

The University of Sydney - 23/06/2013

Although almost all people with Parkinson's disease suffer from impairments in movement, such as tremor, slowness and stiffness, there are a number of other symptoms that commonly affect people with the condition. These symptoms are known as "Non-motor symptoms" of Parkinson's disease, and include problems with sleep, mood, cognition, memory and perception. Unfortunately, these symptoms are not as well understood as those that cause the movement impairments and as such, the treatments for the symptoms are currently underwhelming.

One of the most common non-motor symptoms occurs in advanced Parkinson's disease when patients suffer from disabling breakdowns in their perception of the everyday world<sup>1</sup>. Known as visual misperceptions and hallucinations, these symptoms occur when a patient mistakenly thinks that they see an object that is not in fact present in the physical world. While extensive research has been performed on this symptom, most of the work has been limited to either the post-mortem analysis of brain tissue or the testing of creative hypotheses through plausibility, rather than objective scientific testing. For example, visual hallucinations in Parkinson's disease have been attributed to the intrusion of dreams into everyday reality, or to a breakdown in visual processing.

Recently, our research team has proposed a model that suggests visual hallucinations arise from failing networks across the brain. Normally these networks process available information and allow individuals to make correct responses to what they are seeing. Imagine walking home in the dark after watching a frightening movie – every tree could represent a shadowy threat. However, the brain kicks in and allows you to rationalize that you live on a tree-lined street. In Parkinson's, we believe that the brain's networks intermittently "break down" when having to deal with this type of processing, allowing the mind to play tricks, which results in the emergence of disturbing hallucinations.

Combining results from neuropathology with insights from recent studies in neuroimaging and networks neuroscience, we have proposed instead that visual hallucinations arise from impaired communication between large-scale neural networks<sup>2</sup>. Effectively, patients with these symptoms cannot "problem solve" the presence of an ambiguous stimulus. Instead, they rely on neural networks that are incapable of dealing with these information-processing challenges, leading to incorrect interpretation of the ambiguous stimuli.

When patients develop troublesome hallucinations they often need to reduce their Parkinson's medications. This suggests that dopamine may be affecting the failing networks that underlie this symptom. If we could understand how dopamine is affecting these networks to "drive" hallucinations then we hope to be able to develop more effective treatments that will stop patients entering nursing homes.

#### References

- 1 – Fenelon et al, 2000. *Brain*.
- 2 – Shine et al., 2011. *Mov Disord*.