

## **Conference report**

### **An overview of ataxia research - by Julie Greenfield**

I looked at 3 questions throughout the presentation:

1. "What type of ataxia does a person have?"
2. "What causes the ataxia?"
3. "How can the ataxia be treated?"

#### **What type of ataxia does a person have?"**

Some people have a specific diagnosis, eg Friedreich's ataxia, SCA 1, 2, 3 etc, however there are many people who get a non-specific diagnosis. This means they may be told they have an inherited cerebellar ataxia (if there is more than one family member affected), or they may be told that it is an idiopathic cerebellar ataxia (where the cause is not known). At a recent meeting of European ataxia researchers I attended they reported that about half of people with inherited cerebellar ataxia do not have a specific diagnosis. So considering there are also those with non-inherited cerebellar ataxia it is actually quite common not to know exactly which type of cerebellar ataxia one has. At the moment there are about eight tests for eight different SCAs. Some are done routinely, some only in research labs.

In terms of people who have unidentified cerebellar ataxia the research at the moment is focusing on finding new genes and on finding new forms of cerebellar ataxias. There has been much progress in the last few years in terms of discovering new types of cerebellar ataxias. For example the first SCA gene was found in 1993 and we now know of 21 different SCAs, with new ones being found all the time. Genetic tests are not available for all of them. There are many other types of ataxia being discovered eg ataxia with oculomotor apraxia and gluten ataxia. (These have been discussed in the doctors' questions and answers session).

Another newly identified form of ataxia is ataxia with CoQ10 deficiency. CoQ10 is an antioxidant that is found naturally in the body and it is also involved in the production of energy. This form of ataxia was identified by researchers in the US, and it is still thought to be quite a rare type of ataxia. At a recent conference the researchers quoted that only 18 cases had been identified to date. Having said that, when these same researchers tested 135 people with unidentified cerebellar ataxia they found that 9% actually did have this form of ataxia so it may be more common than originally thought. It is a childhood onset ataxia and it is associated with a number of features such as cerebellar atrophy, weakness, seizures etc. The important thing about this type of ataxia is that children responded to CoQ10 supplements by showing improvement in their ataxia and in their strength. Although this is based on individual case studies and not a large trial, it is very encouraging to find a type of ataxia that could be treatable.

## **'What causes the ataxia?' and 'How can it be treated?'**

Researchers are focusing on trying to understand the causes of the different forms of ataxia and attempting to find therapies that could be tested in cell or animal models and finally in human trials.

### ***Spinocerebellar ataxias (SCAs)***

Good news for spinocerebellar ataxia research. A group of European researchers, including ones in the UK, have recently formed a network and have been successful in obtaining funding from the European Commission for a large multi-site project, known as EuroSCA.

These are their ambitious aims:

- Creation of a large database of clinical and genetic information (to understand the conditions better and to ease recruitment into future trials)
- Creation of world's largest DNA bank
- To halve the number of people with unidentified inherited cerebellar ataxias
- To understand the disease mechanisms at the cell level of a number of different SCAs
- To test five potential new drugs in cell and animal models (and if any prove beneficial this may lead to trials in humans)
- To develop good rating scales for the cerebellar ataxias to measure whether a treatment is having benefits (currently lacking)

### **Trials in the spinocerebellar ataxias**

Much research is focusing on understanding SCAs in detail at the cell level in order to develop possible treatments. However, there have been some trials in people with SCAs in the last few years. These trials were testing medications that may help with ataxia symptoms, maybe because these medications had been successful in treating similar conditions, or maybe because researchers had anecdotal evidence of their benefit.

A few small trials have been published recently from around the world (outside the UK). Researchers who carried out small trials testing ondansetron, trimethoprim sulfamethoxazole or fluoxetine all reported no beneficial effects.

Researchers in Japan carried out a small trial of acetazolamide in SCA 6. Acetazolamide is used in the treatment of episodic ataxia and because there are some similarities in episodic ataxia and SCA 6 researchers have tested whether acetazolamide helped with SCA 6. Initially it looked like there were some positive results for a very short period of time but unfortunately they were not prolonged. When I spoke to these researchers and asked whether they were planning on doing another trial they said they weren't, probably meaning that the results were not as positive as hoped. Another couple of Japanese trials have also been published. These are two very small short trials testing the effect of D-cycloserine or branched chain amino acids. In both trials the researchers concluded that the

medications might have some affect. However they were very short trials, one lasting 2 weeks and the other 4 weeks and involved a small numbers of patients, so they would need to be repeated in larger trials before drawing any conclusions. Lastly a trial using an 'energy enhancer' drug called L-Acetyl carnitine has been ongoing in Italy. Researchers there had anecdotal evidence that it might have some beneficial effect so they wanted to test this in a trial. No results have been reported yet.

### ***Friedreich's ataxia***

I then gave an overview of Friedreich's ataxia research. The causes and potential treatments with iron chelators and antioxidants (including ones targeted to the mitochondria) were described. The update included a description of trials in the UK, Germany, France, Italy, Spain and the US. This information is largely covered in issues 141 and 142 of the *Ataxian* and will therefore not be reproduced here. If you would like a transcript of this section call me at the Office (0207 582 1444).

### ***Common therapeutic approaches - gene therapy***

In a condition such as FA in which both copies of the gene are abnormal and the result is a reduction in frataxin, if you could deliver a normal copy of the gene (gene therapy) it should theoretically be beneficial. Researchers in Australia have successfully injected a normal copy of the FA gene (attached to an inactivated virus particle) into cells taken from people with FA. They have been able to show that this gene actually manages to lead to an increase in the amount of frataxin made. These studies were carried out in cells in test-tubes. Now the researchers plan to test this system in a mouse model of FA.

Another approach that could be used for some of the dominant SCAs, where one copy of the gene is normal and one is abnormal and the abnormal one causes problems (e.g. production of a toxic protein). In this case you could use an approach called RNA interference. This is quite a new approach where you silence the abnormal gene (ie: stop it from making an abnormal toxic protein). There is now a project ongoing in the US on SCA 3 where researchers have succeeded in silencing a SCA 3 gene in cells taken from patients. Further studies are obviously needed. There is also a similar project starting in SCA 1.

### ***Touch therapy***

Lesley Cullen from Coventry University then gave a brief update on the touch therapy project. She explained that we are still looking for volunteers to take part and that the age of the people with ataxia who can take part has now been increased to 21 years old.

The Shorey family, who are the first to complete this study were very pleased with the results and Mrs Shorey said that after seven weeks on the project, their ten year old son was much more relaxed at night. "Normally he would be up for a couple of hours fidgeting. It does relax him and calms him down." She also

commented that “It helps us as well – the fact that we’ve got contact with him on a one-to-one basis”.

There are now a number of therapists around the UK who are trained to run this programme, so if you are interested in taking part please call Julie at the office to see if there is a therapist near you.