

Inherited ataxia in the North of England
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The aim of this study was to carry out an epidemiological study in the north of England between October 2002 and August 2005.

During this period we have established the following:

1. Dominantly inherited ataxia (including the various spinocerebellar ataxias, or SCAs) is far more common than was previously anticipated, affecting ~ 1 in 12,500 individuals.
2. SCA6 is the most common cause of inherited ataxia in this region (1.58 / 100,000 (95% C.I. = 1.04 – 2.13), or 2.18 / 100,000 (95% C.I. = 1.81 – 2.56) adults over 45 years of age). Microsatellite haplotype analysis showed that all 22 SCA6 families in our region descended from a single common founder. Subsequent work showed that the SCA6 haplotype is shared by SCA6 families in Finland, Japan, Thailand and Brazil. We found the same haplotype in a proven de novo SCA6 case. This strongly suggests that the haplotype predisposes to pathological expansion at the SCA6 locus.
3. The recently described SCA17 is the second most common cause of dominant ataxia in our region (0.16/100,000 (upper 95% confidence interval 0.31/100,000)). Our study has shown that it is more common than SCA1,2,3,10,12 and 14 in the UK population. This has now become part of routine diagnostic testing in our region. Our observations suggest that a smaller number of repeats are required to cause disease than was previously thought.
4. SCA 10, 12 and 14 are a rare cause of ataxia. No cases were found in the Northern Region.
5. 4% of patients with undiagnosed ataxia had a pathogenic expansion of the SCA8 gene. In one family the expansion did not segregate with the phenotype, suggesting that the actual expansion is not the primary cause of the disease. Haplotype analysis showed a similar predisposing haplotype in a de novo case to other families around the world.
6. Fragile X premutations are a rare cause of ataxia in our region. No new cases were detected.

Ataxia UK supported this project by funding a PhD studentship. This studentship funded Kate Craig who was awarded her PhD in November 2005. She is now a postdoctoral scientist in my laboratory and is still working on ataxia.

Publications directly arising from this grant:

Craig K, Keers SM, Archibald K, Curtis A, Chinnery PF. Molecular epidemiology of spinocerebellar ataxia type 6. *Ann Neurol* 2004; 55: 752-5.

Craig K, Keers SM, Walls TJ, Curtis A, Chinnery PF. Minimum prevalence of spinocerebellar ataxia 17 in the north east of England. *J Neurol Sci* 2005; 239: 105-9.

Two additional publications are in preparation and will be submitted within the next two months.

Lay summary

Despite growing interest in the different causes of inherited cerebellar ataxia, the actual frequency of these conditions in general population was unknown until recently. Without knowing how common these problems are, it is difficult for the health services to provide enough resources to help affected individuals and their families to cope with the difficulties that ataxia can bring. To tackle this problem we carried out a study of genetic ataxia in the north east of England. We were surprised to find that dominantly inherited ataxia (the kind that does not skip a generation and is passed on from affected individuals to their offspring at 50:50 risk) was much more common than we expected, affecting about 1 in 12,500 of the general population. This translates to around 5000 people in the UK with a dominantly inherited ataxia. This figure does not take into account people with recessively inherited ataxias (such as Friedreich's ataxia) and people with non-inherited ataxias.

Spinocerebellar ataxia type 6 (SCA6) was the most common, with 22 families in our region. Detailed genetic work suggests that all of the affected individuals are related to a single ancestor with SCA6 who lived many years ago. SCA17 was the second most common cause of dominant ataxia in our region of the North East of England. As a result of this research, testing for SCA17 has now been established as a standard diagnostic test in our region. Other dominantly inherited ataxias (such as SCA 1,2,7,8, 10, 12, 14 and late-onset ataxia in the grandfathers of boys with the fragile X syndrome) were very rare indeed. Our work has also helped us to understand how the genetic changes actually occur and spread throughout the population, hopefully leading to the development of new treatments in the future.

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