Novel protein interactions explain memory deficits in Parkinson's disease

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A study published in the journal *Nature Neuroscience* describes the identification of a novel molecular pathway that can constitute a therapeutic target for cognitive defects in Parkinson's disease. The study showed that abnormal forms of Parkinson's disease (PD)-associated protein alpha-synuclein interact with the prion protein (PrP), triggering a cascade of events that culminates in neuronal dysfunction, causing cognitive defects that are reminiscent of those in PD.

"This is the follow-up of a previous study initiated in my laboratory in which we found that particular forms of the protein alpha-synuclein cause dysfunction of neuronal circuits involved in memory formation. We did not know how this was happening. In this new study, we have detailed the molecular mechanisms involved, which suggests we now have new targets for therapeutic intervention," explains Tiago Outeiro.

Using pharmacology and genetics, the team has now defined a series of molecular events that explains the memory defects observed in animals that model some important aspects of PD. Luísa Lopes says, "We used a mouse model of PD in which human alpha-synuclein is produced and found that by blocking this interaction with PrP using a caffeine analogue, reverted the abnormal neuronal activity and memory deficits. This study links nicely with our previous work on Alzheimer's disease, further suggesting that molecules like caffeine may, indeed, have potential benefits against memory deficits upon neurodegeneration."

Parkinson's disease is a devastating disorder affecting millions of people
worldwide. Current therapies are only treat some of the motor symptoms of the disease. "We now know that PD is much more than just a motor disease, and there is a great demand for novel therapies, especially those capable of modulating disease progression or, ideally, capable of preventing the onset of the disease," - says Tiago Outeiro.

![Calcium levels inside a neuron are demonstrated by an intensity scale where blue is low calcium and red high calcium. Credit: Luísa Lopes lab, iMM Lisboa](image)

"We are very excited with the findings of our collaboration, and this study demonstrates that when we pull together our complementary expertise we can make important discoveries that can impact the lives of the millions of people (patients and families) affected by these terrible disorders," says Luísa Lopes.

Provided by Instituto de Medicina Molecular


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