

Linking Olfactory deficits to Neurodegenerative Disorders

<https://neurodegenerationresearch.eu/survey/linking-olfactory-deficits-to-neurodegenerative-disorders/>

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Research Abstract

Project Summary Loss of cholinergic innervation is an early pathological sign in many neurodegenerative disease like Alzheimer's disease (AD) and Parkinson's disease (PD) and it is thought to underlie cognitive deficits in these diseases. Another early symptom, one that precedes the canonical symptoms of these diseases by many years is deficits in olfaction. It

stands to reason that if we can provide a mechanistic explanation linking these early deficits to AD and PD, we will have an early biomarker for these diseases and allow for the design of strategies for early intervention and treatment. In this proposal we test the idea that olfactory insults can cause the degeneration of central neurons that express genes that confer susceptibility to degeneration. To test this idea, we will use mouse models that over-express these genes only in cholinergic neurons. The two genes being tested are the tau, implicated in AD (and now in PD) and the A53T mutant α -synuclein (A53T α -syn) along with a fluorophore (GFP or Td-Tomato). The mice will be subject to either chemically-induced anosmia or treatments that specifically target dopaminergic neurons in the olfactory bulb (intranasal MPTP or stereotactically injected 6-OHDA). We will then examine the cholinergic projections in these mice. For this we will use the CLARITY technique for rendering the brain transparent coupled with light sheet microscopy that allows us to image deep into tissues. Using this technique we will reconstruct and render in 3-D the cholinergic innervation from the basal forebrain to the olfactory bulb. This will allow us to compare changes in cholinergic innervation under conditions of olfactory insults. This project is the first attempt at providing a link between olfactory dysfunction and the cognitive symptoms seen in AD and PD. It will also be the first to provide a detailed 3-D rendering of the basal forebrain cholinergic system. Results from this study will provide the basis for using olfactory dysfunction as an early biomarker for neurodegenerative diseases.

Further information available at:

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