Scientists develop ataxia mouse model

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Scientists at the Ruhr-Universität Bochum established a mouse model for the human disease SCA6. SCA6 is characterised by movement deficits and caused by similar genetic alterations as Chorea Huntington. The mouse model will be used to investigate the disease mechanisms. Experiments suggest that an impairment of eye blink conditioning could be an early disease symptom. The team from the Department of Zoology and Neurobiology published their data in the *Journal of Neuroscience*; the work was highlighted by the editor's commentary.

Spinocerebellar ataxia 6: structural changes in a Calcium channel in cerebellar neurons

SCA6 or spinocerebellar ataxia type 6 is a movement disorder, which results in the loss of a special type of neuron in the cerebellum called Purkinje cells. These neurons process sensory information to coordinate movements. The disease has a late onset and develops in the second period of life. Patients are often wheelchair bound and no therapies are available. "To understand, how the disease originates and progresses and to develop new therapeutic strategies, it was important to establish a new mouse model," says Dr Melanie Mark, a neuroscientist from the Ruhr-Universität Bochum.

Modification of a single protein fragment causes disease symptoms

SCA6 belongs together with Chorea Huntington to the family of

polyglutamine diseases. They are characterised by repetitions of the amino acid glutamine in disease specific proteins. The team of Prof Dr Stefan Herlitze used a human Calcium channel fragment from a SCA6 patient containing stretches of glutamine and brought it in cerebellar Purkinje cells of mice. This protein fragment was sufficient to induce SCA6 like symptoms.

Impairment of eye blink conditioning

However, the animals developed other problems before movement deficits. The physiological properties of the Purkinje cells were altered and conditioning learning was impaired. The scientist presented a tone followed by an air puff onto the eye. Healthy animals learn to close their eyelid, when they hear a tone, before the air puff is applied. However animals with the mutated Calcium channel fragment could not learn this association. "The eye blink conditioning is a noninvasive method, which has the potential to be used to detect cerebellar mediated diseases during early stages before disease symptoms such as movement deficits become obvious," suggests Stefan Herlitze.

More information: "Spinocerebellar ataxia type 6 protein aggregates cause deficits in motor learning and cerebellar plasticity," *Journal of Neuroscience*, DOI: 10.1523/JNEUROSCI.0891-15.2015

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