Cognition, MRI and Wilson's Disease

The CROWD Study, UCL Queen Square Institute of Neurology, London — Update

The CROWD (Cohort Research On Wilson's Disease) Study was launched in December 2018. In Part 1, the aim is to identify genetic factors that determine whether someone with Wilson's disease will develop neurological problems or not. People across the UK were invited to participate by completing an online questionnaire and sending in saliva samples. We have now finished collecting samples, extracting the DNA from the samples and are proceeding with the genetic analyses.

In Part 2 of the Study, the aim is to understand how to measure and monitor the effects of Wilson's disease on the brain. Forty patients attended Queen Square[1] for clinical assessments, blood tests and MRI brain scans in 2019 and this part of the study has been completed. Some findings have been discussed in last year's newsletter. In this article, **Dr Samuel Shribman** and **Miss Maggie Burrows** discuss some of their work looking at cognition in Wilson's disease. Please do not hesitate to contact them at s.shribman@ucl.ac.uk, if you have any questions about their research.

Cognition, MRI and Wilson's disease

Last year we discussed how magnetic resonance imaging (MRI) scans can help us understand how Wilson's disease can affect the brain. This years's article describes research findings exploring the link between cognition and changes on MRI brain scans in Wilson's disease.

What is cognition?

Cognition is the mental action or process of acquiring knowledge and understanding through thought, experience, and the senses. It can be divided into different *cognitive domains* including abstract reasoning, memory, language, calculation, social cognition and executive function. The latter is a term used to describe the mental processes that allow us to plan, focus attention and multitask.

As individuals, we all have strengths and weaknesses in different cognitive areas – some of us may be very competent at map reading and reverse parking our cars – others not so. Some of us may be proficient at having several things on the go at the same time AND hold a conversation on the phone – others would find this very difficult. Some diseases, however, affect cognition in very specific areas. This may not bother the person too much unless it starts to affect their daily life – at this point we would say the person has dementia.

How is cognition measured?

A range of tests can be used to measure different aspects of cognition. This usually involves working through a task with a clinician. There are at least 10 different tests for assessing memory alone, including tests for different types of verbal and visual memory and short- and long-term memory. Tests scores are compared to average scores from the general population to help determine how someone is performing. Where someone performs below the expected level for a given test this is referred to as a *cognitive deficit*.

What was already known about cognition in Wilson's disease?

A number of studies have looked at cognition in patients with movement disorders and/or psychiatric symptoms due to Wilson's disease. They found that several cognitive domains can be affected and that cognitive deficits were often subtle. A small minority of patients only were considered to have cognitive impairment that limited daily life. Patients with Wilson's disease with liver disease only had not been rigorously tested for this. It was also unclear how cognitive problems relate to the changes that can be seen on MRI brain scans.

What did we do in the CROWD study?

We performed a range of cognitive tests in 40 people living with Wilson's disease who visited the National Hospital for Neurology and Neurosurgery as part of the CROWD study. We also performed MRI brain scans to test whether there was an association between test scores and subtle changes in brain structure.

What did we find?

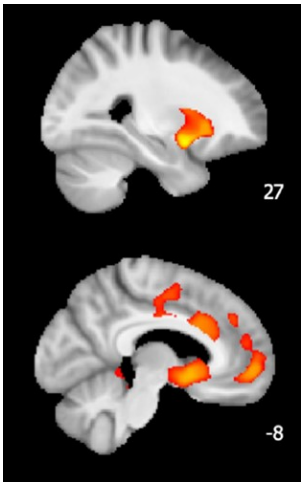
Firstly, we found that patients with movement disorders and/or psychiatric symptoms had lower scores for tests of processing speed and executive function than patients with liver disease only. These scores also correlated with the

severity of the movement disorder meaning that patients with more disabling movement disorders were also more likely to have lower test scores.

Secondly, we found that both patients with movements disorders and/or psychiatric symptoms and patients with liver disease only, had subtle problems with memory, specifically related to recognising faces.

How does this relate to MRI brain scans?

We compared the scores for each cognitive test with the volume of different brain regions. For tests of processing speed and executive function, scores were closely associated with the volume of the basal ganglia. These are the deep structures in the brain that control movements. This area is highlighted in red/yellow in the upper image on the right showing a side view of the brain.



Scores for test of memory for faces were associated with more subtle but widespread changes in the brain. These areas are highlighted in red/yellow in the lower image on the right showing a side view of the brain.

What does this mean?

These findings suggest that the disease process leading to problems with movements and executive function may differ from the disease process responsible for more subtle problems with memory. It is possible that copper affects different parts of the brain in different ways or other consequences of the faulty Wilson's gene might explain our findings.

Why is this important?

A small minority of people living with Wilson's disease have ongoing problems with cognition that limit them at school, college, work or in other aspects of their daily life. It is important that we understand the type of problems with cognition that can occur, so we know how to identify these early and offer support. Developing a clearer understanding of the associated changes in brain structure also provides insights into how Wilson's disease can affect the brain.

Reference
Neuroimaging correlates of cognitive deficits in Wilson's disease: a multimodal, whole-brain MRI study. Shribman S, Burrows M, Convery R, et al. Mov Disord 2022; doi: 10.1002/mds.29123

Dr Samuel Shribman & Miss Maggie Burrows—March 2023