

Expression and quantification of candidate genes of Alzheimer's disease in brain regions primarily affected by disease

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Research question and background

We are studying candidate genes for the neurodegenerative disorders Parkinson's disease (PD) and Alzheimer's disease (AD), with genetic and histological methods.

Methods and tissues used

In situ hybridization, Western blot and immunohistochemistry are used to localize and quantify levels of candidate genes in frontal cortex, putamen, midbrain and hippocampus of patients and matched control subjects. In addition, we analyzed the homologous genes in rodent models of AD or PD respectively. In November 2013 NBB provided us with frozen brain samples from Alzheimer cases (15) and control cases (10).

Results and conclusion

We compared the cellular localization and expression of myeloperoxidase (MPO) in neurodegenerative disease. MPO, a key enzyme in inflammatory processes, has been implicated in neurodegeneration by genetic and histological findings. We detected MPO in monocytes in capillaries, perivascular macrophages and amoeboid microglia in the brain parenchyma. The number of MPO cells was significantly increased in brain areas highly affected by neurodegeneration, for example in frontal cortex of AD patients and putamen of PD. Our results thus highlight the inflammatory component of the pathophysiology of the two neurodegenerative diseases.

In a further analysis we focus on Nogo receptors and other members of the Nogo system, based on results from rodent AD models (Karlsson TE et al, J Alzheimer Dis. 2013, Karlén A et al, PNAS 2009). In ongoing studies we detected significant changes in brain tissue from AD patients compared to control brains, in line with findings in mouse models. Our results point to an unexplored role of the Nogo system in the progression of AD, and highlight the need to characterize gene expression patterns and expression levels at different stages of disease.