

The effect of alcohol on gaze holding in healthy human subjects as a model of gaze-evoked nystagmus and rebound nystagmus induced by impairment of cerebellar function

Summary of the project

Cerebellar diseases usually cause ocular motor disorders like gaze-evoked nystagmus (GEN) and rebound nystagmus (RN). GEN is due to an abnormal centripetal eye drift occurring when the patient moves the eyes toward an eccentric position. It is supposed to be caused by a weakening of the neural integrator, which builds the position command for the eye muscle motoneurons. RN manifests when redirecting fixation to gaze straight ahead after sustained eccentric gaze and it is caused by a transient ocular drift in the direction of the preceding gaze eccentricity. This is probably related to a compensatory mechanism which becomes overactive as cerebellar control decreases in the disease. GEN and RN may lead to disturbing complaints in affected patients including blurred vision and an illusionary percept of motion of the scenery. Subsequently, balance and gait may be hampered, increasing the risk for falls and fall-related injuries. However, as the processes involved are not known, therapeutic options are still very limited for these disabling complaints.

The consumption of alcohol is known to temporarily affect cerebellar function, causing an increase of gaze-evoked centripetal eye drift in healthy subjects. Acute intoxication, by impairing cerebellar control, induces GEN, while chronic intoxication leads to a progressive cerebellar degeneration, with a clinical picture similar to other disorders causing cerebellar loss of function.

We hypothesize that a controlled amount of alcohol can provide a disease model of cerebellar GEN, which allows understanding the pathological mechanism involved and potentially revealing its relation with RN.

We propose to compare centripetal eye drift velocity recorded in a continuous range of gaze eccentricities in healthy subject before and after the intake of a defined amount of alcohol. This will provide us with a unique characterization of the relation between eye drift velocity and gaze eccentricity in normal and altered conditions. Similarly, measuring RN at multiple gaze eccentricities, we will also be able to test if temporary impairment of cerebellar function caused by alcohol induces RN and to investigate the mechanism responsible for it.

The proposed research project will also benefit from the findings of the project on GEN and RN in patients with sporadic cerebellar degeneration, supported by the SNF grant #32003B_130163 of Dr. Sarah Marti, which is currently carried out by the main applicant and will be concluded on April 30th 2014. By comparing the results of the proposed project with the findings in patients with cerebellar disorders we will be able to validate alcohol intake as a disease model of cerebellar GEN and RN, clarifying whether the RN found in patients with cerebellar disease is due to a pathologically overactive compensatory mechanism or a physiological one becoming manifest due to the failure of the gaze holding system causing GEN. On the other hand, investigating the differences between the gaze holding deficits induced by alcohol intake and those encountered in cerebellar disease, will help to clarify and quantify the temporary impairment of cerebellar function caused by alcohol.

Overall, by generating and testing a human model of GEN and RN, the proposed project will provide an opportunity to investigate the ocular motor disorders induced by impairment of cerebellar function, having therefore a double relevance. 1) It will elucidate how alcohol affects gaze holding, possibly suggesting a reliable assessment, and will provide insights into the effect of alcohol on the cerebellum. 2) It will improve our understanding of the functional implications of cerebellar degeneration and may provide the rationale for new therapeutic strategies.