



Investigating neuroinflammation in brain cell death, and reversing Alzheimer's disease with cannabidiol



What is the focus of the research?

1) To examine whether the death of nerve cells in an area of the brain called the basal forebrain exacerbates Alzheimer's disease, and 2) Determine if cannabidiol can reverse the neuroinflammation that leads to cognitive decline.



Why is it important?

Neuroinflammation is the brain's immune response to threat and a hallmark of early Alzheimer's disease. However, scientists still don't understand the exact role it plays. Neuroinflammation appears to interact with other elements of Alzheimer's disease, such as the toxic accumulation of proteins called amyloid beta and tau in brain cells. This interaction may be involved in the dysregulated immune response that causes the death of brain cells and leads to cognitive decline.

The basal forebrain, which regulates sleep, memory and body temperature, is particularly susceptible to neuroinflammation. In Alzheimer's disease, nerve cells that are critical for memory die at an alarming rate. Importantly, basal forebrain degeneration and the loss of these nerve cells can occur before the presence of toxic amyloid beta and tau. This suggests that basal forebrain degeneration may be an early contributor to Alzheimer's disease, instead of a later consequence of disease progression.

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I'm excited to understand how many different factors interact in Alzheimer's disease, instead of looking at one factor in isolation. I think this will help us better comprehend and treat the disease. ”

— Dr Rose Chesworth

For the first time in Alzheimer's disease research, Dr Chesworth will use mice to explore the theory that neuroinflammation and basal forebrain degeneration may exacerbate these other life-threatening characteristics of Alzheimer's disease. Her team will also examine whether cannabidiol, a cannabis plant compound, can reverse neuroinflammation and improve cognitive impairment. If it is successful in mice, the results will provide important evidence that cannabidiol could be a potential treatment option for Alzheimer's disease.



How will this happen?

Stage 1: breed mice that have both chronic neuroinflammation and increased toxic tau aggregation. Determine if these mice develop earlier or more aggressive Alzheimer's disease pathology, cognitive decline and motor impairments, compared with mice that only have tau or neuroinflammation. If so, this would suggest that neuroinflammation and tau can interact to worsen Alzheimer's disease progression.

Stage 2: treat the mice with cannabidiol daily for up to two months to determine if it reverses Alzheimer's disease pathology, neuroinflammation and behavioural impairment.



What does this mean for the future?

- Potential new treatment to reverse Alzheimer's disease.
- A better understanding of Alzheimer's disease pathology.
- Support for cannabidiol to be used in clinical trials.



Why cannabidiol?

Cannabidiol (CBD) is derived from the cannabis plant. The endocannabinoid system (named after the plant) doesn't receive as much attention as our other body systems, but it's critical in the regulation of learning and memory, mood and sleep. This important network of chemicals, called cannabinoids, and the receptors they bind to, are located throughout the entire body. The way CBD interacts with those located in the brain may be protective against Alzheimer's disease by reducing the neuroinflammation that's linked to nerve cell disease and damage.



Who's undertaking the research?

Dr Rose Chesworth, Western Sydney University

Dr Chesworth is a postdoctoral researcher at Western Sydney University, where she uses behavioural neuroscience to investigate mental health and healthy ageing. Dr Chesworth uses preclinical mouse models to investigate novel therapeutics for neurodegenerative disorders such as Alzheimer's disease, as well as comorbidity between schizophrenia and

substance abuse problems.

Dr Chesworth has a strong track record of scientific discovery and funding support, having published 32 papers and book chapters, and being awarded more than \$700,000 in grant funding. She collaborates with leading Australian researchers and supervises several PhD and Master of Research students, as well as international exchange students.

The title of Dr Chesworth's project is *Inflammation and basal forebrain cholinergic degeneration exacerbate tau pathology - a new approach to Alzheimer's disease aetiology and treatment*.