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# How Spinocerebellar Ataxia Affects the Body and the Family

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## Abstract:

This poster project is a literature review that examines the causes, effects, and research being done to treat and prevent some forms of Ataxia. Ataxia is a disorder of the nervous system that causes tremors, and problems with walking, balance, memory, and mood disorders. There are many forms of Ataxia, all affecting various genes, but all have the devastating effect of the loss of the ability to move around without aid. Mental ability is not affected, yet the patient loses the ability to control their body. Most forms are caused by genetic mutations. For example, Fragile X associated tremor/ataxia syndrome (FXTAS) is caused by a mutation of the FMR-1 gene. The base triplet CGG repeats 200-4000 times in people with the disease, and 5-50 times in normal people. Another example is Spinocerebellar Ataxia, which has been tied to many different genes, and is the focus of this project. There is no known cure for this type of ataxia, which is considered a progressive and irreversible disease. Treatments are limited to alleviating symptoms and not fixing the disease itself. Sleep disorders, depression, and joint pain are all side effects that can be treated, but once the disease progresses to the point where the patient can't perform daily tasks, even a rehabilitation therapist cannot help them. Stem cell research, which is still in its early stages, is being looked at as a possible cure for more well-known cerebellar diseases like Parkinson's and hopefully, the cure will help treat diseases like Spinocerebellar Ataxia too.

## Key Points:

- Gradually lose control of your nervous system while retaining all mental capability
- Over 60 different types of Spinocerebellar Ataxia
- Most are polyglutamine diseases with CAG triplet repeat disorders
- No known cure

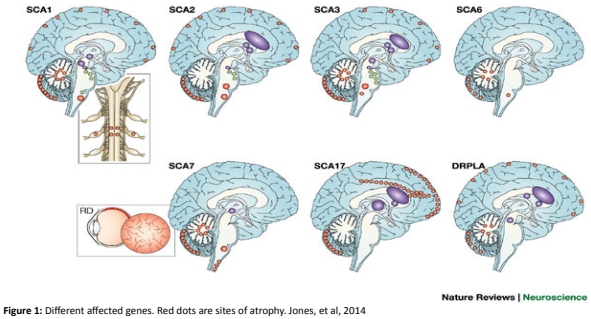


**Figure 1:** Different affected genes. Red dots are sites of atrophy. Jones, et al, 2014

## Hypothesis:

- Do allele frequency distributions at the SCA1 locus differ from population to population?
- Does testing the SCA1 locus make a good paternity test?
- Is there any segregation distortion in testing the SCA1 locus?

## Methods:

- 165 mother/child/potential father trios were tested at the Clínica Civil of the Ribeirão Preto University Hospital, University of São Paulo, Brazil
- Genomic data was extracted from 300 microliter samples
- Fragments containing the CAG repeats of the SCA1 and MJD genes were amplified by PCR, using primers gotten from a collaborating study
- Amplified products were run on a 12% denaturing polyacrylamide gel, followed by silver nitrate staining
- Procedure was repeated with samples of equal mobility placed side by side, allowing them to see an allele ladder and find the samples for sequencing, so that they could determine the exact number of CAG repeats
- To estimate segregation distortion, they selected the 118 related trios
- Then they used a GENEPOP program that allowed them to determine the inherited allele by direct genotype analysis of the trios, and tell which one of the alleles, the larger or the smaller, was transmitted
- Proportions were compared using a $\%^2$ test, and they expected a ratio of 50%.

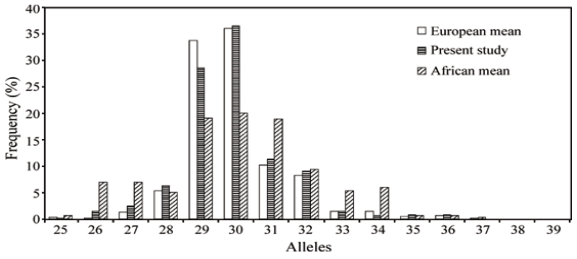


**Figure 2:** Allele frequencies of the *SCA1* locus in three population samples. Weizel, et al, 2003

## Results:

- The allele frequencies found were similar to those reported for European populations, but the most popular alleles (29, 30) were far less frequent in African populations
- Testing the SCA1 locus actually did make a good paternity test as 118 out of 165 fathers were related to one of the children
- 19 different SCA1 alleles were identified, with 19 to 39 repeats
- There was no segregation distortion as shown by table 1

| Meiosis | Transmitted allele | | | | $\chi^2$ |
|---|---|---|---|---|---|
| | Smaller | Larger | Non-informative | Total | |
| Maternal | 130 | 127 | 110 | 367 | 0.035 (p = 0.8516) |
| Paternal | 142 | 127 | 98 | 367 | 0.8364 (p = 0.3604) |
| Total | 272 | 254 | 208 | 734 | 0.6158 (p = 0.4326) |

**Figure 3:** Transmission of larger and smaller alleles by normal individuals. Weizel, et al, 2003

## Future Treatments:

- China is the leading country in stem cell research
- There is a current study being done in China where stem cells are injected and then the patient goes through rehab
- According to the site, 20,000 people have already gotten injections with no side effects.
- In June, 2013, Interferon-beta was injected into mice that had SCA7, a disease that targets infants
- The mice performed better than the control when put to physical tests proving interferon-beta slows down the effects of SCA7.

**References:**

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Thank You!