CANVAS (Cerebellar ataxia, neuropathy and vestibular areflexia syndrome)

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CANVAS is a type of late-onset cerebellar ataxia. CANVAS stands for Cerebellar Ataxia, Neuropathy and Vestibular Areflexia Syndrome. This means that it involves a combination of cerebellar (relating to the part of the brain that regulates movement), proprioceptive (relating to the position and movement of the body) and vestibular impairment (relating to the parts of the brain that control balance and eye movements).

A common genetic cause of CANVAS has recently been identified. The identification of this genetic mutation may mean that more people with late onset ataxia receive a genetic diagnosis for their condition [Cortese, A. et al. Biallelic expansion of an intronic repeat in RFC1 is a common cause of late-onset ataxia. Nature Genet. 51: 649-658, 2019].

What are the symptoms of CANVAS?
CANVAS is a late-onset progressive ataxia, which tends to progress slowly. It is commonly characterised by imbalance, sensory neuronopathy (damage to the sensory nerves), bilateral vestibulopathy (damage to the balance portions of both inner ears), and chronic cough.

What causes CANVAS?
CANVAS is a genetic condition, caused by a defect in the *RFC1* gene. This gene is more extended than normal in people with CANVAS. The *RFC1* gene codes for a protein which is responsible for DNA replication and repair. People may be diagnosed with CANVAS without the confirmation of a genetic test. For information on how to arrange a genetic test, see below.

How is CANVAS inherited?
CANVAS and late-onset ataxia usually occur sporadically (i.e. randomly), but sometimes occur in siblings, suggesting the possibility of recessive transmission (where two copies of a faulty gene must be present in order for the disorder to develop). In such cases parents are carriers but do not have the condition themselves. In a recent study, led by UCL Queen Square Institute of Neurology, genetic testing was undertaken in 29 individuals (23 affected by CANVAS and 6 unaffected) from 11 families. Most of the families consisted of affected siblings and in none was there evidence that the condition had been passed directly from parent to child. All affected individuals were found to have two copies of the *RFC1* gene containing the defect. Genetic CANVAS is therefore inherited in an autosomal recessive way. For more information on inheritance see Ataxia UK's *'Ataxia: what's that'?'* leaflet.

When do symptoms start?
The average age at onset is 50-60 years, but symptoms can appear as young as 30 years old [Szmulewicz, D. J. et al. Cerebellar ataxia, neuropathy, vestibular areflexia syndrome (CANVAS): a review of the clinical features and video-oculographic diagnosis. Ann. N.Y. Acad. Sci. 1233: 139-147, 2011] [Cortese, A. et al. Biallelic expansion of an intronic repeat in RFC1 is a common cause of late-onset ataxia. Nature Genet. 51: 649-658, 2019].

How is CANVAS diagnosed?
A genetic test for CANVAS is not yet widely available. We are hoping the test for the CANVAS gene will be available as a diagnostic test in the near future. In the meantime, if your neurologist contacts Dr Andrea Cortese or Prof Henry Houlden – two of the neurologists involved in the UCL Queen Square Institute of Neurology study – they can provide more information about genetic testing as part of their research project.

Contact details:
Dr Andrea Cortese or Professor Henry Houlden
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How common is CANVAS?
There is no data available for how many people have CANVAS.

The study by UCL Queen Square Institute of Neurology showed that 0.7%-6.8% of healthy controls (i.e. people who don't have CANVAS) are carriers of the *RFC1* genetic mutation. This is similar, if not higher, to the carrier frequency of the GAA expansion in the frataxin gene which causes the most common recessive ataxia, Friedreich's ataxia. By screening additional sporadic cases of late onset ataxia, the researchers confirmed the presence of the mutation in 22% of patients, and higher percentages if sensory neuronopathy and/or bilateral areflexia coexisted. This, researchers say, suggests that the mutation represents a frequent and under recognized cause of late-onset ataxia. This should have major implications for diagnosis and management of ataxia patients.

Management of CANVAS
As with other cerebellar ataxias, physiotherapy and speech therapy can be helpful. A visit by an occupational therapist will be useful in order to assess the need for items such as walking aids, or for adaptations to the home. It is important to see a neurologist, who will monitor the condition, on a regular basis.

This information leaflet was written by Ataxia UK in collaboration with Dr Andrea Cortese and Prof Henry Houlden, UCL Queen Square Institute of Neurology and The National Hospital for Neurology and Neurosurgery, London, UK.

November 2021

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