Decreased postural control in adolescents born preterm and with extremely low birth weight

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Abstract

The survival rates of infants born preterm with extremely low birth weight (ELBW ≤ 1000 g) have gradually improved over the last decades. However, these infants risk to sustain long-term disorders related to poor neurodevelopment. The objective was to determine whether adolescents born with ELBW have decreased postural control and stability adaptation. Twenty-nine ELBW subjects performed posturography with eyes open and closed under unperturbed and perturbed standing by repeated calf vibration. Their results were compared with twenty-one age- and gender-matched controls born after full-term pregnancy. The ELBW group had significantly decreased stability compared with controls in anteroposterior direction, both during the easier quiet stance posturography ($p = 0.007$) and during balance perturbations ($p = 0.007$). The ELBW group had similar stability decrease in lateral direction during balance perturbations ($p = 0.013$). Statistically, the stability decreases were similar with eyes closed and open, but proportionally larger with eyes open in both directions. Both groups manifested significant adaptation ($p \leq 0.023$) to the balance perturbations in anteroposterior direction, though this adaptation process could not compensate for the general stability deficits caused by ELBW on postural control. Hence, adolescent survivors of ELBW commonly suffer long-term deficits in postural control, manifested as use of substantially more recorded energy on performing stability regulating high-frequency movements and declined stability with closed and open eyes both in anteroposterior and lateral direction. The determined relationship between premature birth and long-term functional deficits advocates that interventions should be developed to provide preventive care in neonatal care units and later on in life.

Keywords

Low birth weight Postural control Childhood Adaptation Vision

Introduction

Through modern technical interventions and trained healthcare personnel, the survival rate of preterm-born infants has gradually improved over the last decades (Aylward 2005). This increase, especially of the survival rate of infants born with extremely low birth weight (ELBW ≤ 1000 g), has emphasized the necessity to learn more about this group's neurophysiological development into adolescents and adulthood (Georgsdottir et al. 2013). ELBW infants have elevated risk of suffering a number of deficits related to delayed neurodevelopment of the central nervous system (CNS) and from brain injuries (Samsom and de Groot 2001). However, many of these disorders are commonly difficult to detect in early life, so numerous symptoms may remain undetected until school age (Georgsdottir et al. 2012). Hence, by determining likely relationships between levels of premature birth and deficits in neurodevelopment and in cognitive and physical functions, intervention methods can be developed to provide the correct preventive care in neonatal care units and later on in life (van Lunenburg et al. 2013).

Birth weight is one of the most common markers to rate the degree of premature birth. Infants born with low birth weight (LBW < 2500 g) are generally born before 37 weeks gestational age (Ritchie and McClure 1979), whereas infants born with extremely low birth weight (ELBW ≤ 1000 g) are mostly born before 34 weeks gestational age. The most frequent deficits found after ELBW infancy are moderate-to-severe mental retardation, sensorineural hearing loss, blindness, cerebral palsy (CP) and epilepsy. Infants born with ELBW have a 20–25 % incidence of these disabilities (Halsey et al. 1996; Bennett and Scott 1997; Aylward 2005), whereas full-term-born infants have a 5 % incidence (Paneth 1995). Other common disorders that might be difficult to detect before school age are learning disorders, attention deficiency hyperactivity disorder (ADHD), behavioral problems, sensory and motor system underdevelopment and reduced muscle strength (Samsom et al. 2002; Foulder-Hughes and Cooke 2003). It has been estimated that as many as 50–70 % of infants born ≤1500 g (VLBW) suffers one or several dysfunctions of a severity that tends to increase with smaller birth weight (O'Callaghan et al. 1996; Goyen et al. 1998; Taylor et al. 2000). Brain structures involved in fine motor control such as the cerebellum, basal ganglia, corpus callosum, amygdala and hippocampus are smaller in infants born preterm, even without apparent early brain damage (Maalouf et al.1999; Peterson et al. 2000; Allin et al. 2001; Ferriero 2004; Brandt et al. 2005).

In children, the somatosensory, visual and vestibular systems are in a state of development, which may make these systems more susceptible to neurological long-term damage from unfavorable conditions in childhood (Kovacic and Somanathan 2008). For example, when visual field deficits occur in both eyes and overlap, the corresponding part of the visual cortex may no longer be appropriately stimulated, which in turn can influence the long-term development of the retinotopic organization of the visual cortex (Boucard et al.2009). Hence, modified or absent stimulation of important cortical areas in childhood may affect long-term development.

The ability to maintain an upright stance is extensively dependent on capability to perform fine and complex motor control. The neural systems that regulate postural control continually integrate sensory information from visual, vestibular, proprioceptive and mechanoreceptive sensors and coordinate multiple motor outputs to muscles throughout the body (Lockhart and Ting 2007). One key component for postural control is the ability to adjust the motor programs and reflexive actions to stability-condition changes (Johansson and Magnusson 1991). The stability enhancement gained from this adaptive process depends upon the ability of the CNS to continually select the most accurate and important sensory information from the confluence of signals received and proper process and integrate this information to get the best representation of body position and movement (Fransson 2009).

A common method used to study complex sensorimotor neurophysiological functions such as postural control is posturography with active balance perturbations. The balance perturbations make it easier to detect deficits and limitations in a subjects' stability regulation (Johansson and Magnusson 1991). A well-known method to produce balance perturbations is to disrupt the somatosensory information by applying vibration against muscles or tendons important for standing (Popov et al. 1996). Such vibration simultaneously increases the afferent signals from the muscle spindles and creates a proprioceptive illusion that the vibrated muscle is being stretched. The responses thereafter are intended to return the vibrated muscle to its perceived original length (Goodwin et al. 1972). Calf muscle vibration typically increases movements bidirectionally, though generally more in anteroposterior direction than in lateral direction (Eklund1973). When repeated, balance perturbations normally initiate an adaptive process, which decreases the necessary responsive movements and enhances the stability when the person learns to predict the characteristics of the destabilizing illusory effects and set their balance system to minimize these effects (Corna et al. 1999; Fransson 2009).

To date, it is largely unknown whether adolescents born with ELBW have a normal postural control with properties allowing them effective handling of balance perturbations and operative stability control adaptation. In contrast to previous reports, this study aims to investigate postural control later in life when the balance control development should be completed and, therefore, more likely reflect the long-term conditions these ELBW subjects will live under as adult (Assaiante et al. 2005).

Our hypothesis is that postural stability likely is decreased in adolescents born with ELBW, particularly with eyes open since the visual and oculomotor systems are known to be affected by ELBW at 6–7 years of age (Atkinson and Braddick 2007). We also hypothesize that postural adaptation is affected after ELBW birth, as postural adaptation depends upon attention and fine motor control (Patel et al. 2008). Detecting these derivatives from normal may improve the awareness of how complex the deficit pattern might be after ELBW birth, promoting that better intervention methods are designed to improve the general health and well-being of individuals born with ELBW.

Materials and methods

Subjects

The total number of births and survival of ELBW (<1000 g) preterm infants in Iceland in the years 1991–1995 was obtained from the National Hospital Birth registry in Iceland. Exclusion criteria for participation in the study were mental retardation, sensorineural hearing loss and blindness, cerebral palsy and epilepsy. From the original group, thirty-five teenagers still living in the selected area were eligible for participation, thereof six declined participation. All of the ELBW subjects were born before the 34-week gestation age, and 33 of the 35 subjects were treated with ampicillin and neomycin after birth. The final selectively recruited ELBW group comprised of twenty-nine teenage participants, 25 females and 4 males of mean age 17.2 years old (SD 1.4 years), mean height 1.65 m (SD 0.09 m) and mean mass 62.6 kg (SD 12.4 kg).

Twenty-one age- and gender-matched healthy participants, 18 females and 3 males of mean age 17.0 years old (SD 1.4 years), mean height 1.69 m (SD 0.07 m) and mean mass 64.7 kg (SD 7.7 kg) were recruited from local schools as control group for comparison. All in the control group were born after 37 gestational weeks and had a birth weight >2500 g. The control group had normal otological status, normal vestibular status and no history of any major injury or neurological disorder.

Signed consent was obtained from adult participants or from both the teenager and his/her parent/guardian. The experiments were all performed in accordance with the most recent Declaration of Helsinki and approved by Scientific Ethical Committee and The Data Protection Authority in Iceland. This study was part of a larger assessment on the long-term effects of preterm birth on social, neurological and intellectual performance (Georgsdottir et al. 2012, 2013; Jonsdottir et al. 2012).

Equipment

A custom-built force platform recorded torques and sheer forces with six degrees of freedom using force transducers with an accuracy of 0.5 N. A customized computer program controlled the vibratory stimulation and sampled the data of the individual measurements from the platform at 50 Hz. The vibrators had vibration amplitude of 1.0 mm and frequency of 85 Hz, were 6 cm long and 1 cm in diameter and strapped over the gastrocnemius muscles of both legs.

Posturography assessment

Each subject stood barefoot on the force platform in a relaxed posture with arms folded across the chest. This posture was used to maintain consistency and to avoid inappropriate arm movements. The participant's heels were 3 cm apart and feet positioned at an angle of 30° along guidelines on the platform. Participants were instructed to focus on a target 1.5 m in front of them at eye level or keep their eyes closed depending on the test condition. If the subjects used visual correction media such as glasses or contact lenses, then these were used also during the assessments. The participants listened to music through headphones in order to reduce possible movement references from external noise sources and to avoid extraneous sound distractions (Petersen et al. 1995). To ensure no prediction of the balance perturbation, all participants were naive to the stimulus and were not informed about the effect calf vibration would have on their balance.

The stability during the following two conditions was investigated in a randomized order, using a Latin Square design, by all subjects:

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

Before the vibration commenced, a 30-s control period of quiet stance was recorded. The vibratory stimulations were applied according to a pseudorandom binary sequence (PRBS) schedule (Johansson et al.1988) during a period of 200 s making each trial 230 s long. The PRBS schedule defined the periodicity of stimulation pulses, where each pulse and each interval between pulses had random time duration from 0.8 s up to 6.4 s, 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 preemptive responses. An identical PRBS sequence was applied to all subjects during all tests, and the stimuli were simultaneously applied to the gastrocnemius muscles of both legs. A 5-min rest period was given to the subjects between EO and EC tests.

Analysis

Postural stability was measured by a force platform as the variance of anteroposterior and lateral torque values used toward the support surface. Recorded torque contains the same information about movement fluctuations as the traditional method of calculating CoP (Patel et al. 2008). However, the information is presented in the form of energy used toward the support surface to maintain stability (Johansson et al.2009), and the data analysis process includes that the values are always normalized before statistical analysis for anthropometrical variations in height and mass. Moreover, torque variance values correspond to the efficiency of standing (Riccio and Stoffregen 1988) (for a detailed explanation on torque and its relationship to standing postural control, see Patel et al. 2008; Fransson 2009; Johansson et al. 2009). The force platform recordings were divided into total torque variance, torque below 0.1 Hz (low frequency), and torque above 0.1 Hz (high frequency) using a fifth-order digital finite-duration impulse response filter, with filter components selected to avoid aliasing. These separations were used to distinguish better between smooth corrective changes of posture and voluntary movements (i.e., <0.1 Hz) and fast corrective largely reflexive movements made to maintain balance (i.e., >0.1 Hz) (Kristinsdottir et al. 2001). Torque variance values were normalized to account for anthropometric differences between the subjects, using the subject's squared height and squared weight (Johansson et al. 2009). The squared nature of the variance algorithm made it necessary to use normalization with squared parameters to achieve unit agreement.

Mean values for all parameters were obtained for five periods for each trial condition: the quiet stance period (0–30 s), and from four 50-s periods (period 1: 30–80 s; period 2: 80–130 s; period 3: 130–180 s; period 4: 180–230 s) during the vibration. The selection of 50-s analysis periods for a total of 200-s stimulation period 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 50 s period contained a similar amount of long and short vibration pulses validated by fast Fourier transform analysis of spectral contents in the stimulation. Hence, the selected periods and perturbation sequence allowed analysis of whether the stability changed over time and possibly caused an adaptation to the unpredictable balance perturbations.

Statistical analysis

The torque variance values during quite stance and during balance perturbations were analyzed using repeated-measures GLM ANOVA on log-transformed values. The log transformation made prior to the statistical analysis was done to reduce the nonnormal distribution of the data sets, produced partly by that the variance algorithm used in the data analysis includes calculating the sum of squared values. The main factors included in the GLM model were as follows: the effect of preterm ELBW birth (denoted 'ELBW': yes or no [degrees of freedom (*df*) = 1], availability of visual information ('Vision': eyes closed or eyes open; *df* 1) and when applicable the period of vibration ('Period': periods 1–4; *df* 3).

The Mann–Whitney test (Altman 1991) was used for the post hoc statistical comparisons between groups. The Wilcoxon matched-pairs signed-rank test (Altman 1991) was used for the post hoc statistical analysis of stability variations over time, i.e., the torque variance changes between Period 1 and Period 4 were evaluated to determine how assessed stability was affected by repeated vibratory stimulation, quantifying the accumulated effects of adaptation (Patel et al. 2008). In the analysis, *p* values <0.05 were considered statistically significant.

Results

Quiet stance stability

The GLM ANOVA of the quiet stance stability in anteroposterior direction showed that the ELBW subjects had poorer stability compared with healthy controls as reflected by significantly higher total (*p* = 0.007, +53 %), low-frequency (*p* = 0.018, +83 %) and high-frequency (*p* = 0.022, +38 %) torque variance (Table 1). Vision increased anteroposterior stability in both the ELBW group and controls, i.e., significantly reduced, total (*p* = 0.033, −32 %) and high-frequency (*p* < 0.001, −40 %) torque variance. No significant interaction was found in the GLM ANOVA between the main factors investigated.

The analysis of quiet stance stability in lateral direction showed that the ELBW subjects had poorer stability also in this direction compared with healthy controls as reflected by significantly higher high-frequency torque variance (*p* = 0.009, +48 %) (Table 1). Vision did not improve the quiet stance stability in lateral direction, and no significant interaction was found between the main factors investigated.

The post hoc group-wise analysis of the GLM ANOVA findings confirmed generally poorer quiet stance stability in the anteroposterior direction in the ELBW group compared with controls, both with eyes closed and eyes open (Fig. 1). The analysis also confirmed decreased quiet stance stability in lateral direction in the ELBW group, though here only during tests standing with eyes open.

Perturbed stance stability

The GLM ANOVA showed that the ELBW group had poorer stability compared with controls in anteroposterior direction, as reflected in significantly higher total (*p* = 0.007, +78 %) and high-frequency torque variance (*p* = 0.003, +127 %) (Table 2). Vision increased stability in both groups, i.e., significantly reduced total (*p* < 0.001, −34 %), low-frequency (*p* = 0.043, −16 %) and high-frequency torque variance (*p* < 0.001, −44 %). The significant Period factor of total (*p* < 0.001, −35 %), low-frequency (*p* < 0.001, −51 %) and high-frequency torque variance (*p* < 0.001, −21 %) shows that when repeated, the balance perturbations caused a lower stability challenge over time in both groups. Furthermore, the significant interaction between vision and period for high-frequency torque variance (*p* = 0.036) shows that the increase in stability over time was larger with eyes closed (−30 %) than with eyes open (−12 %) (see also Table 4).

In a further analysis of the effects of ELBW, the data were analyzed for eyes closed and eyes open tests separately (Table 3). With eyes closed, the ELBW subjects had poorer stability compared with healthy controls, reflected by significantly higher total (*p* = 0.017, +59 %) and high-frequency torque variance (*p* = 0.012, +69 %). Additionally, the Period factor shows that the balance perturbations caused a lower stability challenge over time in all spectral categories, i.e., total (*p* < 0.001, −39 %), low-frequency (*p* < 0.001, −53 %) and high-frequency torque variance (*p* < 0.001, −30 %), in both groups. With eyes open, the findings were largely the same as with eyes closed, though the differences between groups were proportionally larger. The ELBW subjects had poorer stability compared with healthy controls, as reflected by significantly higher total (*p* = 0.013, +97 %) and high-frequency torque variance (*p* = 0.006, +185 %). However, as shown by the Period factor, the stability adaptation over time with eyes open was effective only on total (*p* = 0.002, −30 %) and low-frequency torque variance (*p* < 0.001, −50 %).

The analysis of the stability in lateral direction showed that the ELBW group, during balance perturbations, had poorer stability compared with controls as reflected in significantly higher total ($p < 0.013$, +84 %) and high-frequency torque variance ($p < 0.001$, +93 %) (Table 2). Vision increased stability in both groups, i.e., significantly reduced total ($p < 0.001$, −25 %) and high-frequency torque variance ($p < 0.001$, −37 %). The nonsignificant Period factor shows that the balance perturbations caused about the same stability challenge over time.

In the further analysis of the effects of ELBW, separately for eyes closed and eyes open, some findings were different from those found in anteroposterior direction (Table 3). With eyes closed, the ELBW subjects had poorer stability compared with healthy controls, as reflected by significantly higher total ($p = 0.030$, +83 %) and high-frequency torque variance ($p = 0.004$, +74 %). However, the nonsignificant Period factor shows that the repeated balance perturbations caused no stability improvements from adaptation as found in anteroposterior direction. With eyes open, the ELBW subjects had also poorer stability, as reflected by significantly higher total ($p = 0.011$, +85 %) and high-frequency torque variance ($p < 0.001$, +112 %). Again, however, the nonsignificant Period factor shows that the repeated balance perturbations caused no stability improvements from adaptation.

The post hoc group-wise analysis confirmed poorer stability in anteroposterior direction in the ELBW group compared with controls during balance perturbations both with eyes closed and eyes open during most periods, though the differences between groups were somewhat more pronounced with eyes open (see Fig. 1). The post hoc group-wise analysis of the lateral data revealed that also the lateral stability was poorer in the ELBW group both with eyes closed and eyes open during most periods, though again the differences between groups were statistically more pronounced with eyes open.

Adaptation capacity

The analysis of the adaptation ability showed that healthy controls did significantly adapt to the balance perturbations in anteroposterior direction, as reflected in reductions of the measured torque variances in all frequency spectra with eyes closed ($p \leq 0.014$) and with eyes open ($p \leq 0.023$) (Table 4). The ELBW group also showed significant adaptation in all frequency spectra with eyes closed ($p \leq 0.008$) and with eyes open ($p \leq 0.004$), though the average quantitative improvements gained through adaptation tended to be smaller in the high-frequency range and larger in the low-frequency range compared with controls especially with eyes open.

When investigating the adaptation ability in lateral direction, neither healthy controls nor the ELBW group showed significant adaptation with eyes closed or eyes open. However, an inspection of the quantitative values suggests that the healthy controls tend to increase the stability in lateral direction over time, whereas the ELBW group instead tended to decrease the stability over time (Table 4). None of these changes reached significant levels though.

Discussion

Preterm birth presents a substantial challenge for the neurodevelopment of the postural control systems, because the infants are born with an immature and more vulnerable motor and sensory system, and because the infants commonly suffer brain injuries such as periventricular hemorrhage and leukomalacia or ventricular enlargement (Schmidt et al. 2003; Fallang and Hadders-Algra 2005). As a result, preterm birth commonly causes dysfunctional postural control with delayed onset and poor quality of early walking. The functional deficits observed up to the age of 1 year are often associated with poorer neurodevelopmental outcome also later at 6–7 years of age (Fallang and Hadders-Algra 2005), expressed as problems with standing on one leg, poor hopping and clumsy walking (Sommerfelt et al. 1993). The present study shows that functional deficits of postural control from ELBW are not limited to younger children, but persist into adolescence, i.e., the deficits persist after the developmental stages of postural control are completed. This finding is in keeping with other recent reports of persistent motor control problems in adolescents and adults after preterm birth and VLBW (Evensen et al. 2004; de Kieviet et al. 2009). Moreover, since presence of CP was one of the exclusion criteria in this study, persisting postural control issues into adulthood was not limited only to subjects suffering from severe lesions such as CP from preterm birth, but seemingly, subjects born with ELBW generally perform worse than controls. The postural control strategies in the ELBW subjects utilized a higher-frequency torque variance and a movement pattern, which consumes much more energy. The stability deficits had similar properties with closed and open eyes and in anteroposterior and lateral direction. However, the deficits were proportionally more pronounced versus controls with eyes open. Moreover, the stability decline was apparent already during the easier quiet stance posturography but more marked when being exposed to straining balance perturbations.

Decreased postural control has previously been reported after preterm birth with VLBW with eyes open and closed, though in that study the differences found were small compared with a control group born after full-term pregnancy (Kluenter et al. 2008). Moreover, the study was performed on VLBW children of 7 years of age without major neurological disorders. The postural control systems are generally not fully developed before 12 years of age (Assaiante et al. 2005), so the properties of postural control in adolescence and adulthood and thus the full extent of deficits experienced after completed development might not be discernible while the development still is ongoing, as is the case in young children.

One circumstance that should be noted is that females markedly dominated the ELBW group, and 25 out of 29 ELBW subjects were girls. Whether this was an effect of random local variations or that females do dominate among those who survive birth of extremely low weight is an aspect that merits more research. The practical consequences on the assessments and statistical analysis of the gender imbalance were addressed by performing anthropometrical normalization of all recorded data before statistical analysis and by comparing all results to a gender-matched control group. However, the gender imbalance may still have implications on the findings presented, in that the results might not accurately reflect the performance of males ELBW.

ELBW and postural control adaptation

The ability to adapt and habituate based on prior experiences is important for human movement control, fall prevention (Eccles 1986; Fransson et al. 2003) and for the ability to enhance the performance during various human activities (Horak and Nashner 1986; Keshner et al. 1987). Postural control adaptation including optimizing integration of information from the visual, vestibular and somatosensory receptors and motor coordination are complex processes, especially when information from any of the sensory systems is not reliable (Redfern et al. 2001). Neurophysiological data associated with postural control tasks at young age indicate a reduced capacity to modulate the postural activity, which has been characterized by temporal disorganization of EMG responses (Fallang and Hadders-Algra 2005). Moreover, during the last months of pregnancy, the cerebellum goes through a vital phase in which the hierarchy of motor activities and mechanisms that influences and maintains motor control is laid down (Brodal 1998). Animal studies have also shown a reduction in the number of pyramidal cells in the hippocampus and Purkinje cells in the cerebellum (Mallard et al. 2000) and disturbed myelination of oligodendrocytes (Tolcos et al. 2011).

In this study, the adolescent ELBW subjects displayed an active and effective adaptation of postural control to the artificial balance perturbations, achieving the same proportional enhancement of stability as observed in the control group. This finding suggests that the cerebellar and the other CNS structures used for short-term enhancements of motor programs and adjustments of reflexive stability responses may still largely be intact after premature birth. However, these adaptation processes had seemingly not the capacity or properties suitable to compensate for the deficits causing the general decline of postural control. Moreover, though it could not be confirmed statistically on group level, some individual ELBW subjects had marked difficulties to control and enhance the stability using adaptation in lateral direction, mostly with eyes open.

ELBW and vision

Vision generally provides a robust source of reliable stability information to postural control. The present study shows that ELBW subjects utilize visual information to improve stability, confirming that visual information served a vital role for enhancing postural control (Le and Kapoula 2008). However, although vision improved the stability, the ELBW subjects performed noticeably poorer compared with controls with eyes open than with eyes closed. Moreover, the relatively poorer stability with eyes open was apparent already during the easier quiet stance posturography but more pronounced when being exposed to straining balance perturbations. During quiet stance, the ELBW subjects used in anteroposterior direction on average only 3 % more energy with eyes closed compared with controls. However, the differences between groups increased to 73 % with eyes open. During balance perturbations, the corresponding differences between groups were 69 % with eyes closed and 185 % with eyes open. Hence, although visual information improved stability, this additional information seemed to be used far less effective to enhance postural control in ELBW subjects, which advocate for more research to investigate in what ways ELBW compromises the ability to collect, analyze or utilize visual information for better postural control. One possible explanation could be that the visual information quality is compromised by the common deficits among VLBW children and adolescents of poorer visual functions, including poorer visual acuity, stereoacuity, contrast sensitivity and more strabismus than controls (Powls et al. 1997; Evensen et al. 2009). Moreover, one of the common morbidities with premature birth is severe retinopathy, which to various degree may affect vision and in worst case cause blindness if not properly treated

(Eckert et al. 2012). However, the complex combination of deficits observed with eyes open in this study also has many similarities with those observed under severe alcohol intoxication (Modig et al. 2012), i.e., conditions under which the oculomotor functions are compromised (Fransson et al. 2010).

Spectral characteristics of ELBW subject’s postural control

From the standpoint of mechanical engineering, the frequency domain characteristics of the physical actions taken to maintain stability may provide more detailed information about the properties and potential weaknesses of the movement pattern used, e.g., about the contents of slow and rapid movements and ability to respond appropriately to balance perturbations. The present study revealed that primarily the high-frequency regulation activity of postural control was significantly increased in the ELBW subjects. Effective visual feedback can usually significantly reduce the requirements of using high-frequency movement to maintain stability, thus reducing both the energy requirement used for stability control and the physical strain on postural muscles (Kristinsdottir et al. 2001). The same effect was also found in the ELBW subjects, but vision was in these cases not near as effective to reduce the high-frequency activity as found in healthy controls. Similar extensive use of high-frequency activity with eyes open is commonly found among elderly with deficits in mechanoreceptive and proprioceptive sensation in the feet and lower legs from factors such as polyneuropathy (Kristinsdottir et al. 2001; Patel et al. 2009) or in subjects under severe alcohol intoxication (Modig et al. 2012). Hence, more research needs to be done to explain why ELBW subjects show the same pattern, suggesting lack of or poor use of certain sensory information by postural control.

Postural control issues and neurological disorders

ELBW and low gestational age has been associated with three common morbidities: bronchopulmonary dysplasia, brain injury identified via ultrasound (periventricular leukomalacia or ventricular enlargement) and severe retinopathy (Schmidt et al. 2003). However, even in the absence of identifiable CNS events, preterm birth is characterized by a potential disruption in the typical temporal and spatial progression of development of brain structures. Peak brain growth, synaptogenesis and developmental regulation of specific receptor populations (*N*-methyl-d-aspartate, AMPA, glutamate) are affected during the critical developmental window that occurs around the time of premature birth (Huttenlocher and Dabholkar 1997; Bhutta and Anand 2002). Therefore, the brain of the baby born prematurely is not organized in the same manner as that of a full-term infant (Ferriero 2004; Aylward 2005).

Vulnerable processes due to preterm birth include establishment and differentiation of subplate neurons, alignment, orientation, and layering of cortical neurons (Aylward 2005). The subplate neuron layer is a transient structure that is located beneath the cortical plate and peaks in activity between 22 and 36 weeks of gestation (Back et al. 2001; Perlman 2003). Removal of subplate neurons profoundly affects cortical development and plasticity (Kanold 2009). This structure is important in cerebral organization because it is the area where growing axons from the thalamus and other key cortical sites “wait” because their ultimate neuronal targets in the cortical plate have not yet been developed (Aylward 2005), and this is particularly true for the visual system (Kanold et al. 2003; Kanold 2009).

In MRI investigations of the brain structures in adults born with VLBW, the lateral ventricular volume and the ratio of gray to white matter were found to be significantly increased, the latter including widespread changes in the distribution of gray and white matter (Brandt et al. 2005). Several white matter regions, in particular the corpus callosum, internal capsule and superior fasciculus have shown less integrity on fractional anisotropy maps in VLBW adolescents compared with controls (Skranes et al. 2007). Furthermore, lower IQs in children born preterm are related to poorer development of the caudate relative to the rest of the brain, independent of other lesions. These findings suggest that abnormal brain development after perinatal injury or postnatal nutritional deficits are responsible for cognitive deficits in preterm children (Abernethy et al. 2004) and for small white matter lesions (Abernethy et al. 2003).

The motor proficiency has been described as consistently poorer in very preterm and VLBW children than in normative samples, influencing both fine and gross motor skills (de Kieviet et al. 2009). However, the observable motor deficits may vary with age, i.e., decrease within the first years of development but then stabilize or increase later in development (de Kieviet et al. 2009). Moreover, in children showing no apparent signs of dysfunction at a young age, functional deficit and motor problems may appear first with increasing age when the complexity of the motor tasks performed set higher demands on the neural functions (de Graaf-Peters and Hadders-Algra 2006). For example, some movement components for the acquisition of motor abilities showed a different trend in the development of preterm infants when compared to full-term infants, e.g., the onset for the acquisition of the extensor and flexor patterns was slower and the distribution of the load bearing was less mature at 2 and 3 months of age, but not before (Gaetan and Moura-Ribeiro2002). VLBW infants typically sit unsupported and walk later than full-term infants (Marin Gabriel et al. 2009). Moreover, higher weight and partly higher height have been identified as possible confounding factors increasing the risks of postural control problems (Evensen et al. 2004). A possible cause could be that the muscles produce lower strength, which may act as a limiting factor of activities involving the lower extremities (de Groot et al. 2012).

References

1. Abernethy LJ, Klafkowski G, Foulder-Hughes L, Cooke RW (2003) Magnetic resonance imaging and T2 relaxometry of cerebral white matter and hippocampus in children born preterm. Pediatr Res 54:868–874.

2. Abernethy LJ, Cooke RW, Foulder-Hughes L (2004) Caudate and hippocampal volumes, intelligence, and motor impairment in 7-year-old children who were born preterm. Pediatr Res 55:884–893.

3. Allin M, Matsumoto H, Santhouse AM et al (2001) Cognitive and motor function and the size of the cerebellum in adolescents born very pre-term. Brain 124:60–66

4. Assaiante C, Mallau S, Viel S, Jover M, Schmitz C (2005) Development of postural control in healthy children: a functional approach. Neural Plast 12:109–118. doi:10.1155/NP.2005.109 (discussion 263–172)

5. Atkinson J, Braddick O (2007) Visual and visuocognitive development in children born very prematurely. Prog Brain Res 164:123–149.

6. Aylward GP (2005) Neurodevelopmental outcomes of infants born prematurely. J Dev Behav Pediatr 26:427–440

7. Back SA, Luo NL, Borenstein NS, Levine JM, Volpe JJ, Kinney HC (2001) Late oligodendrocyte progenitors coincide with the developmental window of vulnerability for human perinatal white matter injury. J Neurosci 21:1302–1312

8. Bennett FC, Scott DT (1997) Long-term perspective on premature infant outcome and contemporary intervention issues. Semin Perinatol 21:190–201

9. Bhutta AT, Anand KJ (2002) Vulnerability of the developing brain. Neuronal mechanisms. Clin Perinatol 29:357–372

10. Boucard CC, Hernowo AT, Maguire RP, Jansonius NM, Roerdink JB, Hooymans JM, Cornelissen FW (2009) Changes in cortical grey matter density associated with long-standing retinal visual field defects. Brain 132:1898–1906.

11. Brandt T, Schautzer F, Hamilton DA et al (2005) Vestibular loss causes hippocampal atrophy and impaired spatial memory in humans. Brain 128:2732–2741.

12. Brodal P (1998) The central nervous system, structure and function. Oxford University Press, Oxford

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

14. de Graaf-Peters VB, Hadders-Algra M (2006) Ontogeny of the human central nervous system: what is happening when? Early Hum Dev 82:257–266.

15. de Groot S, Dallmeijer AJ, Bessems PJ, Lamberts ML, van der Woude LH, Janssen TW (2012) Comparison of muscle strength, sprint power and aerobic capacity in adults with and without cerebral palsy. J Rehabil Med 44:932–938.

16. de Kieviet JF, Piek JP, Aarnoudse-Moens CS, Oosterlaan J (2009) Motor development in very preterm and very low-birth-weight children from birth to adolescence: a meta-analysis. JAMA 302:2235–2242.

17. Eccles JC (1986) Learning in the motor system. Prog Brain Res 64:3–18

18. Eckert GU, Fortes Filho JB, Maia M, Procianoy RS (2012) A predictive score for retinopathy of prematurity in very low birth weight preterm infants. Eye (Lond) 26:400–406.

19. Eklund G (1973) Further studies of vibration-induced effects on balance. Ups J Med Sci 78:65–72

20. Evensen KA, Vik T, Helbostad J, Indredavik MS, Kulseng S, Brubakk AM (2004) Motor skills in adolescents with low birth weight. Arch Dis Child Fetal Neonatal Ed 89:F451–F455.

21. Evensen KA, Lindqvist S, Indredavik MS, Skranes J, Brubakk AM, Vik T (2009) Do visual impairments affect risk of motor problems in preterm and term low birth weight adolescents? Eur J Paediatr Neurol 13:47–56.

22. Fallang B, Hadders-Algra M (2005) Postural behavior in children born preterm. Neural Plast 12:175–182 (discussion 263–172)

23. Ferriero DM (2004) Neonatal brain injury. N Engl J Med 351:1985–1995.

24. Foulder-Hughes LA, Cooke RW (2003) Motor, cognitive, and behavioural disorders in children born very preterm. Dev Med Child Neurol 45:97–103

25. Fransson PA (2009) Adaptation of human postural control: learning, sensorimotor and analysis aspects. VDM, Saarbrücken

26. Fransson PA, Hafstrom A, Karlberg M, Magnusson M, Tjader A, Johansson R (2003) Postural control adaptation during galvanic vestibular and vibratory proprioceptive stimulation. IEEE Trans Biomed Eng 50:1310–1319

27. Fransson PA, Modig F, Patel M, Gomez S, 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.

28. Gaetan EM, Moura-Ribeiro MV (2002) Developmental study of early posture control in preterm and fullterm infants. Arq Neuropsiquiatr 60:954–958

29. Georgsdottir I, Erlingsdottir G, Hrafnkelsson B, Haraldsson A, Dagbjartsson A (2012) Disabilities and health of extremely low-birthweight teenagers: a population-based study. Acta Paediatr 101:518–523.

30. Georgsdottir I, Haraldsson A, Dagbjartsson A (2013) Behavior and well-being of extremely low birth weight teenagers in Iceland. Early Hum Dev 89:999–1003.

31. Goodwin GM, McCloskey DI, Matthews PB (1972) The contribution of muscle afferents to kinaesthesia shown by vibration induced illusions of movement and by the effects of paralysing joint afferents. Brain 95:705–748

32. Goyen TA, Lui K, Woods R (1998) Visual-motor, visual-perceptual, and fine motor outcomes in very-low-birthweight children at 5 years. Dev Med Child Neurol 40:76–81

33. Halsey CL, Collin MF, Anderson CL (1996) Extremely low-birth-weight children and their peers: a comparison of school-age outcomes. Arch Pediatr Adolesc Med 150:790–794

34. Horak FB, Nashner LM (1986) Central programming of postural movements: adaptation to altered support-surface configurations. J Neurophysiol 55:1369–1381

35. Huttenlocher PR, Dabholkar AS (1997) Regional differences in synaptogenesis in human cerebral cortex. J Comp Neurol 387:167–178.

36. Johansson R, Magnusson M (1991) Human postural dynamics. Crit Rev Biomed Eng 18:413–437

37. Johansson R, Magnusson M, Akesson M (1988) Identification of human postural dynamics. IEEE Trans Biomed Eng 35:858–869

38. Johansson R, Fransson PA, Magnusson M (2009) Optimal coordination and control of posture and movements. J Physiol Paris 103:159–177.

39. Jonsdottir GM, Georgsdottir I, Haraldsson A, Hardardottir H, Thorkelsson T, Dagbjartsson A (2012) Survival and neurodevelopmental outcome of ELBW children at 5 years of age: comparison of two cohorts born 10 years apart. Acta Paediatr 101:714–718.

40. Kanold PO (2009) Subplate neurons: crucial regulators of cortical development and plasticity. Front Neuroanat 3:16.

41. Kanold PO, Kara P, Reid RC, Shatz CJ (2003) Role of subplate neurons in functional maturation of visual cortical columns. Science 301:521–525.

42. Keshner EA, Allum JH, Pfaltz CR (1987) Postural coactivation and adaptation in the sway stabilizing responses of normals and patients with bilateral vestibular deficit. Exp Brain Res 69:77–92

43. Kluenter H, Roedder D, Kribs A, Fricke O, Roth B, Guntinas-Lichius O (2008) Postural control at 7 years of age after preterm birth with very low birth weight. Otol Neurotol 29:1171–1175.

44. Kovacic P, Somanathan R (2008) Ototoxicity and noise trauma: electron transfer, reactive oxygen species, cell signaling, electrical effects, and protection by antioxidants: practical medical aspects. Med Hypotheses 70:914–923.

45. Kristinsdottir EK, Fransson PA, Magnusson M (2001) Changes in postural control in healthy elderly subjects are related to vibration sensation, vision and vestibular asymmetry. Acta Otolaryngol 121:700–706

46. Le TT, Kapoula Z (2008) Role of ocular convergence in the Romberg quotient. Gait Posture 27:493–500.

47. Lockhart DB, Ting LH (2007) Optimal sensorimotor transformations for balance. Nat Neurosci 10:1329–1336.

48. Maalouf EF, Duggan PJ, Rutherford MA et al (1999) Magnetic resonance imaging of the brain in a cohort of extremely preterm infants. J Pediatr 135:351–357

49. Mallard C, Loeliger M, Copolov D, Rees S (2000) Reduced number of neurons in the hippocampus and the cerebellum in the postnatal guinea-pig following intrauterine growth-restriction. Neuroscience 100:327–333

50. Marin Gabriel MA, Pallas Alonso CR, De La Cruz Bertolo J et al (2009) Age of sitting unsupported and independent walking in very low birth weight preterm infants with normal motor development at 2 years. Acta Paediatr 98:1815–1821.

51. Modig F, Patel M, Magnusson M, Fransson PA (2012) Study I: effects of 0.06 % and 0.10 % blood alcohol concentration on human postural control. Gait Posture 35:410–418.

52. O'Callaghan MJ, Burns YR, Gray PH, Harvey JM, Mohay H, Rogers YM, Tudehope DI (1996) School performance of ELBW children: a controlled study. Dev Med Child Neurol 38:917–926

53. Paneth NS (1995) The problem of low birth weight. Future Child 5:19–34

54. Patel M, Gomez S, Berg S et al (2008) Effects of 24-h and 36-h sleep deprivation on human postural control and adaptation. Exp Brain Res 185:165–173

55. Patel M, Magnusson M, Kristinsdottir E, Fransson PA (2009) The contribution of mechanoreceptive sensation on stability and adaptation in the young and elderly. Eur J Appl Physiol 105:167–173.

56. Perlman JM (2003) The genesis of cognitive and behavioral deficits in premature graduates of intensive care. Minerva Pediatr 55:89–101

57. Petersen H, Magnusson M, Johansson R, Akesson M, Fransson PA (1995) Acoustic cues and postural control. Scand J Rehabil Med 27:99–104

58. Peterson BS, Vohr B, Staib LH et al (2000) Regional brain volume abnormalities and long-term cognitive outcome in preterm infants. JAMA 284:1939–1947

59. Popov K, Lekhel H, Bronstein A, Gresty M (1996) Postural responses to vibration of neck muscles in patients with unilateral vestibular lesions. Neurosci Lett 214:202–204

60. Powls A, Botting N, Cooke RW, Stephenson G, Marlow N (1997) Visual impairment in very low birthweight children. Arch Dis Child Fetal Neonatal Ed 76:F82–F8

61. Redfern M, Jennings J, Martin C, Furman J (2001) Attention influences sensory integration for postural control in older adults. Gait Posture 14(3):211–216

62. Riccio GE, Stoffregen TA (1988) Affordances as constraints on the control of stance. Hum Mov Sci 7:265–300

63. Ritchie K, McClure G (1979) Prematurity. Lancet 2:1227–1229

64. Samsom JF, de Groot L (2001) Study of a group of extremely preterm infants (25–27 weeks): how do they function at 1 year of age? J Child Neurol 16:832–837

65. Samsom JF, de Groot L, Bezemer PD, Lafeber HN, Fetter WP (2002) Muscle power development during the first year of life predicts neuromotor behaviour at 7 years in preterm born high-risk infants. Early Hum Dev 68:103–118

66. Schmidt B, Asztalos EV, Roberts RS, Robertson CM, Sauve RS, Whitfield MF (2003) Impact of bronchopulmonary dysplasia, brain injury, and severe retinopathy on the outcome of extremely low-birth-weight infants at 18 months: results from the trial of indomethacin prophylaxis in preterms. JAMA 289:1124–1129

67. Skranes J, Vangberg TR, Kulseng S et al (2007) Clinical findings and white matter abnormalities seen on diffusion tensor imaging in adolescents with very low birth weight. Brain 130:654–666.

68. Sommerfelt K, Ellertsen B, Markestad T (1993) Personality and behaviour in eight-year-old, non-handicapped children with birth weight under 1500 g. Acta Paediatr 82:723–728

69. Taylor HG, Klein N, Minich NM, Hack M (2000) Middle-school-age outcomes in children with very low birthweight. Child Dev 71:1495–1511

70. Tjernstrom F, Fransson PA, Hafstrom A, Magnusson M (2002) Adaptation of postural control to perturbations—a process that initiates long-term motor memory. Gait Posture 15:75–82

71. Tolcos M, Bateman E, O’Dowd R, Markwick R, Vrijsen K, Rehn A, Rees S (2011) Intrauterine growth restriction affects the maturation of myelin. Exp Neurol 232:53–65.

72. van Lunenburg A, van der Pal SM, van Dommelen P, van der Pal-de Bruin KM, Bennebroek Gravenhorst J, Verrips GH (2013) Changes in quality of life into adulthood after very preterm birth and/or very low birth weight in the Netherlands. Health Qual Life Outcomes 11:51.

Torque	***p* values**		
Quiet stance	**ELBW**	**Vision**	**ELBW × vision**
Anteroposterior			
Total	**0.007 [7.8]**	**0.033 [4.8]**	0.794 [0.1]
<0.1 Hz	**0.018 [6.0]**	0.403 [0.7]	0.247 [1.4]
>0.1 Hz	**0.022 [5.6]**	**<0.001 [30.2]**	0.170 [1.9]
Lateral			
Total	***0.055 [3.9]***	0.646 [0.2]	0.198 [1.7]
<0.1 Hz	0.418 [0.7]	***0.068 [3.5]***	0.966 [0.0]
>0.1 Hz	**0.009 [7.3]**	0.236 [1.4]	***0.057 [3.8]***

Table 1: Statistical evaluation of torque variance values, reflecting the energy used during quiet stance toward the supporting surface, comparing subjects born with ELBW with controls. The notation "<0.001" means that the *p* value is smaller than 0.001. Values in bold show *p* values <0.05, and values in bold italic show *p* values <0.1. *F* values are presented within the squared parenthesis. The interaction values between main factors ELBW and vision are presented in the column denoted ELBW × vision

Torque variance	***p* values**[#]			
Balance perturbations	**ELBW**	**Vision**	**Period**	**Vision × period**
Anteroposterior				
Total	**0.007 [8.0]**	**<0.001 [62.0]**	**<0.001 [29.3]**	***0.097 [2.9]***
<0.1 Hz	***0.069 [3.5]***	**0.043 [4.3]**	**<0.001 [28.2]**	0.275 [1.2]
>0.1 Hz	**0.003 [9.7]**	**<0.001 [97.3]**	**<0.001 [18.1]**	**0.036 [4.7]**
Lateral				
Total	**0.013 [6.7]**	**<0.001 [26.9]**	0.386 [0.8]	0.339 [0.9]
<0.1 Hz	0.397 [0.7]	***0.099 [2.8]***	0.133 [2.3]	0.648 [0.2]
>0.1 Hz	**<0.001 [12.4]**	**<0.001 [87.9]**	0.475 [0.5]	***0.092 [3.0]***

Table 2: Statistical evaluation of torque variance values during balance perturbations comparing subjects born with ELBW with controls[#] The repeated-measures GLM ANOVA interaction combinations not presented contained no significant results or trends. The interaction values between main factors vision and period are presented in the column denoted Vision × period

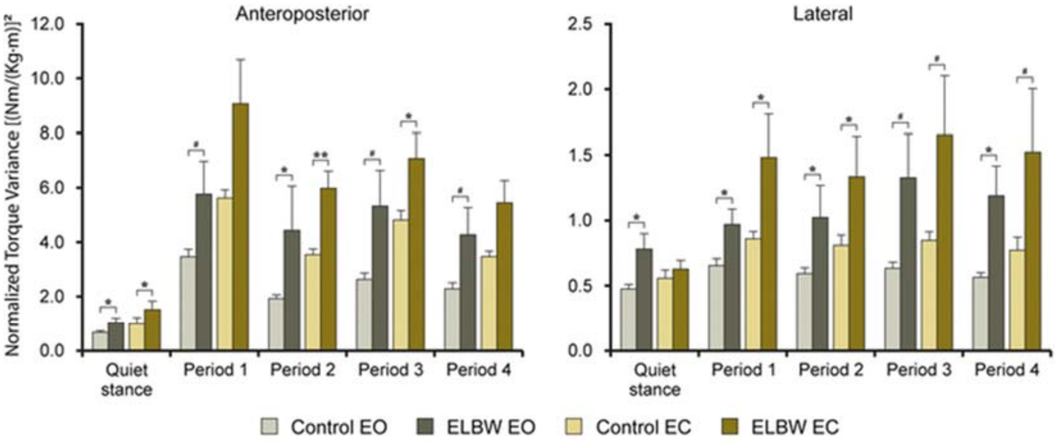
Torque variance	***p* values**$^{\#}$					
	Eyes closed			**Eyes open**		
Balance perturbations	**ELBW**	**Period**	**ELBW × period**	**ELBW**	**Period**	**ELBW × period**
Anteroposterior						
Total	**0.017 [6.1]**	**<0.001 [23.3]**	0.308 [1.1]	**0.013 [6.7]**	**0.002 [11.3]**	0.443 [0.6]
<0.1 Hz	0.119 [2.5]	**<0.001 [14.0]**	0.113 [2.6]	0.100 [2.8]	**<0.001 [17.1]**	0.483 [0.5]
>0.1 Hz	**0.012 [6.8]**	**<0.001 [20.0]**	0.423 [0.7]	**0.006 [8.2]**	***0.063 [3.6]***	0.236 [1.4]
Lateral						
Total	**0.030 [5.0]**	0.242 [1.4]	0.528 [0.4]	**0.011 [7.0]**	0.654 [0.2]	0.309 [1.1]
<0.1 Hz	0.593 [0.3]	0.276 [1.2]	0.269 [1.3]	0.282 [1.2]	0.246 [1.4]	0.835 [0.0]
>0.1 Hz	**0.004 [9.1]**	0.172 [1.9]	0.557 [0.4]	**<0.001 [12.8]**	0.478 [0.5]	0.337 [0.9]

Table 3: Statistical evaluation of torque variance values during balance perturbations, analyzing separately the data from tests standing with eyes closed and eyes open $^{\#}$**The interaction values between main factors ELBW and period are presented in the column denoted ELBW × period**

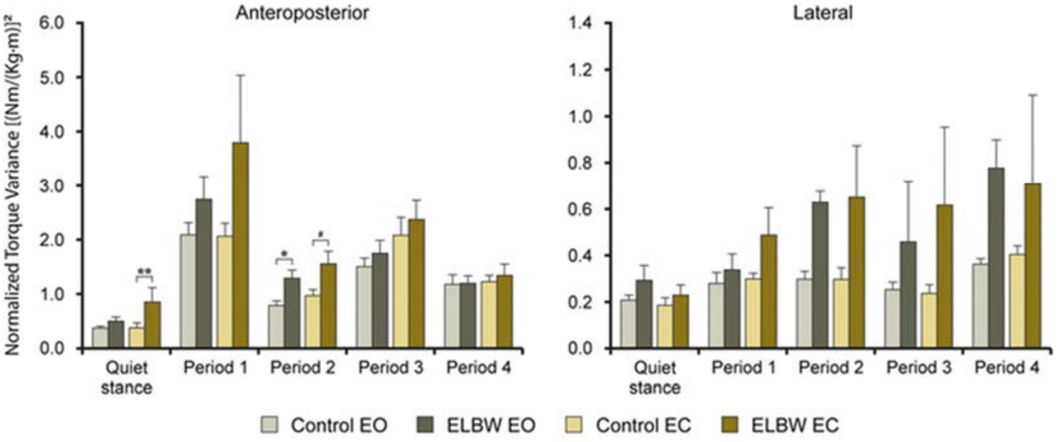
Table 4 Statistical differences and the torque variance changes in percent found between vibration period 1 and vibration period 4 with eyes closed and eyes open for subjects born with ELBW and for controls. The changes in percentage are presented within the squared parenthesis, where (−) represent a reduction of the energy used over time and (+) an increase over time. The tables present the statistical findings made in the post hoc evaluation of the main factor period

P1 versus P4	**Eyes closed**	**Eyes open**
Anteroposterior adaptation		
Controls		
Total	**<0.001 [−38 %]**	**0.007 [−34 %]**
<0.1 Hz	**0.014 [−41 %]**	**0.023 [−44 %]**
>0.1 Hz	**<0.001 [−38 %]**	**0.010 [−23 %]**
ELBW		
Total	**0.001 [−40 %]**	**0.002 [−26 %]**
<0.1 Hz	**<0.001 [−65 %]**	**<0.001 [−56 %]**
>0.1 Hz	**0.008 [−23 %]**	**0.004 [−1 %]**
Lateral adaptation		
Controls		
Total	0.166 [−10 %]	0.176 [−14 %]
<0.1 Hz	0.276 [−12 %]	0.325 [−27 %]
>0.1 Hz	0.100 [−12 %]	0.627 [−2 %]
ELBW		
Total	0.666 [+3 %]	0.882 [+23 %]
<0.1 Hz	0.339 [+37 %]	0.481 [+11 %]
>0.1 Hz	0.766 [−14 %]	0.498 [+22 %]

A Total Torque Variance



B Low Frequency Torque Variance <0.1 Hz.



C High Frequency Torque Variance >0.1 Hz.

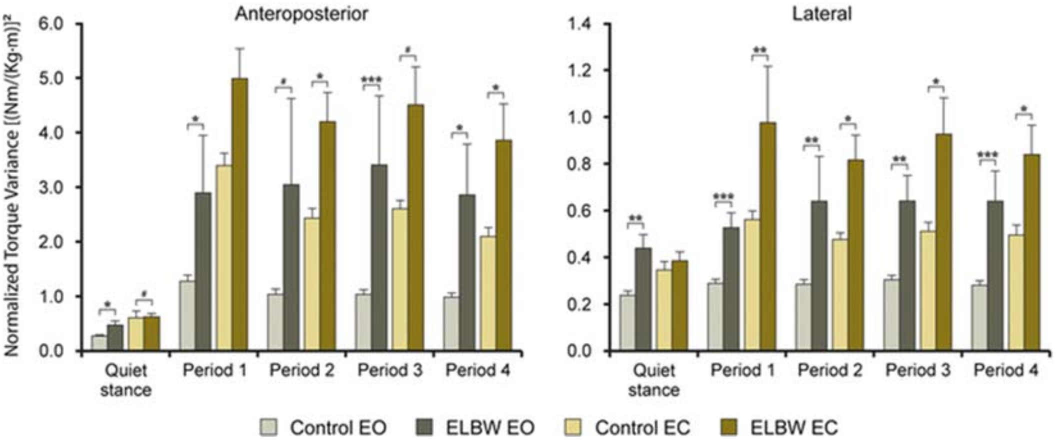


Figure 1: Anthropometrical height and mass-normalized values for a total torque variance, b low-frequency torque variance and c high-frequency torque variance with eyes closed and eyes open (mean and SEM) for subjects born with ELBW (*n* = 29) and for controls (*n* = 21). The figures present the statistical findings made in the repeated-measures GLM ANOVA post hoc evaluation of the main factor ELBW. $^{\#}$ *p* < 0.1 (trends), **p* < 0.05, ***p* < 0.01 and ****p* < 0.001