Role of N-cadherin in the aging human brain and in Alzheimer´s disease

Aksana Andreyeva and Kurt Gottmann

Institute for Neuro- and Sensory Physiology, University Düsseldorf, Universitätsstr. 1, 40225 Düsseldorf, Germany. Kurt.Gottmann@uni-duesseldorf.de

Research question and background

During aging of the human brain, synapses are thought to undergo molecular changes that have not been well characterized. Because Alzheimer's disease (AD) is associated with aging and affects the function of excitatory synapses, these changes might be important in AD. Synaptic adhesion molecules such as N-cadherin have been shown to stabilize pre- and postsynaptic structure and function. Presynaptically, vesicle clustering and recruitment of vesicles to the active zone have been demonstrated to depend on the N-cadherin/catenin system. Postsynaptically, dendritic spines are well known to be influenced by N-cadherin function. Therefore altered N-cadherin expression might influence the long-term stability of synapses. Moreover, N-cadherin is proteolytically processed leading to the formation of a C-terminal fragment CTF1 that is further cleaved by γ-secretase.

Methods and tissues used

We analysed changes in the expression of N-cadherin and N-cadherin CTF1 in the post-mortem brains (cortical samples) of normal donors and AD patients using Western blotting as major method.

Results and conclusion

We studied the expression of N-cadherin and of a C-terminal fragment of N-cadherin (CTF1, which is created by proteolytic processing) in post-mortem brains from non-demented individuals and AD patients by using Western blot technology. No differences in N-cadherin expression were detectable. Intriguingly, the expression of the C-terminal N-cadherin fragment CTF1 was clearly increased in about 50% of the AD patient brain samples (Andreyeva et al., 2012). Because N-cadherin CTF1 is a γ-secretase substrate this might indicate an altered function of γ-secretase in AD patients. Moreover, as indicated by experiments in cultured mouse neurons (Andreyeva et al., 2012), N-cadherin CTF1 appears to accelerate synaptotoxic effects of amyloid-β peptides and thus might contribute to the progression of AD.