JPND research
EU Joint Programme – Neurodegenerative Disease Research

# CircProt

**Synaptic circuit protection in Alzheimers's disease (AD) and Huntington's disease (HD): BDNF/TrkB and Arc signaling as rescue factors**

Alzheimer's (AD) and Huntington's disease (HD) result from the erroneous communication of neurons at synapses in different brain areas (neocortex, hippocampus, striatum). The protein BDNF regulates synaptic communication under healthy conditions. However, insufficient release of BDNF from neurons and defective BDNF signaling in target neurons contribute to cellular malfunctions in AD and HD. Although they are essential to the development of effective therapies, the underlying molecular mechanisms for deficits in synaptic communication in these diseases are not understood.

CircProt will employ AD and HD mouse models to investigate the synapse communication deficits for both diseases. Using microscopy methods to investigate BDNF trafficking and release, electrophysiological recordings to check for altered synaptic activity, structural analysis of synaptic contact points (spines), analysis of intracellular protein networks, and behavioral analysis of memory dysfunction (AD) and motor/ cognitive deficits (HD), CircProt will disentangle the role of defective BDNF function in both diseases. Diseased mice will be treated with drugs that either speed up BDNF release or boost BDNF signaling to investigate how drug treatment ameliorates synaptic communication. Computational modeling of neuronal circuits will assist in the quantitative analysis of improved synaptic function in response to treatment. Thus, CircProt will aid the development of effective future therapies for both diseases.

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**Duration:** 3 years

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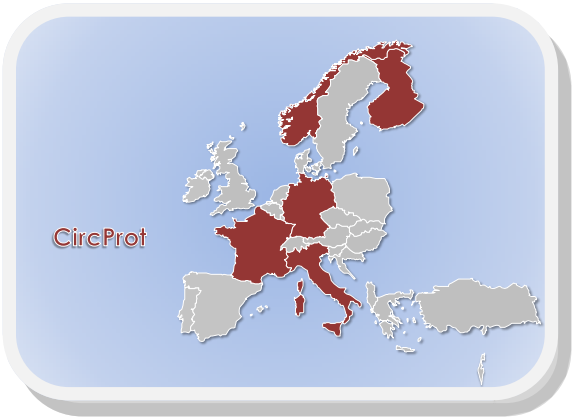


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