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Blood Alcohol Concentration at 0.06% and 0.10% causes a complex multifaceted deterioration of body movement control

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Running title: Alcohol intoxication, postural control and adaptation.

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Abstract

Alcohol-related falls are recognized as a major contributor to the occurrence of traumatic brain injury. The control of upright standing balance is complex and comprises contributions from several partly independent mechanisms like appropriate information from multiple sensory systems and correct feedback and feedforward movement control. Analysis of multi-segmented body movement offers a rarely used option for detecting the fine motor problems associated with alcohol intoxication.

The study aims were: 1) to investigate whether alcohol intoxication at 0.06% and 0.10% blood alcohol concentration (BAC) affected linear body movement under unperturbed and perturbed standing; and 2) to investigate whether alcohol affected the ability for sensorimotor adaptation.

Body movements were recorded in 25 participants (13 women and 12 men, mean age 25.1 years) at five locations (ankle, knee, hip, shoulder and head) during quiet standing and during balance perturbations from pseudorandom pulses of calf muscle vibration over 200s with eyes closed or open. Tests were performed at 0.00%, 0.06% and 0.10% BAC.

The study revealed several significant findings: 1). An alcohol dose-specific effect; 2). A direction-specific stability decrease from alcohol intoxication; 3). A movement pattern change related to the level of alcohol intoxication during unperturbed standing and perturbed standing; 4). A sensorimotor adaptation deterioration with increased alcohol intoxication; and 5). That vision provided a weaker contribution to postural control during alcohol intoxication.

Hence, alcohol intoxication at 0.06% and 0.10% BAC causes a complex multifaceted deterioration of human postural control.

Key Words: Postural control; Balance; Alcohol; Adaptation; Vision

Introduction

Consumption of large amounts of alcohol results in alcohol intoxication and signs such as slurred speech, reduced inhibition, decreased coordination and impaired balance. Alcohol-related falls are recognized as a major contributor to hospitalization, particularly for limb breakages or traumatic brain injury (Talving et al., 2010) and the severity of these injuries correlates directly with Blood Alcohol Concentration (BAC) (Johnston and McGovern, 2004).

The simple act of standing is a common and essential motor behavior. The neural systems that regulate postural control integrate a large array of sensory inputs from visual, vestibular, and somatosensory receptors (proprioception and mechanoreceptors) and coordinate multiple motor outputs to muscles throughout the body (Lockhart and Ting, 2007). However, alcohol intoxication may disrupt the neural control of standing at several points. The presence of ethyl alcohol in the central nervous system (CNS) can interfere with the transmission of nerve impulses at the synapse (Mullikin-Kilpatrick and Treistman, 1994; Treistman et al., 1991). Alcohol intoxication impairs vestibular senses (Kubo et al., 1990; Tianwu et al., 1995), reduces the amplitude of mono- and poly- synaptic reflexes (Ashby et al., 1977), and prolongs the latency and reduces the amplitude of long latency muscle responses (Woollacott, 1983). Therefore, alcohol intoxication leads to deleterious effects on both the sensory and motor systems (Fuster et al., 1985) and is likely to have profound effects on body movement control while standing.

Humans have a complex biomechanical body design, with multiple degrees of freedom allowing for various movements (Todorov and Jordan, 2002). In the upright standing position, the least straining and most common movement pattern to maintain postural stability in unperturbed and perturbed standing is the often called single–link pattern or ankle strategy (Fransson et al., 2007b). This movement pattern is identified by similar movements of all body segments with the ankle acting as the only movement joint around which corrective movements are introduced. However, during more challenging situations, this simplified movement strategy may become insufficient and is subsequently replaced by strategies where corrective movements are introduced about other joints such as at the knees or hip. Such movement patterns are indications of a multi-segmented movement pattern (Horak and Nashner, 1986). Body movement can be captured through kinematic analysis, which is sometimes employed to evaluate the severity or rehabilitation status of a disorder (Blackburn et al., 2003). Body movement analysis has proven more sensitive in detecting motor control changes than traditional force platform recordings (Fransson et al., 2007b; Gomez et al., 2008; Gomez et al., 2009). However, this method has not yet been used to study the effects of alcohol intoxication on human postural control.

One way to monitor the prospective risk of falling when intoxicated is to measure an individual's ability to maintain an upright standing particularly when the task is challenged (Granata and Lockhart, 2008). When balance is threatened by a large sensory perturbation, the differences in postural control between healthy and patient groups are more easily recognized. One method commonly employed to find balance deficits in patients is proprioceptive vibration of skeletal muscles or tendons specifically involved in the regulation of balance, such as the calf muscles (Patel et al., 2009). Moreover, when repeated, balance perturbations of healthy sober subjects are usually accompanied over time by sensorimotor adaptation (motor learning), which may cause sensory re-weighting and altered feedback and feedforward motor control responses (Bastian, 2008), resulting in decreased fall risk (Pai and Iqbal, 1999; Pavol and Pai, 2002). Sensory re-weighting when determining the body's spatial orientation and movements is defined as a process where less reliable sensory information gradually diminishes in influence relative to other sources of sensory information found more reliable (Oie et al., 2002). Human postural control adaptation also involves recalibration of motor programs, sensorimotor pathways and strategies, such as changes of the body movement pattern (Fransson et al., 2007b; Pavol and Pai, 2002). In this study, both the initial effects of alcohol intoxication and its effects on the ability for adaptation and maintaining accurate body movement control during sustained sensorimotor challenges will be investigated. Noteworthy, Connor (Connor et al., 2004) showed an increased number of traffic accidents at levels below 0.05% BAC, which suggests that alcohol intoxication may affect performance even at low levels of intoxication in conditions where sustained attention or performing challenging sensorimotor tasks are necessary.

To date, only Woollacott has studied the effects of alcohol intoxication on adaptation, although in that study electromyographic muscle activity was considered and subjects were submitted to only 5 repeated balance perturbations (Woollacott, 1983). Woollacott found that alcohol intoxication at about 0.10% BAC caused significantly delayed compensatory muscle responses. However, in that study, subjects were able to adapt normally (Woollacott, 1983). This finding is not consistent with others reports showing that acute alcohol intoxication appears to affect the cerebellum (Belmeguenai et al., 2008; Diener et al., 1983; Servais et al., 2005), a CNS structure known to be extensively involved in adaptive motor control.

Alcohol-related effects on postural control have been the topic of previous studies based on force platform recordings. These have revealed that BAC above 0.07% - 0.08% impairs postural control in unperturbed standing (Dick et al., 1989; Nieschalk et al., 1999; Thyssen et al., 1981), whereas perturbed standing can be affected from about 0.06% BAC (Woollacott, 1983). However, most studies performed on human postural control and alcohol intoxication were done over 20 years ago. Since then, a new generation of alcohol analysis devices has been introduced, providing the necessary means to introduce more accurate measurements. Moreover, new techniques have also been developed to assess and quantify disorders in human postural control.

One of the limitations in many previous studies of human postural control and alcohol intoxication is that subjects were assessed a fixed time after alcohol consumption. One problem with this approach is illustrated in the study by Nieschalk and colleagues (Nieschalk et al., 1999) showing that the BAC in the 30 subjects assessed ranged from 0.022% to 1.59%, 30 minutes after consumption. This finding highlights the importance in the study design to consider the large individual difference in absorption of alcohol, anthropometrical influences and the risk of assessing the alcohol intoxication effects in different Mellanby states. The Mellanby effect notes the observation that the impairments caused by alcohol intoxication in performance are often greater when BAC is ascending than descending (Wang et al., 1992; Vogel-Sprott, 1979).

Hence, a major improvement introduced in the present study is the use of the new generation of very accurate breath analysers. This allows all subjects to be investigated at exactly the same BAC level and in the same alcohol absorption phase, meaning that systematic biases from the Mellanby effect can now be controlled. Furthermore, the same subjects can be assessed as sober and at different exact BAC levels so that effects observed can be explicitly determined to be caused by BAC. Moreover, systematic findings made in a large group of subjects assessed at the same BAC means that the statistical evaluation becomes more accurate, and specifically, it ensures that responses recorded at the investigated BAC level are more likely to be representative of a larger population. Finally, in this study a Latin square test order will be used to avoid systematic biasing order effects from psychological expectation as well as from being more familiar with the test conditions.

The aim of the present study was to evaluate the effects of alcohol intoxication on human postural control using the new generation of alcohol analysis. Postural control will be assessed by recording body movement and analyzing the multi-segmented movement pattern. The effect of alcohol intoxication will be assessed in unperturbed and perturbed standing at exact, pre-specified, alcohol levels just below (0.06% BAC) and above (0.10% BAC) the legal blood alcohol level for driving in the United Kingdom and United States (0.08% BAC). Another aim was to evaluate the effects of alcohol on sensorimotor adaptive capabilities. This report is part of a larger project investigating the effects of alcohol intoxication on the visual (Hafstrom et al., 2007), oculo-motor (Fransson et al., 2010) and postural control systems (Patel et al., 2010).

Methods and Materials

Participants

Twenty-seven consenting healthy adults initially volunteered to participate in the study. Two participants from this group were excluded: one for not reaching intended BAC and one due to failing an otolith test (Hafstrom et al., 2007). The final study group consisted of 25 participants, 13 women and 12 men of mean age 25.1 years (range 19-41), mean height 1.75 meters (range 1.60-1.92), mean weight 68.8 kilograms (range 50.05-106.3) and mean BMI 22.2 (range 17.9-30.7). The study was approved by the local ethics committee at Lund University, Lund, Sweden, and performed in accordance with latest version of the Declaration of Helsinki.

The participants were screened for any medical reasons that might exclude them from participating in the study such as a history of vertigo, balance problems, inner ear disease, acute bacterial meningitis, major CNS-trauma, cardiovascular disease or serious injuries involving their lower extremities or known eye movement disorders. The medical examination was performed by an Otorhinolaryngology physician and included hearing, visual and vestibular tests; the Weber test, otolith rod and frame test, eye movement saccade and pursuit tests, head impulse test and a headshake test using magnifying video glasses. The subjects were also interviewed about drinking habits. None of the participants were regular smokers.

Participants were instructed not to consume any alcohol, sleep-inducing or revitalizing products, such as caffeine, 48 hours before and during testing other than the alcohol provided to the participants. At the time of the study, no participant was on any form of medication and smoking was not allowed.

Equipment

The balance perturbations during posturography were produced by applying vibrations to the calf muscles. The vibrations was produced by a revolving DC-motor (Escap, Geneva, Switzerland) equipped with a 3.5g weight attachment contained within a cylindrical plastic coating (6cm x 1cm). The vibrators had vibration amplitude of 1.0 mm and a vibration frequency of 85 Hz. Prior to testing, the vibrators were placed vertically over the belly of the gastrocnemius muscles of both legs and secured by elastic straps. A customized computer program controlled the vibratory stimulation and sampled the body movement data at 50 Hz.

An ultrasound 3D-Motion Analysis system (Zebris™) measured the linear movements of five markers positioned at anatomical landmarks. The first marker (‘Head’) was attached to the participant's cheekbone (os zygomaticum), the second (‘Shoulder’) to tuberculum majus, the third (‘Hip’) to the crista iliaca, the fourth (‘Knee’) to the lateral epicondyle of femur, and the fifth (‘Ankle’) to the lateral distal fibula head. Each marker was tracked in three directions, i.e., anteroposterior, lateral and vertical. The measurement resolution in all dimensions was 0.4mm.

Procedure

Each participant performed the tests at three different blood alcohol concentrations (BAC): 0.00%, 0.06% and 0.10%, in a randomized order. The tests were conducted once a week for three consecutive weeks and participants were blinded to the amount of alcohol they consumed. They were allowed 30 minutes in a quiet environment to drink 750ml of either a mixture of 70% ethanol diluted in elderflower juice or only elderflower juice (0.00% BAC).

The amount of alcohol given to each participant depended on their gender and weight and was calculated to achieve the intended BAC of 0.00%, 0.06% and 0.10% BAC. Women were given 1.0g alcohol/kg body weight and men 1.1g alcohol/kg body weight to reach 0.10% BAC, and women were given 0.6g alcohol/kg body weight and men 0.7g alcohol/kg to reach 0.06% BAC. After consuming the drink, alcohol concentration was measured every 15 minutes by an Evidenzer breath analyzer (Nanopuls AB, Uppsala, Sweden). The breath analyzer measured in real-time BAC with a precision of 0.001% (Fransson et al., 2005). The Evidenzer™ system fulfills the requirements found in OIML R126E (1998) and has been approved by U.S. department of transport. The subjects provided also every 15 minutes a subjective score of drunkenness using a Visuo-Analogue Scale (VAS). The VAS scores assigned ranged from 1 to 10, where 1 = "sober" and 10 = "extremely drunk". The following criteria ensured that all participants were assessed during similar alcohol intoxication conditions:

- A plateau phase was identified in the BAC recordings with no further tendency of increasing BAC values.
- At least one BAC value was recorded with decreasing BAC level compared with peak BAC.
- The measurements were performed as closely as possible to planned BAC (0.06% BAC or 0.10% BAC) in the descending BAC phase. The 0.00% BAC assessments were performed after about the same time as it took for the subjects to reach planned BAC in the alcohol intoxication tests. This procure was used to avoid participants predicting their alcohol dose from when the assessments were performed after drinking the liquid.

Posturography assessment

The five Zebris markers were attached on the right side of the participant facing the Zebris transmitter. With the vibrators attached, each participant was instructed to stand barefoot in an erect and relaxed posture with arms folded across the chest. This posture was chosen to maintain consistency between subjects and to avoid inappropriate arm and head movements. The participant's heels were 3cm apart and the feet were placed at an angle of approximately 30º open to the front using guidelines. The participants stood 1.5m in front of a wall and were instructed to focus on an image (6cm x 4cm large) directly ahead of them at eye level or stand with their eyes closed depending on the test condition. All participants were naive to the stimulus and were not informed about the effect calf vibration would have on their balance. The participants listened to calm classical music through headphones during the balance tests to avoid extraneous sound distractions.

The following 2 tests were performed in a randomized order, using a Latin Square design, by all participants during three different test conditions: I) 0.00% BAC, II) 0.06% BAC and III) 0.10% BAC.

- Vibration of the calf muscles with eyes closed (EC).
- Vibration of the calf muscles with eyes open (EO).

Before the vibratory stimulation commenced, a 30 second control period of quiet standing was recorded for separate analysis. The vibratory stimulations were applied according to a pseudorandom binary sequence (PRBS) schedule (Johansson, 1993) during a period of 200 seconds making each trial 230 seconds long. The PRBS schedule defined the periodicity of stimulation pulses, where each pulse had random time duration and interval from 0.8 seconds up to 6.4 seconds, which yielded an FFT- validated effective bandwidth of the test stimulus in the region of 0.1-2.5 Hz. The PRBS sequence was selected because this randomized stimulation sequence is difficult to predict and therefore lessens the likelihood of pre-emptive responses (Fransson et al., 2007b). A five minute rest period was given between EO and EC tests.

Analysis

The body movements were quantified by calculating the variance of the linear head, shoulders, hip and knee movements in the anteroposterior and lateral directions. A movement variance value shows how much the body position marker has moved without being affected by average body leaning (Fransson et al., 2007a; Fransson et al., 2007b; Gomez et al., 2009; Patel et al., 2009).

Mean values for all parameters were obtained for five periods for each trial condition: the quiet standing period (0–30s), and from four 50-second periods (period 1: 30–80s; period 2: 80–130s; period 3: 130–180s; period 4: 180–230s) during the vibration. The separation of the 200s stimulation period into four sequential 50s periods was done to allow the study of changing effects of the balance perturbations over time. The selection of studying the recorded data in 50s time intervals was based on prior studies on how postural control is gradually affected by prolonged randomized vibratory proprioceptive stimulation (Tjernstrom et al., 2002). The vibration sequence was randomized, but each 50s period contained a similar amount of long and short vibration pulses, validated by Fast Fourier Transform analysis of the spectral contents. Hence, the selected periods and perturbation sequence allowed analysis of adaptive changes over time to unpredictable balance perturbations.

The linear movement variance values were normalized using the participant's squared height before the statistical analysis thus providing inter-individual compensation for individual variation in height (Fransson et al., 2007a).

Statistical analysis

The data was analyzed with a multifactorial statistical method, which consists of 2 statistical evaluation levels of the data, the main level of a multifactorial univariate GLM ANOVA (General Linear Model univariate Analysis of Variance) analysis followed by a second step of post hoc pair-wise analysis of the significances found in the main ANOVA analysis. The multifactorial analysis was performed both on the data from the quite stance recordings and on the data from the four 50s periods of vibratory proprioceptive balance perturbations. The effects of the main factors alcohol intoxication ('Alcohol': 0.0%, 0.06% or 0.10% BAC; (degrees of freedom (d.f.) 2), availability of visual information ('Vision': eyes closed or eyes open; d.f. 1), direction of recorded movement ('Direction': anteroposterior or lateral; d.f. 1), and when applicable the period of vibration ('Period': periods 1-4; d.f. 3) and their interactions were analyzed with an univariate GLM ANOVA with log-transformed linear movement variance values as outcome parameter (Altman, 1991). The interaction evaluation in the GLM ANOVA analysis reveals whether the outcome might be influenced by certain combinations of factors. The GLM model accuracy was evaluated by testing the model residual for normal distribution and the model accuracy was in all evaluations approved when the analysis was performed on log-transformed movement variance values. In the GLM analysis, p-values < 0.05 were considered statistically significant.

Wilcoxon matched-pairs signed-rank test (Exact sig. 2-tailed) (Altman, 1991) was used for the post hoc pair-wise analysis of the significances found in the main ANOVA analysis. Moreover, quotients were calculated between the movement variance values at 0.06% BAC divided by the values at 0.00% BAC respectively between the values at 0.10% BAC divided by 0.06% BAC to describe the destabilization rates between these different BAC levels. Wilcoxon pair-wise tests were then used to determine whether the destabilization rates were significantly different between 0.00% BAC and 0.06% BAC compared with between 0.06% BAC and 0.10% BAC. Non-parametric statistical tests were used in the post hoc evaluation since the Shapiro-Wilk test revealed that the data sets analyzed with pair-wise statistics were not normally distributed and normal distribution could not be obtained by log-transformation. The pair-wise statistical analysis was carried out with Bonferroni correction for multiple comparisons when appropriate.

Results

The posturography tests were performed in the decreasing phase of alcohol intoxication on average 83 minutes (0.06% BAC, SEM 5 min) and 84 minutes (0.10% BAC, SEM 4 min) after the participants had finished drinking. The 0.00% BAC tests were performed after about the same time as the alcohol intoxication tests (76 minutes, SEM 4 min). The measured BAC levels when the posturography tests were performed were on average 0.057% (SEM 0.001%) for the 0.06% BAC aimed test and 0.101% (SEM 0.002%) for the 0.10% BAC aimed test.

The participant's subjective feeling of drunkenness, quantified by VAS scores, were on average 1.0 (SEM 0.0) for the 0.00% BAC test, 2.6 (SEM 0.3) for 0.06% BAC test and 4.9 (SEM 0.4) for 0.10% BAC test, where 1 = "sober" and 10 = "extremely drunk". The statistical differences between 0.00% BAC vs. 0.06% BAC; 0.00% vs. 0.10% BAC and 0.06% BAC vs. 0.10% BAC VAS scores were all significant at $p<0.001$.

Multifactorial univariate GLM ANOVA analysis of linear body movement variance during quiet standing and perturbed standing

Multifactorial univariate GLM ANOVA analysis of linear body movement variance during quiet standing

	p-value						
	Alcohol	Vision	Direction	Alcohol x Vision	Alcohol x Direction	Vision x Direction	Alcohol x Direction x Period
Head	<0.001 [8.3]	NS [2.7]	<0.001 [150.2]	NS [0.2]	NS [0.4]	NS [1.4]	NS [0.5]
Shoulder	<0.001 [10.7]	NS [2.7]	<0.001 [141.4]	NS [0.3]	NS [0.7]	NS [1.7]	NS [0.3]
Hip	<0.001 [9.5]	NS [1.5]	<0.001 [104.1]	NS [0.3]	NS [2.0]	NS [0.3]	NS [0.8]
Knee	<0.001 [9.1]	NS [1.0]	<0.001 [42.4]	NS [0.2]	NS [1.9]	NS [0.9]	NS [0.6]

Table 1, Statistical evaluation of the linear movement variance values during quiet standing using a multifactorial univariate GLM ANOVA analysis. "NS" signifies no significant difference. The notation "<0.001" means that the p-value is smaller than 0.001. F-values are presented in the squared parenthesis.

Alcohol intoxication significantly increased the amplitude of the body movements in quiet standing as expressed by increased linear movement variances at all recorded positions and by the significant Alcohol factor in the GLM ANOVA analysis (table 1, figures 1 and 2). Vision did not significantly affect linear movement variance at any position. Linear movement variances were larger at all positions in the anteroposterior direction compared with the lateral direction as illustrated by the significant Direction factor.

Multifactorial univariate GLM ANOVA analysis of linear body movement variance during perturbed standing

	p-value						
	Alcohol	Vision	Direction	Period	Alcohol x Period	Vision x Direction	Direction x Period
Head	<0.001 [113.5]	<0.001 [96.4]	<0.001 [2211.0]	<0.001 [7.7]	0.006 [3.1]	<0.001 [25.2]	0.004 [4.5]
Shoulder	<0.001 [97.3]	<0.001 [82.2]	<0.001 [2202.4]	<0.001 [9.8]	0.003 [3.3]	<0.001 [20.4]	0.002 [5.1]
Hip	<0.001 [90.9]	<0.001 [54.7]	<0.001 [1696.9]	<0.001 [10.0]	0.019 [2.5]	<0.001 [10.2]	0.001 [5.5]
Knee	<0.001 [75.5]	<0.001 [41.3]	<0.001 [1076.5]	<0.001 [13.4]	0.014 [2.7]	NS [1.5]	0.001 [5.5]

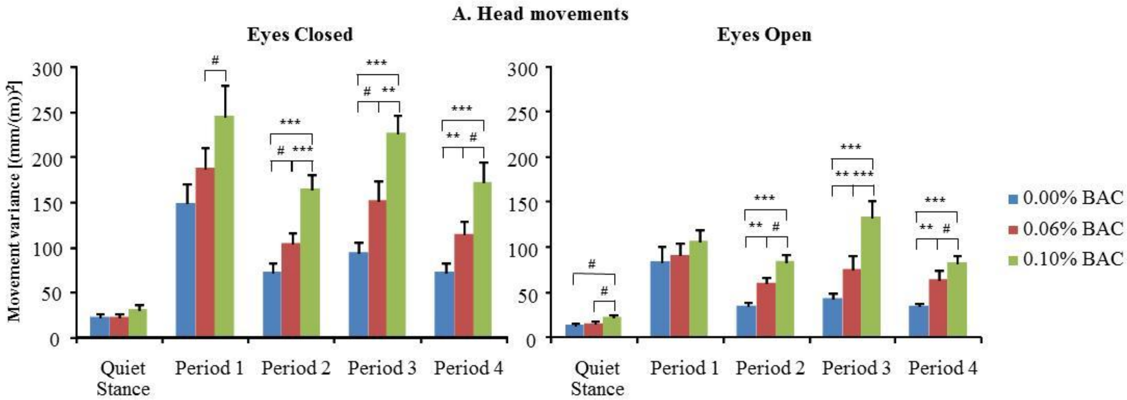
Table 2. Statistical evaluation of the linear movement variance values during balance perturbations using a multifactorial univariate GLM ANOVA analysis. The interaction combinations not presented in the table were not significant.

During balance perturbations, Alcohol intoxication significantly increased linear movement variance at all positions (table 2, figures 1 and 2) and Vision significantly decreased linear movement variance at all positions. As expected, the linear movement variance was affected more in anteroposterior direction than lateral direction at all positions as illustrated by the significant Direction factor. The significant Period factor shows that the balance perturbations caused a different stability challenge over time when repeatedly submitted to balance perturbations.

Three main factor interactions were found significant. The significant Alcohol x Period interaction shows that the effects of alcohol intoxication on linear body movement was influenced by under how many time periods the subject had been exposed to balance perturbations. The Vision x Direction interaction at the head, shoulder and hip shows that vision increased the stability at these positions significantly less in lateral direction than in anteroposterior direction. The Direction x Period interaction shows that the stability changes over time to sustained balance challenges were different in anteroposterior direction compared with lateral direction.

Post Hoc analysis of the multifactorial univariate GLM ANOVA findings

Effects of alcohol intoxication on linear body movement variance



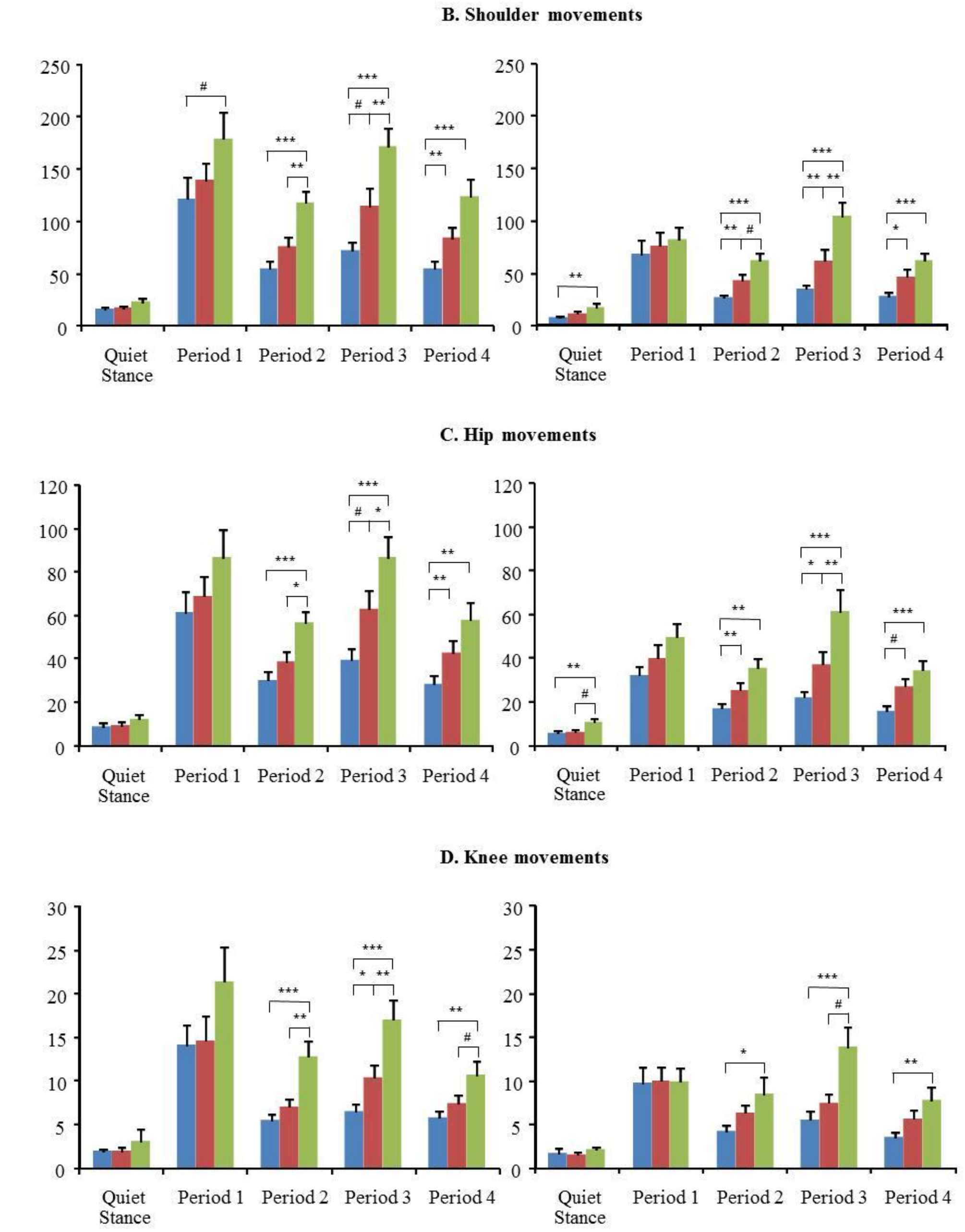
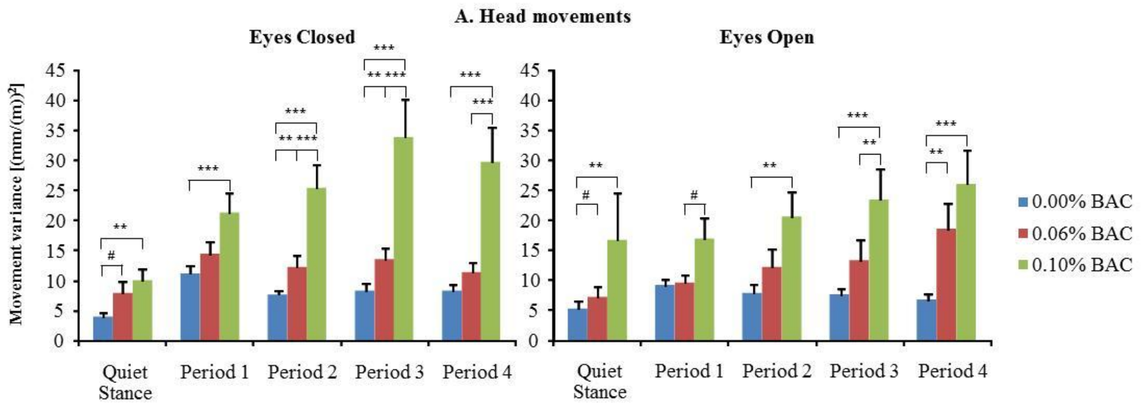


Figure 1. Normalized anteroposterior linear movement variance values (mean and SEM) during tests with A: Head movements; B: Shoulder movements; C: Hip movements and D: Knee movements. Note the difference in scales. The figures present the statistical findings made in the post hoc evaluation of the main factor Alcohol, the interaction between Alcohol x Period and the interaction between Direction x Period. # denotes p<0.05, * denotes p<0.0167, ** denotes p<0.01 and *** denotes p<0.001.



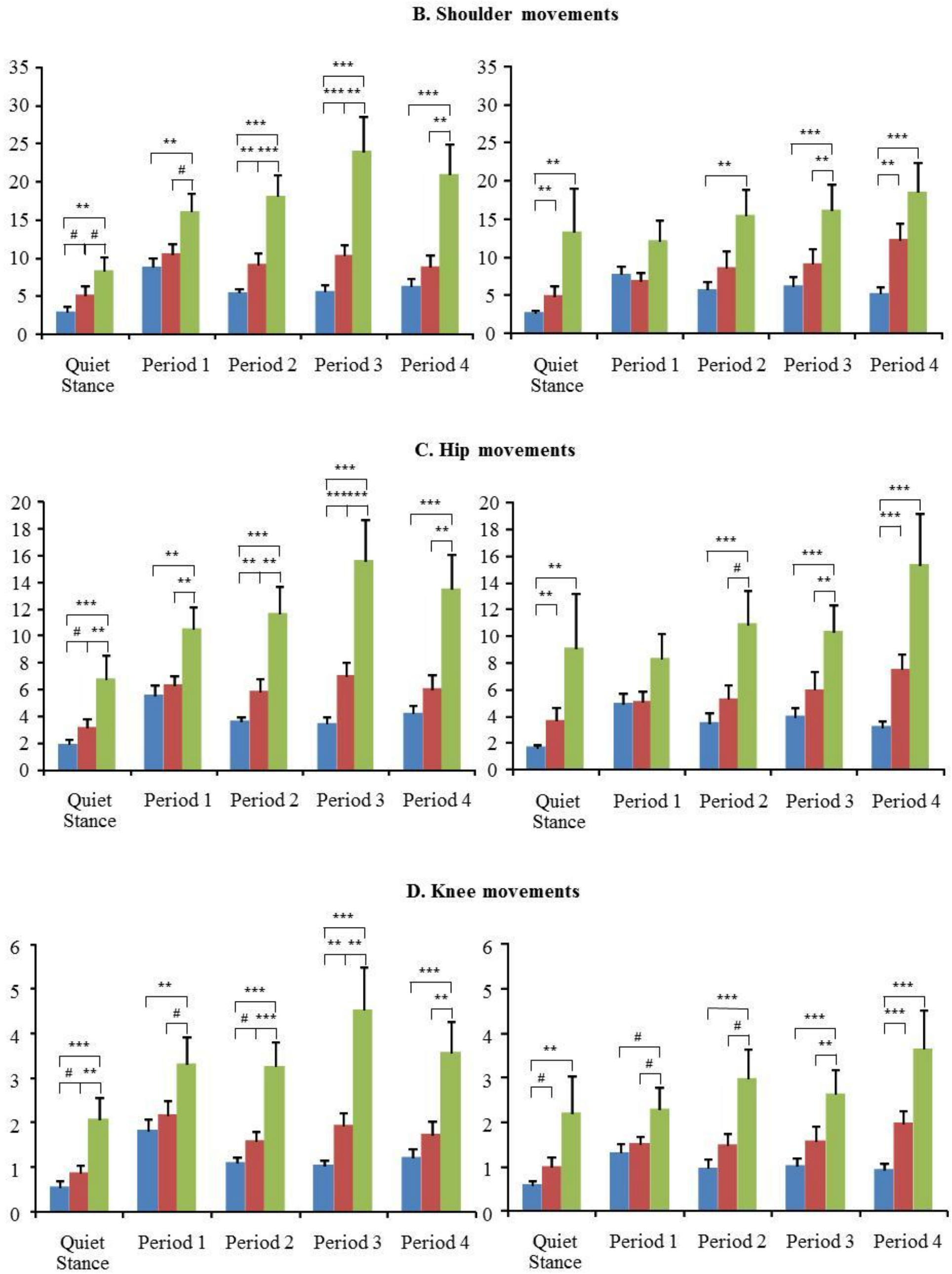


Figure 2. Normalized lateral linear movement variance values (mean and SEM) during tests with A: Head movements; B: Shoulder movements; C: Hip movements and D: Knee movements.

Figures 1 and 2 present the statistical findings made in the post hoc evaluation of the main factor Alcohol, the interaction between Alcohol x Period and interaction between Direction x Period. The post hoc findings illustrate that the effects of alcohol intoxication became larger with increasing BAC and larger in periods 2, 3 and 4, when submitted for a longer duration to sustained balance perturbations. There was a clear progressive decline in stability from period to period in lateral direction (figure 2), whereas the stability was maintained over time much better in anteroposterior direction (figure 1).

Dose-dependent alcohol intoxication effects on linear body movement variance

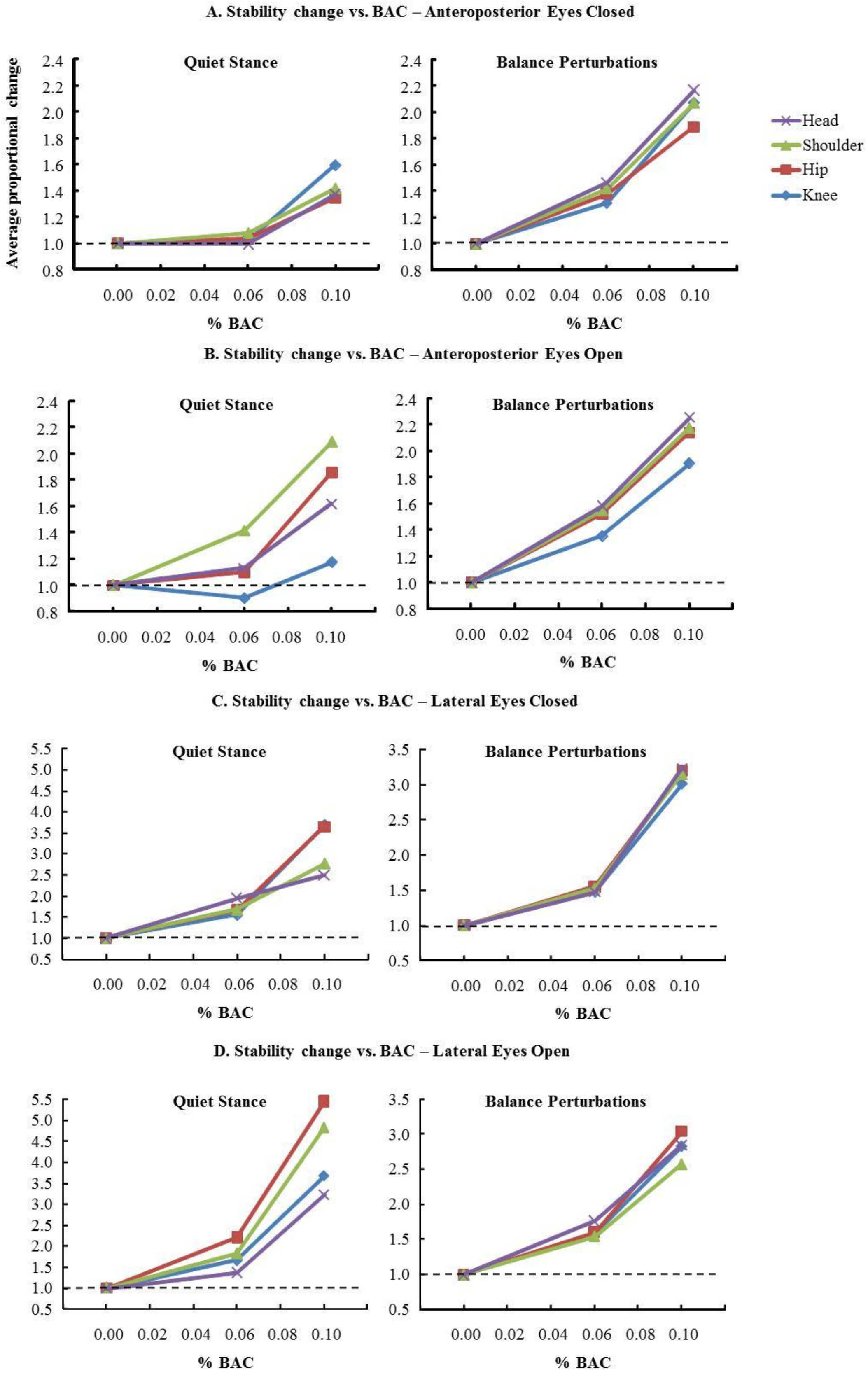


Figure 3. Average proportional change of linear knee, hip, shoulder and head movement variances during quiet standing and balance perturbations with A: Anteroposterior - eyes closed, B: Anteroposterior - eyes open, with C: Lateral - eyes closed, D: Lateral - eyes open. A value of 1 on the y-axis represent the baseline value while sober (0.0% BAC) and a value of 2 on the y-axis represent that the recorded movement variance has doubled compared with the base-line value. Notice the anteroposterior and lateral scale differences. The figures illustrates the significant main effect of Alcohol in the multifactorial univariate GLM ANOVA analyses.

Figure 3 illustrates the significant main effect of Alcohol in the multifactorial univariate GLM ANOVA analyses. The proportional changes found confirm that alcohol intoxication increased linear body movement in quiet standing in both the anteroposterior and lateral directions. During balance perturbations, the detrimental effects of alcohol intoxication were more prominent at 0.10% BAC than at 0.06% BAC, both in anteroposterior and lateral directions. In most statistical evaluations the difference between sober vs. 0.10% BAC reached $p<0.001$ in the post hoc pair-wise comparisons whereas the sober vs. 0.06% BAC comparisons ranged from non-significant to $p<0.01$, see figure 1 and 2.

In quiet standing, the destabilization rate of anteroposterior linear body movement variance was different with eyes closed and eyes open. With eyes closed, the destabilization rates of linear movement variance at all positions were increased similarly between 0.00% BAC and 0.06% and between 0.06% BAC and 0.10% BAC. The presented values are consistent with a single-link movement pattern between the feet and head, i.e., the movement amplitudes increased by alcohol intoxication but without causing an alteration of the general movement pattern. With eyes open, linear movement variance was affected somewhat different at each position by increasing alcohol intoxication. The destabilization rates between 0.06% BAC and 0.10% BAC were significantly higher compared with rates between 0.00% BAC and 0.06% for the upper body movements (head, $p<0.01$; shoulder, hip, $p<0.05$). For the lower body movements the destabilization rates were more similar (knee, p=ns) between 0.0% BAC and 0.06% compared with between 0.06% BAC and 0.10% BAC.

The destabilization rates of lateral linear body movement variance during quiet stance was also different with eyes closed and eyes open, though in another way as was found in anteroposterior direction. With eyes closed, the destabilization rate differences between 0.06% BAC and 0.10% BAC compared with between 0.00% BAC and 0.06% were less pronounced for upper body movements (head, p=ns, shoulder, $p<0.05$), whereas the destabilization rates were markedly higher for the lower body movements (hip, $p<0.01$; knee, $p<0.05$) between 0.06% BAC and 0.10% BAC compared with the destabilization rates found between 0.0% BAC and 0.06%. These findings are consistent with a multi-segmented response to increased alcohol intoxication. With eyes open, the destabilization rates of linear movement variance at all positions were increased similarly between 0.0% BAC and 0.06% and between 0.06% BAC and 0.10% BAC consistent with a single-link movement pattern response.

During balance perturbations, the destabilization rates between 0.06% BAC and 0.10% BAC were higher than the destabilization rates between 0.0% BAC and 0.06% BAC in both anteroposterior and lateral directions. The destabilization rates were significantly different ($p<0.05$) for all positions and tests apart from the anteroposterior knee movements with eyes open ($p=0.076$), see figure 3.

Linear body movement variance changes over time during alcohol intoxication

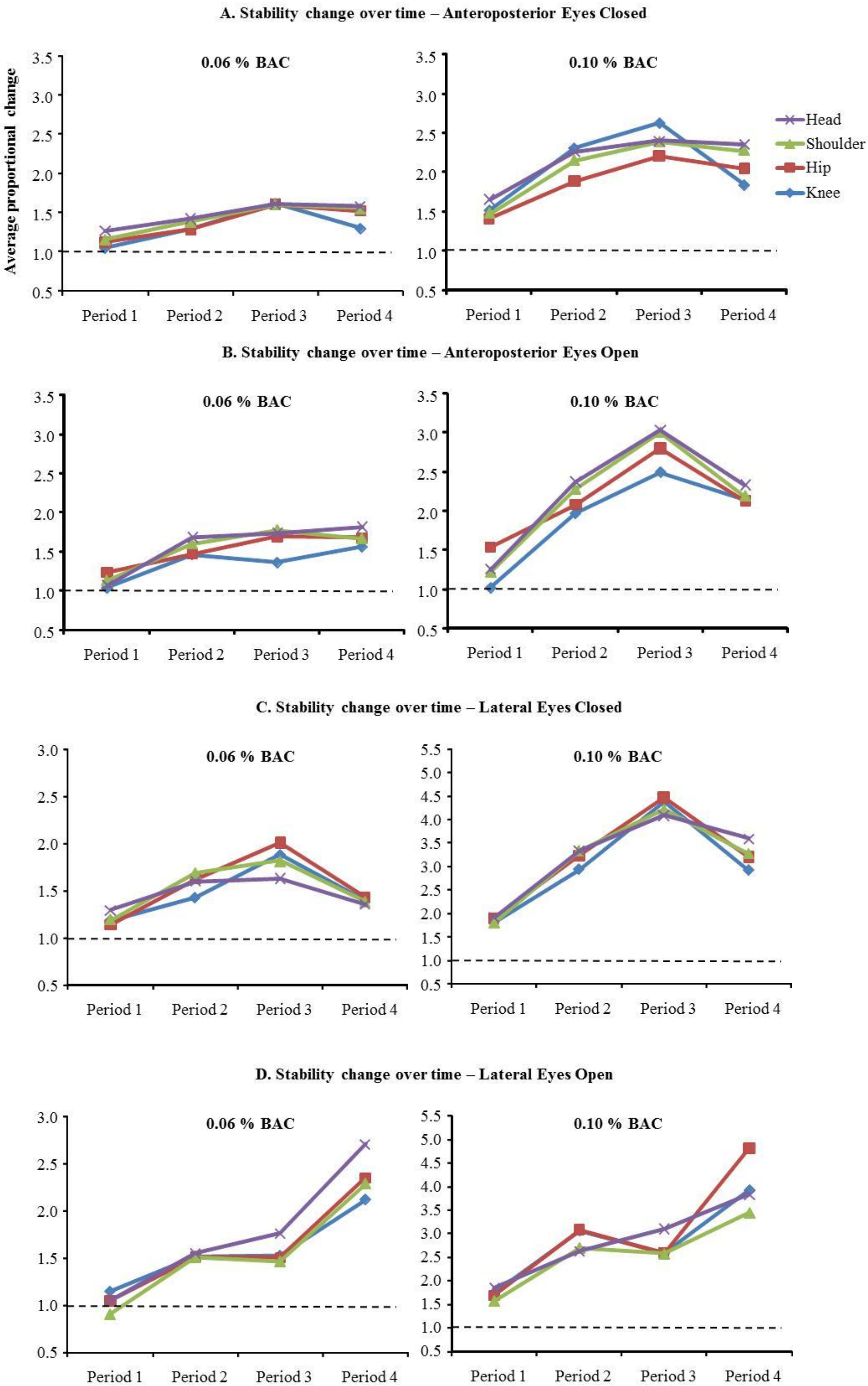


Figure 4. Average proportional change of linear knee, hip, shoulder and head movement variances during quiet standing and each of the 4 stimulation periods of balance perturbations at different BACs with A: Anteroposterior - eyes closed, B: Anteroposterior - eyes open, with C: Lateral - eyes closed, D: Lateral - eyes open. A value of 1 on the y-axis represent the baseline value while sober (0.0% BAC) and a value of 2 on the y-axis represent that the recorded movement variance has doubled compared with the base-line value. The figures illustrates the significant interaction effects of Alcohol x Period and Direction x Period in the multifactorial univariate GLM ANOVA analyses.

Figure 4 illustrates the significant interaction effect of Alcohol x Period and Direction x Period in the multifactorial univariate GLM ANOVA analyses. During balance perturbations, the alcohol intoxication had a non-linearly growing destabilizing effect over time on the recorded body movements (figure 4). In period 1, the body movements were up to +74% larger than normal levels (lateral direction 0.10% BAC, EC). However, the stability continued to decline at all recorded positions compared with normal levels during the following 3 periods reaching up to 381% larger values than normal (period 4, lateral direction, 0.10% BAC, EO). The non-linear increase of the alcohol intoxication effects over time on postural control were markedly larger at 0.10% BAC compared with 0.06 % BAC and distinct both in anteroposterior and lateral directions. However, the stability decrease over time was significantly larger in lateral direction compared with anteroposterior direction.

The statistical values presented in figure 1 and 2 and the amplitude of proportional changes presented in figure 4 illustrate that the movements at all recorded body positions were similar increased over time by the alcohol intoxication. However, the knee movements amplitude decreased markedly ($p<0.05$) with eyes closed between periods 3 and 4 in anteroposterior direction at 0.10% BAC whereas the other recorded body movements remained the same. This finding is consistent with that the knee movements had a changed roll in period 4 and that a more complex multi-segmented movement pattern was used to address the alcohol intoxication effects.

Analysis of alcohol intoxication on adaptation

Anteroposterior P1/P4		*p*-value		
		0% BAC	0.06% BAC	0.10% BAC
Head	EC	<0.001 [>51%]	<0.001 [>39%]	***0.019 [>30%]***
	EO	<0.001 [>58%]	NS [>30%]	NS [>23%]
Shoulder	EC	<0.001 [>55%]	<0.001 [>46%]	***0.022 [>34%]***
	EO	<0.001 [>60%]	NS [>43%]	NS [>25%]
Hip	EC	<0.001 [>51%]	<0.001 [>44%]	***0.019 [>35%]***
	EO	<0.001 [>47%]	NS [>37%]	***0.042 [>28%]***
Knee	EC	<0.002 [>61%]	<0.001 [>52%]	0.001 [>40%]
	EO	<0.001 [>55%]	0.008 [>37%]	***0.039 [>14%]***

Lateral P1/P4		*p*-value		
		0% BAC	0.06% BAC	0.10% BAC
Head	EC	***0.048 [>25%]***	NS [>22%]	NS [<40%]
	EO	***0.045 [>26%]***	***0.034 [<92%]***	0.016 [<54%]
Shoulder	EC	0.011 [>38%]	NS [>13%]	NS [<13%]
	EO	NS [>26%]	NS [<24%]	0.011 [<28%]
Hip	EC	***0.020 [>35%]***	NS [>7%]	NS [<10%]
	EO	***0.034 [>28%]***	NS [<3%]	0.015 [<31%]
Knee	EC	0.005 [>39%]	NS [>27%]	NS [>2%]
	EO	NS [>26%]	NS [>2%]	NS [<30%]

Table 3. Statistical differences found between vibration period 1 and vibration period 4 with Eyes Closed (EC) and Eyes Open (EO). The '<' or '>' notation before the percentage difference shows whether the first value was larger (>) or smaller (<) compared with the second value with respect to the comparison presented in each row. "NS" signifies no significant difference. Values in italic show p-values <0.05 but not reaching the Bonferroni corrected level of significance of p<0.0167. The tables present the statistical findings from a simplified post hoc evaluation of the main factor Period and the interaction between Alcohol x Period.

Table 3 present the statistical findings from a simplified post hoc evaluation of the main factor Period and the interaction between Alcohol x Period. When the progressive effects of repeated balance perturbations were investigated, a clear difference was found in the ability to adapt to balance perturbations while sober and intoxicated (table 3). At 0.00% BAC, both anteroposterior and lateral movement variance decreased through adaptation between periods 1 and 4, though the decrease in lateral direction did not always reach Bonferroni corrected level of significance. When intoxicated, the quantitative adaptation found in anteroposterior direction was poorer than at 0.00% BAC, i.e., the reduction of body movements over time in percentage was smaller, though the stability was still somewhat increased over time by adaptation. However, in the lateral direction with eyes open the stability became quantitatively decreased reflected by increasingly larger body movements over time at 0.06% BAC. Moreover, the body movements became increasingly larger over time both with eyes closed and open at 0.10% BAC and at 0.10% BAC the stability decline over time was significant for the hip, shoulder and head movements with eyes open ($p<0.0167$).

Discussion

This study revealed: 1) A relationship between blood alcohol concentration and amplitude of recorded body movements; 2) That alcohol intoxication caused a substantially larger stability decrease in lateral direction than anteroposterior direction; 3) That the body movement pattern changed in relation to alcohol concentration and in relation to whether stance was unperturbed or repeatedly perturbed; 4) That the sensorimotor adaptation capacity deteriorated with increasing alcohol intoxication; and 5) That the visual information provided a weaker contribution to postural control during alcohol intoxication. These alcohol-related changes of postural control often occurred simultaneously, which suggests that alcohol intoxication cause a complex multifaceted deterioration of human postural control.

Dose-related effects of alcohol intoxication in unperturbed and perturbed standing

In unperturbed standing, the alcohol-related increase in segmental body movements was non-linearly related to the blood alcohol concentration (figure 3). The changes in stability were small between sober and 0.06 % BAC but the stability declined fast between 0.06% BAC to 0.10% BAC, particularly with eyes open. The rapid decrease in postural control found above 0.06% BAC is in line with a prospective study by Kool et al (Kool et al., 2008) showing that approximately 20% of falls at home can be attributed to drinking more than two alcoholic drinks in the 6 hours preceding the fall. Two 30% alcohol drinks yields about 0.06% BAC in a person of 73kg weight. The falls and poorer postural control is probably related to an interference by ethyl alcohol on the sensory and motor synapses in the CNS, causing difficulty in nerve firing and transmission of nerve impulses (Moser et al., 1998).

The effects of alcohol intoxication were quite different on the postural control during unperturbed stance and during balance perturbations. During unperturbed standing, the stability was only marginally affected at 0.06% BAC, whereas under balance perturbations the body movement increases were almost linearly related to the increase in BAC and the stability was substantially deteriorated already at 0.06% BAC. In accordance with our findings, previous studies have revealed that the unperturbed standing is only marginally impaired by alcohol intoxication below 0.08% BAC (Nieschalk et al., 1999). Hence, while a subject with 0.06% BAC may find the quiet stance stability almost unaffected, the subject may find a balance perturbation unexpectedly already difficult to handle at 0.06% BAC.

Direction specific effects of alcohol intoxication in unperturbed and perturbed standing

The significant interaction between period and direction in the multivariate GLM ANOVA analysis revealed increasingly poorer stability with repeated perturbations in lateral direction. The finding of a large deterioration of postural control in the lateral direction through alcohol intoxication is consistent with other reports (Woollacott, 1983). However, the asymmetrical directional deterioration in stability suggests that the postural control system modifies its control from “multi-directional” to “unidirectional”. Such control allows postural control to focus resources, already limited by alcohol intoxication, on stability in the direction believed to be most unsteady. In fact, the subjects were exposed to balance perturbations with predominant destabilizing effect in anteroposterior direction (Fransson et al., 2007b), so the observed focus on stability in anteroposterior direction is in that sense rational. However, focus on stability mainly in one direction could substantially increase the risk of falls in the direction receiving less attention.

Time varying effects of alcohol intoxication during balance perturbations

In this study, both the initial effects of alcohol intoxication and the ability to maintain accurate motor control during sustained sensorimotor challenges with eyes closed and eyes open were investigated. Repeated balance challenges in healthy sober subjects usually introduce an adaptive process enabling them to handle the balance challenges more easily after a learning phase (Corna et al., 1999). However, as illustrated by the significant interaction between period and alcohol in the multivariate GLM ANOVA analysis for all recorded body positions, alcohol intoxication had a very strong and growing destabilizing influence on the ability to handle sustained balance perturbations. When intoxicated at 0.06% BAC a growing inability to maintain stability was already observed in lateral direction. At 0.10% BAC, the stability decline was significant with eyes open, and the body movement had increased by more than 25% at all recorded positions from period 1 to period 4. This could be associated with poorer attention towards the end of the posturography tests or that sustained sensorimotor challenges causes a further breakdown of the postural control mechanisms. Importantly, these findings suggest that the true extent of the incapacity caused by alcohol intoxication may not be revealed through short assessments and during assessments of unperturbed stance. Noteworthy, a recent article by Conner and colleagues (Connor et al., 2004) have shown that the number of traffic accidents also increased at levels below 0.05% BAC, which suggests that the true risks at a certain BAC might be underestimated if influential additional factors are not considered. In line with these observations by Conner and colleagues, this study showed that a combination of alcohol intoxication and sustained exposure to challenging conditions, requiring sustained attention or complex sensorimotor activity, produces a substantial sensorimotor control capacity loss already at low BAC levels.

Alcohol-related changes of multi-segmental movement pattern

The presented findings revealed that participants used a single-link movement pattern between the feet and head during most of the tests. Alcohol intoxication increased the movement amplitudes at all recorded positions but generally did not cause an altered movement pattern. However, several findings suggest that towards the end of the tests, subjects were more prone to alter to a multi-segmented movement pattern to meet the increasing challenges caused by the alcohol intoxication at that time. Interestingly, at 0.10% BAC with eyes closed, there was an increase in knee movement between periods 2 and 3, followed by a large decrease in period 4 (figure 4), which explains the noteworthy significant decrease of the knee movement between periods 1 and 4 with eyes closed at this intoxication level (table 3). One explanation for these findings could be that the growing stability problems reached a threshold in period 3 and alerted the intoxicated participants about their growing instability. The subjects addressed this stability threat by choosing a multi-segmented movement pattern, which better suited the stability conditions at that time. The presented values, supported by visual inspection of the raw data recordings, suggest that this new multi-segmented movement strategy chosen involved a change in the role of the knee. During the initial three 50s balance perturbation periods, the body moved predominantly according to a single-link movement pattern between the feet and head. However, in period 4 the knee movements decreased extensively and partly overtook the role the ankle had in the single-link movement pattern, acting as a correctional reference joint above which the upper body moved as a single link segment. This finding of a new movement pattern while intoxicated at 0.10% BAC, where particularly the knees serve a new role in postural control, is supported by investigations of the co-variances between the recorded movements (Patel et al., 2010).

Sensorimotor adaptation and alcohol intoxication

Alcohol had a strong influence on the ability to adapt to the balance perturbation. In anteroposterior direction, there was a clear decrease in the quantitative improvement obtained from adaptation with increasing BAC. However, the effects of alcohol intoxication were clearest in lateral direction, evidenced by increasing destabilization of postural control over time. This signifies a directional-specific loss of ability to learn and enhance postural control from repeated exposures to balance perturbations.

Several studies have reported that acute alcohol intoxication appears to cause a cerebellar deficit (Belmeguenai et al., 2008; Diener et al., 1983; Servais et al., 2005). Interestingly, damage to the cerebellum can produce profound impairments in learning e.g., patients with cerebellar lesions have difficulties to adapt to predictable large perturbations (Bastian, 2008). Another possibility is that alcohol intoxication cause decreased attention (Abroms et al., 2006), which may slow or delay the initiation of sensorimotor adaptation.

Visual contribution is changed by alcohol intoxication

The present study revealed that the visual system was not able to compensate or even reduce the relative destabilizing effects caused by alcohol intoxication on postural control. On the contrary, the relative impact of alcohol intoxication on unperturbed and perturbed standing was the same or even larger when visual information was available (figures 3 and 4). In unperturbed standing, the movements of the knee, hip, shoulder and head were equally affected by alcohol intoxication with eyes closed and the subjects used the same movement pattern as when sober (figure 3). However with eyes open, the segmental movement pattern was unequally affected by alcohol intoxication, particularly at 0.10% BAC, which suggests a less systematic and multi-segmented handling of the challenges introduced by alcohol intoxication. Furthermore, there was a significantly growing lateral destabilization of head, shoulder and hip movement at 0.10% BAC with eyes open during repeated balance perturbations. Moreover, as evidenced by the significant interaction between vision and direction in the GLM analysis, vision provided poorer stabilization in lateral direction compared with anteroposterior direction.

Boonstra et al. have proposed that the inability for the visual system to compensate for alcohol intoxication might suggest that the neural site affected is located in the central vestibular system or perhaps in the vestibulo-cerebellum (Boonstra et al., 2008). Another explanation could be that the information provided by vision is distorted by alcohol intoxication effects on the vestibular system through visual-vestibular interactions. Hafström and colleagues reported that spatial orientation was increasingly more dependent on visual information with increasing alcohol intoxication (Hafstrom et al., 2007). Hence, if the CNS regards vision as a reliable source for spatial orientation even when the information is unreliable, there could be larger proportional destabilizing effects of alcohol intoxication with eyes open compared with eyes closed, as revealed in the present study.

Subjective feeling of drunkenness

If individuals feel that they are not impaired after consuming alcohol they might be more inclined to engage in activities such as driving. Conversely, when performing alcohol intoxication studies, subjective expectancy of certain effects have substantial impact on the results (Testa et al., 2006), e. g., sober subjects may behave as intoxicated if they believe they have drunk alcohol. This problem was addressed here by a blinded approach providing the subjects with the same information and following the same procedure during all BAC test conditions. To monitor the subjective feeling of drunkenness, a subjective score of feeling of drunkenness was collected every 15 minutes. Those values showed that some subjects felt intoxicated even when receiving placebo drinks whereas some of those who got 0.06% initially felt sober after the first 15 minutes. However, at the time of measurements, after about 85 minutes, almost all subjects were quite aware of their correct status in terms of intoxicated or not and aware of their degree of intoxication.

Conclusions

Alcohol intoxication at 0.06% and 0.10% BAC causes a complex multifaceted deterioration of human postural control. This stability deterioration was expressed by a direct relationship between increased BAC and increased recorded body movements and a large stability decrease in lateral direction. Alcohol intoxication also influenced the movement pattern and reduced the ability for sensorimotor adaptation to such an extent in lateral direction that the stability became progressively poorer to handle repeated balance perturbations. Furthermore, vision provided a weaker contribution to postural control during alcohol intoxication.

Conflict of Interest

There are no conflicts of interest.

References

Abroms, B.D., Gottlob, L.R., and Fillmore, M.T. (2006). Alcohol effects on inhibitory control of attention: distinguishing between intentional and automatic mechanisms. Psychopharmacology (Berl) *188*, 324-334.

Altman, D. (1991). Practical statistics for medical research (New York, NY: Chapman & Hall).

Ashby, P., Carlen, P.L., MacLeod, S., and Sinha, P. (1977). Ethanol and spinal presynaptic inhibition in man. Ann Neurol *1*, 478-480.

Bastian, A.J. (2008). Understanding sensorimotor adaptation and learning for rehabilitation. Curr Opin Neurol *21*, 628-633.

Belmeguenai, A., Botta, P., Weber, J.T., Carta, M., De Ruiter, M., De Zeeuw, C.I., Valenzuela, C.F., and Hansel, C. (2008). Alcohol impairs long-term depression at the cerebellar parallel fiber-Purkinje cell synapse. J Neurophysiol *100*, 3167-3174.

Blackburn, J.T., Riemann, B.L., Myers, J.B., and Lephart, S.M. (2003). Kinematic analysis of the hip and trunk during bilateral stance on firm, foam, and multiaxial support surfaces. Clin Biomech (Bristol, Avon) *18*, 655-661.

Boonstra, T.W., Roerdink, M., Daffertshofer, A., van Vugt, B., van Werven, G., and Beek, P.J. (2008). Low-alcohol doses reduce common 10- to 15-Hz input to bilateral leg muscles during quiet standing. J Neurophysiol *100*, 2158-2164.

Connor, J., Norton, R., Ameratunga, S., and Jackson, R. (2004). The contribution of alcohol to serious car crash injuries. Epidemiology *15*, 337-344.

Corna, S., Tarantola, J., Nardone, A., Giordano, A., and Schieppati, M. (1999). Standing on a continuously moving platform: is body inertia counteracted or exploited? Exp Brain Res *124*, 331-341.

Dick, R.B., Setzer, J.V., Taylor, B.J., and Shukla, R. (1989). Neurobehavioural effects of short duration exposures to acetone and methyl ethyl ketone. Br J Ind Med *46*, 111-121.

Diener, H.C., Dichgans, J., Bacher, M., Hulser, J., and Liebich, H. (1983). Mechanisms of postural ataxia after intake of alcohol. Z Rechtsmed *90*, 159-165.

Fransson, M., Jones, A.W., and Andersson, L. (2005). Laboratory evaluation of a new evidential breath-alcohol analyser designed for mobile testing--the Evidenzer. Med Sci Law *45*, 61-70.

Fransson, P.A., Gomez, S., Patel, M., and Johansson, L. (2007a). Changes in multi-segmented body movements and EMG activity while standing on firm and foam support surfaces. Eur J Appl Physiol *101*, 81-89.

Fransson, P.A., Hjerpe, M., and Johansson, R. (2007b). Adaptation of multi-segmented body movements during vibratory proprioceptive and galvanic vestibular stimulation. J Vestib Res *17*, 47-62.

Fransson, P.A., Modig, F., Patel, M., Gomez, S., and Magnusson, M. (2010). Oculomotor deficits caused by 0.06% and 0.10% blood alcohol concentrations and relationship to subjective perception of drunkenness. Clin Neurophysiol *121*, 2134-2142.

Fuster, J.M., Willey, T.J., and Riley, D.M. (1985). Effects of ethanol on eye movements in the monkey. Alcohol *2*, 611-616.

Gomez, S., Patel, M., Berg, S., Magnusson, M., Johansson, R., and Fransson, P.A. (2008). Effects of proprioceptive vibratory stimulation on body movement at 24 and 36 h of sleep deprivation. Clinical Neurophysiology *119*, 617-625.

Gomez, S., Patel, M., Magnusson, M., Johansson, L., Einarsson, E.J., and Fransson, P.A. (2009). Differences between body movement adaptation to calf and neck muscle vibratory proprioceptive stimulation. Gait Posture *30*, 93-99.
Granata, K.P., and Lockhart, T.E. (2008). Dynamic stability differences in fall-prone and healthy adults. J Electromyogr Kinesiol *18*, 172-178.
Hafstrom, A., Modig, F., Karlberg, M., and Fransson, P.A. (2007). Increased visual dependence and otolith dysfunction with alcohol intoxication. Neuroreport *18*, 391-394.
Horak, F.B., and Nashner, L.M. (1986). Central programming of postural movements: adaptation to altered support-surface configurations. J Neurophysiol *55*, 1369-1381.
Johansson, R. (1993). System Modeling and Identification (Englewood Cliffs, N.J. USA., Prentice Hall).
Johnston, J.J., and McGovern, S.J. (2004). Alcohol related falls: an interesting pattern of injuries. Emerg Med J *21*, 185-188.
Kool, B., Ameratunga, S., Robinson, E., Crengle, S., and Jackson, R. (2008). The contribution of alcohol to falls at home among working-aged adults. Alcohol *42*, 383-388.
Kubo, T., Sakata, Y., Koshimune, A., Sakai, S., Ameno, K., and Ijiri, I. (1990). Positional nystagmus and body sway after alcohol ingestion. Am J Otolaryngol *11*, 416-419.
Lockhart, D.B., and Ting, L.H. (2007). Optimal sensorimotor transformations for balance. Nat Neurosci *10*, 1329-1336.
Moser, A., Heide, W., and Kompf, D. (1998). The effect of oral ethanol consumption on eye movements in healthy volunteers. J Neurol *245*, 542-550.
Mullikin-Kilpatrick, D., and Treistman, S.N. (1994). Ethanol inhibition of L-type Ca2+ channels in PC12 cells: role of permeant ions. Eur J Pharmacol *270*, 17-25.
Nieschalk, M., Ortmann, C., West, A., Schmal, F., Stoll, W., and Fechner, G. (1999). Effects of alcohol on body-sway patterns in human subjects. Int J Legal Med *112*, 253-260.
Oie, K.S., Kiemel, T., and Jeka, J.J. (2002). Multisensory fusion: simultaneous re-weighting of vision and touch for the control of human posture. Brain Res Cogn Brain Res *14*, 164-176.
Pai, Y.C., and Iqbal, K. (1999). Simulated movement termination for balance recovery: can movement strategies be sought to maintain stability in the presence of slipping or forced sliding? J Biomech *32*, 779-786.
Patel, M., Gomez, S., Lush, D., and Fransson, P.A. (2009). Adaptation and vision change the relationship between muscle activity of the lower limbs and body movement during human balance perturbations. Clin Neurophysiol *120*, 601-609.
Patel, M., Modig, F., Magnusson, M., and Fransson, P.A. (2010). Alcohol intoxication at 0.06 and 0.10% blood alcohol concentration changes segmental body movement coordination. Exp Brain Res *202*, 431-443.
Pavol, M.J., and Pai, Y.C. (2002). Feedforward adaptations are used to compensate for a potential loss of balance. Exp Brain Res *145*, 528-538.
Servais, L., Bearzatto, B., Delvaux, V., Noel, E., Leach, R., Brasseur, M., Schiffmann, S.N., and Guy, C. (2005). Effect of chronic ethanol ingestion on Purkinje and Golgi cell firing in vivo and on motor coordination in mice. Brain Res *1055*, 171-179.
Talving, P., Plurad, D., Barmparas, G., Dubose, J., Inaba, K., Lam, L., Chan, L., and Demetriades, D. (2010). Isolated severe traumatic brain injuries: association of blood alcohol levels with the severity of injuries and outcomes. J Trauma *68*, 357-362.
Testa, M., Fillmore, M.T., Norris, J., Abbey, A., Curtin, J.J., Leonard, K.E., Mariano, K.A., Thomas, M.C., Nomensen, K.J., George, W.H., *et al.* (2006). Understanding alcohol expectancy effects: revisiting the placebo condition. Alcohol Clin Exp Res *30*, 339-348.
Thyssen, H.H., Brynskov, J., and Jansen, E.C. (1981). Alcohol and postural imbalance. A force plate study. Z Rechtsmed *87*, 257-260.

Tianwu, H., Watanabe, Y., Asai, M., Shimizu, K., Takada, S., and Mizukoshi, K. (1995). Effects of alcohol ingestion on vestibular function in postural control. Acta Otolaryngol Suppl *519*, 127-131.
Tjernstrom, F., Fransson, P.A., Hafstrom, A., and Magnusson, M. (2002). Adaptation of postural control to perturbations--a process that initiates long-term motor memory. Gait Posture *15*, 75-82.
Todorov, E., and Jordan, M.I. (2002). Optimal feedback control as a theory of motor coordination. Nat Neurosci *5*, 1226-1235.
Treistman, S.N., Bayley, H., Lemos, J.R., Wang, X.M., Nordmann, J.J., and Grant, A.J. (1991). Effects of ethanol on calcium channels, potassium channels, and vasopressin release. Ann N Y Acad Sci *625*, 249-263.
Wang, M.Q., Taylor-Nicholson, M.E., Airhihenbuwa, C.O., Mahoney, B.S., Fitzhugh, E.C., and Christina, R. (1992). Psychomotor and visual performance under the time-course effect of alcohol. Percept Mot Skills *75*, 1095-1106.
Vogel-Sprott, M.D. (1979). Acute recovery and tolerance to low doses of alcohol: differences in cognitive and motor skill performance. Psychopharmacology (Berl) *61*, 287-291.
Woollacott, M.H. (1983). Effects of ethanol on postural adjustments in humans. Exp Neurol *80*, 55-68.