Comprehensive characterization of alcohol-induced postural instability and walking ataxia in healthy participants: a new model to mimic sensory and cerebellar ataxia?

Summary of the project

Alcohol is a socially well-accepted drug being regularly consumed by people of different social classes and age levels. Psychomotor dysfunctions upon alcohol consummation are well known and are associated with enhanced risk for traffic accidents [1] or increased incidence of falls and related injuries [2, 3]. Imaging studies during controlled alcohol-intoxication revealed altered levels of brain glucose metabolism and cerebral blood flow that were most pronounced in cerebellar neural circuits and the occipital lobe [4, 5]. The cerebellum is a key neural structure for coordinated movements, as it receives afferent feedback from different sensory organs including visual, vestibular, and ascending proprioceptive inputs [6]. These sensory afferents are essential to interact with our surrounding and to react to fast changes in the environment (e.g. retaining dynamic stability after stumbling). Real-time sensory information is integrated and compared to feed-forward motor efferent copies originating from the cortico-ponto-cerebellar pathway. Based on sensory information and motor copies, the cerebellum generates well-coordinated motor outputs to the cortex and brainstem motor systems that initiate, modulate and control movement patterns. Not surprisingly, cerebellar hypofunction as observed in conditions of inherited cerebellar neurodegeneration, ischemic-derived cerebellar lesions or also alcohol administration lead to major motor pathologies of posture and gait [7-9]. One of the most characteristic signs of cerebellar impairment is walking ataxia, which describes a condition where locomotion is poorly coordinated, instable and variable [10]. Due to the similar phenotype of ataxic gait deviations in neurological patients and healthy people with alcohol-induced postural and walking deficits (e.g. variable foot placing and movement patterns, reduced intra-limb coordination, enhanced trunk sway and increased step width), gait ataxia is often referred as to "drunken gait" [11]. First studies investigating the acute, short-term effects of alcohol on human posture and locomotion appeared 3 decades ago [12, 13]. Several trials examined the effects of alcohol on postural stability in healthy subjects so far [14-17]. Whereas there is a consensus about the destabilizing effect of alcohol on static and dynamic posture, the exact pathomechanisms (e.g. malfunction of individual sensory inputs (such as vestibular or somatosensory input) vs. altered cerebellar weighting of sensory inputs vs. cerebellar paralysis leading to impaired cerebellar afferents to brainstem or thalamic neurons etc.) underlying postural imbalance are still debated. The effects of controlled, low-dose application of alcohol on walking function are less understood and reported heterogeneous findings on alcohol-induced gait deviations [9, 12, 18]. The inconsistent results might be explained by differential blood alcohol concentrations (BAC) or by non- controlled walking speeds with and without alcohol, leading to velocity-dependent alterations in walking patterns that are not specific to alcohol-related effects.

The aim of this project is to characterize the effects of controlled, low-dose administration of alcohol using cutting-edge technologies of movement analysis involving 3D kinematic gait analysis, electromyographic recordings, pressure plate data and computerized, dynamic posturography.

Comprehensive assessment of postural and locomotor dysfunctions upon controlled alcohol administration in healthy individuals will shed more light on the detailed effects of alcohol on sensory and motor modalities of the neural system.

We hypothesize that controlled, low-dose administration of alcohol in healthy individuals is able to mimic walking ataxia observed in neurological patients by reversibly disturbing sensory or cerebellar neural circuits. Ataxic postural and walking disorders are frequent in the clinical setting and clinical manifestation is often heterogeneous. Thus, a valid model of sensory or cerebellar ataxia based on healthy controls with low inter-subject variability is relevant and would facilitate the investigation of neural pathomechanisms underlying clinical ataxia. In addition, a well-validated model of ataxia might be used to screen for anti-ataxic treatments in the future.