA neurons in vivo.

To investigate potential changes in MANF and CDNF levels connected to neurodegeneration, we investigated mRNA levels using radioactive oligonucleotide based in situ hybridization in key regions of the brain affected by degeneration in MitoPark mice, APP transgenic mice and postmortem human tissue. The MitoPark mouse is a genetic PD model, which displays slow progression of key pathological symptoms. In old MitoPark mice displaying advanced symptoms of PD, we found a significant decrease of MANF mRNA expression in the striatum as well as in cortex. We extended the study to APP mice, an AD mouse model. Our results in human postmortem tissue indicate that mRNA levels of the two neurotrophic factors are reduced also in PD and AD brains. We conclude that other neurotrophic factors than GDNF and NGF are affected in PD and AD respectively, and that factors such as MANF and CDNF might lead to new therapeutically approaches for neurodegenerative diseases.