WHAT WE KNOW ABOUT SCHIZOPHRENIA

Schizophrenia and schizoaffective disorder cause a person to avoid family and friends, have difficulty thinking, be unable to work, and have unusual experiences including hearing voices or having unwavering false beliefs. Current treatments are not aimed at the cause (which is unknown), do not completely relieve the symptoms, and produce unwanted side effects. Schizophrenia is first diagnosed in adolescents and young adults and impacts millions of people world-wide. Currently we think that genetic and environmental influences combine to create changes in brain development that cause schizophrenia.

ABOUT OUR RESEARCH

The Macquarie Group Foundation Chair of Schizophrenia Research, Professor Cyndi Shannon Weickert*, and her research team aim to understand how biological changes in the brain during development cause schizophrenia. A more complete knowledge can lead to new and more effective treatments aimed at the root of the problem in schizophrenia. Dr Tom Weickert’s research group takes the lab-based discoveries into clinical trials to test new treatments aimed at reducing symptoms, improving thinking, and restoring normal social function in people with schizophrenia.

WHAT WE HAVE DISCOVERED

People with schizophrenia have difficulty planning tasks, problem solving, focusing attention, remembering information and interacting with others. Antipsychotic medication treatment may reduce some symptoms but they do not return people to their level of function before the illness. Some people with schizophrenia have a gene that does not allow the brain to respond to hormones during development which may put those people at risk for schizophrenia. We have recently successfully completed a clinical trial that repurposes a drug treatment (raloxifene) aimed at stimulating a hormone receptor that improved attention and memory in some people with schizophrenia.
CURRENT PROJECTS

CANAKINUMAB ADD-ON TREATMENT FOR SCHIZOPHRENIA (CATS).
Earlier studies by the Weickert lab revealed elevated levels of cytokines (a sign of infection) in people with schizophrenia. Dr Tom Weickert is currently conducting a clinical trial that uses an already established medication (canakinumab) to reduce levels of one of the elevated cytokines in people with schizophrenia.

This new treatment would, in theory, potentially reduce or eliminate their psychotic symptoms and improve cognitive abilities. We have begun recruiting people into the study and if this treatment is found to be beneficial, then it may provide completely new ways to successfully treat schizophrenia.

COGNITION AND SELECTIVE ESTROGEN RECEPTOR MODULAR-RELATED TREATMENT.
Our previous clinical trial using raloxifene showed that it improved memory and attention in people with schizophrenia. The current task is to determine how raloxifene is working mechanistically. We aim to conduct a truly “reverse translational” approach, taking observations of the clinical benefit of raloxifene back to the lab which will allow us to better understand the molecular changes that occur in schizophrenia.

Using rodent models to determine the mechanism of action of raloxifene and relate molecular changes to specific behaviors will allow us to improve hormonal treatments of people with schizophrenia for even better cognitive outcomes.

CORTICAL NEUROPROTECTION IN SCHIZOPHRENIA.
Brain imaging studies have revealed widespread thinning of the brain’s grey matter in people with schizophrenia, with this thinning being linked to symptoms. This project will investigate if brain inflammation contributes to grey matter thinning. Next, we will determine if higher inflammation measured in blood predicts those people with a thinner grey matter in the brain. Third, we will test if a protective agent can reverse inflammation in the blood and restore brain health in people with schizophrenia.

IS THE BLOOD BRAIN BARRIER AT RISK IN PSYCHOSIS?
The blood brain barrier (BBB) is a structure that normally prevents large molecules from entering the brain and protects the brain. Recent studies have shown that inflammatory processes in either the blood or the brain can damage the BBB and may lead to conditions that are harmful to brain health. Our lab and others have recently shown that there is evidence for inflammation processes in the blood and brains of people with schizophrenia.

In this work we will test if people with psychosis who also have increased cytokines (signs of infection) may also have a damaged BBB. We aim to use post-mortem brain tissue from deceased people with psychosis, blood serum from living people with psychosis, and a cellular culture laboratory model to test the relationship between elevated cytokines and a damaged BBB in people with psychosis. This work also may help determine whether it is possible to reverse the inflammation damage and restore healthy BBB function.

* Prof Shannon Weickert is the Macquarie Group Foundation Chair of Schizophrenia Research, a joint venture between NeuRA, UNSW, Schizophrenia Research Institute and Macquarie Group Foundation. It is supported by NSW Health.

HOW YOUR SUPPORT HELPS
We are able to make significant advances due to the dedication and generosity of countless people who come to NeuRA every day. Your donation, or a gift in your will, play a key role in allowing us to continue to work towards transforming the lives of all Australians through medical breakthroughs. For further information on how you can support our research phone 1300 888 019 or make a secure donation at neura.edu.au/donate.