

## **The effect of a gluten-free diet on patients with gluten ataxia- the use of MRS as a tool to measure ataxia**

*A research project that started over 3 years ago by Dr Hadjivassiliou and colleagues at Sheffield Royal Hallamshire Hospital and was funded by Ataxia UK has recently been completed.*

*Here Dr Hadjivassiliou reports on the findings of his research.*

### **Background and aims**

The aim of the study was to look at the usefulness of magnetic resonance (MR) spectroscopy as a monitoring tool in patients with ataxia. Ataxia rating scales are a notoriously crude means of assessing ataxia, yet most studies looking at interventions have used such rating scales as the only means of assessing the effect of therapeutic agents. In addition, MR imaging (MRI), the standard tool used in hospitals to detect atrophy of the cerebellum, is also a crude instrument in assessing changes that result from progression of the condition or from treatment.

### **Project details**

The general principle was to see if a) MRS is good tool to use to detect cerebellar dysfunction, b) this technique could be used to measure progression of ataxia and c) such dysfunction is reversible with dietary treatment in patients with gluten and anti-GAD ataxia

The specific aims of the project were to use MRS to study people with gluten ataxia and anti-GAD ataxia and to test whether differences could be detected by MRS before and after one year on a gluten free diet. The controls for this study were people with inherited ataxias (primarily FA and SCA6) and people without ataxia ('healthy' controls). A further aim was to see if MRS is also a useful tool in monitoring disease progression in the genetic ataxias. The idea here was that MRS can then be used for the evaluation of interventions such as for example the use of idebenone in FA.

### **Outcomes**

MR spectroscopy appears to be a sensitive method of assessment of cerebellar functioning. It appears that it has a higher sensitivity than MRI alone. This is demonstrated by the fact that patients with normal MRI (ie no detectable cerebellar atrophy) had evidence of abnormality on MR spectroscopy (Wilkinson et al. JNNP 2005; 76:1011-1013). Further refining of the technique is needed (eg using new software on a newer stronger magnetic field MR scan and altering the target of interest within the cerebellum) and we hope to achieve this. This tool may prove very helpful in assessing medical interventions that ultimately may benefit patients with ataxia.

Overall, we have been unable to demonstrate significant changes in MR spectroscopy following intervention with a gluten free diet in those patients with gluten ataxia and anti-GAD ataxia. We already know however that these patients stabilise or improve on clinical grounds following the introduction of a strict gluten free diet. The failure to demonstrate significant MR spectroscopy changes may be due to a number of reasons: the one year duration of the study may not be sufficient to detect changes, stabilisation of the condition may not be associated with changes on MRS, patient numbers being too small and that the target area of the cerebellum chosen may not be representative of the pathology in different ataxias (ie different parts of the cerebellum can be affected in different ataxias). However, there have been some notable exceptions. One patient with anti-GAD ataxia who started a gluten free diet was found to have a dramatic improvement on MR spectroscopy at one year. The improvement was sustained on repeat scanning. The patient is now stable without further deterioration (paper in preparation).

The researchers have published one paper and are currently working on three others. The work has been presented at national and international conferences. In addition they have obtained a large research grant from the Department of Health that matched funds from Ataxia UK and will also enable to take this research forward. The MRI data collected on patients with different types of ataxias provides a potential source of further study of which parts of the cerebellum are affected in different types of ataxias.

**Papers:**

Wilkinson ID, Hadjivassiliou M, Dickson JM, Grünewald RA, Wallis L, Griffiths PD. Cerebellar abnormalities on proton MR spectroscopy in gluten ataxia. *JNNP* 2005; 76:1011-1013.

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