

## **SUMMARY OF FINAL REPORT**

### **The cognitive effects of cerebellar disorder**

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**Start date:** November 2006

**End date:** November 2009

#### **Background and aims:**

The purpose of this PhD studentship was to investigate the role of the cerebellum in aspects of perception, thinking, intellect and memory. SCA6 is a genetic condition that causes a gradual degeneration of the cerebellum. By looking at the cognitive and perceptual profile of people with SCA6, we can make inferences about the role of the cerebellum in cognitive and perceptual processes. This is important information, not only for people with SCA6, but for people with disorders involving the cerebellum.

The following goals were outlined for the project:

1. Acquisition of neuropsychological, perceptual and imaging data
2. Analysis of neuropsychological, perceptual and imaging data
3. Report of data to international neurology or neuroscience meeting
4. Preparation of data for full report(s) in international peer-reviewed neurology or neuroscience journal of the calibre of Brain
5. First draft of PhD thesis

#### **Results:**

Of the above goals, numbers one to four were achieved during the timescale of the project. For goal five, the student's PhD thesis was submitted within two months of completing the project, and has now been successfully awarded.

Analysis of the rhythm measures comparing the 34 SCA6 patients to the control group (n=40) was carried out in the past year. It was discovered that in tests of absolute timing (measuring lengths of intervals between two tones) patients were significantly impaired relative to controls, yet in tests of relative timing (discriminating between two rhythmic patterns), no differences between patients and controls were found. This suggests the cerebellum may play a role in the timing of intervals, with other brain mechanisms being responsible for rhythmic pattern perception. These results have been published in 'Proceedings of National Academy of Sciences'.

Analysis of the neuropsychological assessment was carried out and completed from a group of 27 SCA6 patients. Detailed analysis showed that general intellect and memory are not affected in SCA6, but that specific executive functions, such as verbal and non-verbal response inhibition, mental flexibility, and the abstraction of concepts are impaired in SCA6. These results have been published in a special issue of Behavioural Neurology.

MRI structural scans were collected from 15 patients. The aim here was to look at the relationship between the structure of the cerebellum and the group's performance on the cognitive assessment to investigate if specific areas of the cerebellum are important for certain cognitive tasks. Analysis is now complete and showed that the cerebellum is important for verbal working memory, particularly the posterior (back) and inferior (bottom) parts of the cerebellar hemispheres. These results were presented at the Society for Neuroscience conference in November 2009 and have been submitted for publication in the journal Neuropsychologia.

### **Lay summary of the results:**

The purpose of these studies was to investigate the role of the cerebellum in aspects of perception, thinking, intellect and memory. SCA6 is a genetic condition that causes a gradual degeneration of the cerebellum. By looking at the cognitive and perceptual profile of people with SCA6, we can make inferences about the role of the cerebellum in cognitive and perceptual processes. This is important information, not only for people with SCA6, but for people with disorders involving the cerebellum.

We looked at the role of the cerebellum in time perception. Timing is very important for coordinated movement. The cerebellum is known to be involved in the control and correction of movement. When the cerebellum is damaged, movement becomes clumsy and less balanced and controlled. This is affected in people who have ataxia. In this study we found that in auditory tests of absolute timing (measuring lengths of intervals between two beeps) people with SCA6 were significantly impaired compared to controls, yet in tests of relative timing (discriminating between two rhythmic patterns), no differences between people with SCA6 and controls were found. This suggests the cerebellum may play a role in the timing of intervals, with other brain mechanisms being responsible for rhythmic pattern perception. The test we used does not require motor coordination and suggest a fundamental role of the cerebellum in the analysis of time, independent of its role in motor control.

We investigated the involvement of the cerebellum in cognitive processes, and found that there was no difference between people with SCA6 and those without SCA6 (standardised control data), in terms of memory and general intellectual ability. However we did find that people with SCA6 were worse than we would expect at tasks where two or more things have to be done at once, where the task requires mental inhibition of a response, and in tasks where it is required to mentally switch backwards and forwards between different rules or ways of doing things (these are known as 'executive functions'). The results show that having SCA6 does not affect memory or general intellectual ability, but that people with SCA6 may find that trying to do more than one thing at once and juggling different tasks in mind may become a little harder than before.

We also wanted to see if there was a relationship between the structure of the cerebellum and the performance of the participants on the thinking and memory assessment. This would tell us if certain parts of the cerebellum were important for certain cognitive tasks. We found that the posterior (back) and the inferior (bottom) of the cerebellum are important for tasks where you have to do two things at once. In SCA6, cells in only the cerebellum gradually die from the top of the cerebellum to the bottom, over many years. This suggests that as the disease progresses, people with SCA6 may find it harder to do tasks that require two things to be done at once.

The frontal lobe of the brain is important for the control of tasks where two things need to be done at once; suppressing a response and mentally switching between tasks and ideas. We know that the cerebellum has connections to the frontal lobe and we think that through these connections that the cerebellum supports the frontal lobe in its control of these types of tasks. People with SCA6 may find that, although they can still perform such tasks, because the frontal lobe is not affected, it may become harder and less automatic over time. This is because, due to the degeneration of the cerebellum in SCA6, it cannot support the frontal lobe as efficiently as it could before.

#### **Benefits to people with ataxia arisen/likely to arise from this research:**

This work will allow patients with cerebellar disorder, and those at genetic risk of such disorders, to be informed about the effect of such disorders on cognition. The role of the cerebellum in time perception will have important implications for optimising the home and working environment of patients with cerebellar disorder.

#### **Publications arisen from this project:**

Cooper FE et al The contribution of the cerebellum to cognition in Spinocerebellar Ataxia type 6. Behavioural Neurology 2010; 23(1-2): 3-15

Cooper F E et al Critical cerebellar subregions for verbal working memory. Neuropsychologia (in press).

Grube M et al Neuropsychological evidence for a cerebellar clock Proceedings of National Academy of Sciences 107(25): 11597-11601

#### **Conferences/ meetings where this research has been presented:**

Society for Cognitive Neuroscience (April 2008, San Francisco)

Newcastle University Postgraduate Research Conference (July 2009)

Society for Neuroscience (November 2009, Chicago)

#### **If the grant awarded funded a PhD studentship, has the student obtained their PhD? If not please give details of current status.**

The student working on this project, Freya Cooper, successfully obtained her PhD.

**For more support or information please contact: Ataxia UK, Lincoln House,  
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