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Original Article

Advanced sleep–wake rhythm in adults born prematurely: confirmation by actigraphy-based assessment in the Helsinki Study of Very Low Birth Weight Adults

Johan Björkqvist [a,c,*], Juulia Paavonen [b,c], Sture Andersson [a], Anu-Katriina Pesonen [d], Jari Lahti [d], Kati Heinonen [d], Johan Eriksson [c,e,f,g,h], Katri Räikkönen [d], Petteri Hovi [a,c], Eero Kajantie [a,c], Sonja Strang-Karlsson [a,c]

[a] Children's Hospital, Helsinki University Central Hospital and University of Helsinki, Helsinki, Finland
[b] Child Psychiatry, Helsinki and Uusimaa Hospital District, Helsinki, Finland
[c] National Institute for Health and Welfare, Helsinki, Finland
[d] Institute of Behavioural Sciences, University of Helsinki, Helsinki, Finland
[e] Department of General Practice and Primary Health Care, University of Helsinki, Helsinki, Finland
[f] Vasa Central Hospital, Vasa, Finland
[g] Unit of General Practice, Helsinki, Finland
[h] Folkhälsan Research Centre, Helsinki, Finland

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ABSTRACT

Objective: Previous studies have suggested a propensity towards morningness in teenagers and adults born preterm. We set out to study sleep in a subsample from The Helsinki Study of Very Low Birth Weight Adults cohort, with emphasis on sleep timing, duration, and quality. We compared young adults who were born prematurely at very low birth weight (VLBW; <1500 g) with controls born at term.
Methods: We measured sleep by actigraphy in young adults aged 21–29 years. A total of 75 individuals (40 VLBW and 35 controls) provided adequate data. Group differences in sleep parameters were analyzed using *t*-test and linear regression models.
Results: VLBW adults woke up on average 40 min earlier [95% confidence interval (CI), 9–70] and reported 40 min earlier get up time (95% CI, 8–71) than did the controls. The difference remained after adjustment for confounders. We found no group difference in sleep duration or measures of sleep quality.
Conclusion: Our findings of earlier rising in the VLBW group are suggestive of an advanced sleep phase in that group. These results reinforce previous suggestions that chronotype may be programmed early during life.

1. Introduction

About 0.8–1.5% of children born in developed countries today are born prematurely (<37 completed weeks of gestation) with very low birth weight (VLBW; <1500 g) [1,2]. In earlier decades, being born preterm with VLBW implied a low chance of survival. For example, in the 1960s, only about half of live-born VLBW infants in industrialized countries survived, whereas 85–90% do so today [1,3,4]. This is mainly due to the remarkable advances witnessed in modern neonatal intensive care from the 1970s onwards, such as improvements in ventilation strategies and introduction of antenatal glucocorticoids and surfactant. Therefore there is today a considerable number of young adults who were born with VLBW and whose health prospects may differ from those of individuals born at term.

Previous studies indicate that some mental health problems such as symptoms of depression and attention deficit/hyperactivity disorder (ADHD) are more common among people born preterm or subgroups of them [5–8]. Differences regarding somatic health have also been described, eg higher levels of insulin resistance [9] and blood pressure [9–11].

Abnormalities in sleep are linked to many of the aforementioned conditions associated with prematurity, including ADHD, insulin resistance, hypertension, and depression [12–15]. The question arises whether sleep characteristics of ex-preterms differ from those of term-borns. If they do differ, this could be a link between preterm birth and prematurity-associated health sequelae. Whereas sleep of ex-preterms during early childhood has been studied to some extent, yielding somewhat discrepant results [16–19], only a few

* Corresponding author at: National Institute for Health and Welfare, Department of Chronic Disease Prevention, PL 30, 00271 Helsinki, Finland. Tel.: +35829 524 6000.
E-mail address: johan.bjorkqvist@helsinki.fi (J. Björkqvist).

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studies range beyond early childhood [20], not to mention adulthood [21].

In our previous study performed in 2004–2005 [21] using actigraphy and questionnaires, it was found that VLBW adults went to bed earlier than their term-born control group. That was a post-hoc finding and we set out to confirm this in a prospective setting. We subsequently reported that adults born with VLBW have a propensity towards morningness, a trait indicating personal preference for an early rhythm [22]. The current follow-up study aimed to further validate our earlier findings in a somewhat different subsample, and with improvements in methodology. We used actigraphy to assess sleep timing, sleep duration, and sleep quality. We hypothesized that VLBW adults, as compared with term-born controls, would show signs of an earlier sleep phase.

2. Methods

2.1. Participants

The Helsinki Study of Very Low Birth Weight Adults is a case–control cohort study that has been described in detail previously [9]. The original cohort consisted of 335 VLBW children treated in the neonatal intensive care unit (NICU) of the Children's Hospital at Helsinki University Central Hospital between January 1978 and December 1985. In 2003, we traced the original VLBW cohort using the National Population Register, and invited to a clinical study those 255 individuals (76%) who were still living in the greater Helsinki area. A comparison group of 314 individuals was formed, consisting of the next singleton, term-born (gestational age ≥37 weeks), same-sex, non-SGA child born in the same hospital after each corresponding VLBW birth.

All these individuals (255 VLBW and 314 term-born controls) were invited to participate in a first clinical study, consisting of extensive cardiovascular and metabolic assessments and detailed questionnaires regarding medical history, mental health, socio-economic characteristics, and physical activity. This examination was performed in the years 2004–2005 and was completed by 338 individuals (166 VLBW, 65% of those invited; and 172 term controls, 55% of those invited).

Several results from this first clinical study have been published, eg data on blood pressure [9,23], glucose regulation and insulin resistance [9], symptoms of depression [7] and attention deficit/hyperactivity disorder [8], cognitive functions [24,25], and personality [26]. In addition, data on sleep quality and sleep duration, by means of actigraphy and questionnaire, have been reported [21,27].

During 2007–2008, a follow-up study was performed. Of the previous 338 participants, 11 lived abroad, four refused to be contacted again, one person was developmentally delayed, two could not be traced, and seven did not fulfil the inclusion criteria for an intravenous glucose tolerance test that was performed in conjunction with the follow-up, leaving 313 persons who were eligible and invited. Of these 313 persons, 218 (69.6%) participated (113 VLBW, 105 controls).

In conjunction with this follow-up examination, an actigraphy-based sleep study was again conducted within a subsample. All 218 participants were offered an actigraph if there was one available at the time, resulting in 116 individuals who were asked to take part in the actigraphy study. Of these 116 individuals, 106 produced 1 or more nights of actigraphy data (57 VLBW, 49 controls). A total of 48 participants (33 VLBW and 15 controls) participated in both the original actigraphy study 2004–2005 and the follow-up actigraphy study 2007–2008.

There were no statistically significant differences in the perinatal and young adult characteristics presented in Table 1 between the participants in the actigraphy study and those who participated in the rest of the second clinical examination, except regarding employment; the actigraphy participants were more likely to be in paid employment ($P = 0.011$) both in the VLBW group and the control group. Each participant gave written informed consent to this study, which was approved by the local ethics committee and was carried out according to the Declaration of Helsinki.

Table 1
Characteristics of the VLBW and control groups.

Variable	VLBW ($n = 40$)	Control group ($n = 35$)	*P*-value
	Mean (SD)	Mean (SD)	
Birthweight (g)	1096 (224)	3640 (514)	<0.001[a]
Gestational age (weeks)	29.2 (2.5)	40.0 (1.2)	<0.001[a]
Relative birthweight SD[b]	−1.4 (1.6)	0.23 (1.1)	<0.001[a]
Singleton pregnancy, *n* (%)	35 (87.5)	35 (100)	0.030[c]
SGA[b], *n* (%)	15 (37.5)	0 (0.0)	<0.001[c]
Maternal pre-eclampsia, *n* (%)	7 (17.5)	2 (5.7)	0.12[c]
Maternal smoking during pregnancy, *n* (%)	7 (18.9)	6 (17.1)	0.85[c]
Firstborn, *n* (%)	16 (41.0)	15 (42.9)	0.87[c]
Caesarean, *n* (%)	22 (56.4)	4 (11.4)	<0.001[c]
Daily smoking, *n* (%)	6 (15.0)	8 (22.9)	0.38[c]
Using antidepressants, *n* (%)	6 (15.0)	1 (2.9)	0.071[c]
Paid employment, *n* (%)	25 (62.5)	16 (45.7)	0.15[c]
Men, *n* (%)	15 (37.5)	7 (20.0)	0.097[c]
Age during study (years)	25.0 (2.1)	24.9 (2.2)	0.81[a]
Body mass index (kg/m^2)	23.1 (4.1)	24.1 (5.3)	0.35[a]
Parental education			0.18[c]
Elementary school, *n* (%)	5 (12.5)	2 (5.7)	
High school level, *n* (%)	14 (35.0)	6 (17.1)	
Intermediate level, *n* (%)	7 (17.5)	10 (28.6)	
University degree, *n* (%)	14 (35.0)	17 (48.6)	

VLBW, very low birthweight; SD, standard deviation; SGA, small for gestational age. Missing data for the following variables: maternal smoking during pregnancy ($n = 3$), firstborn ($n = 1$), caesarean ($n = 1$).

[a] *t*-Test.

[b] Relative birthweight is given in SD units, e.g. SGA (small for gestational age) = birthweight below −2 SD of the Finnish mean after adjusting for sex and gestational age.

[c] χ^2-Test.

2.2. Actigraphy

For sleep measurement we used actigraphy (Actiwatch AW4 model, Cambridge Neurotechnology Ltd, Papworth Everard, UK). An actigraph is an accelerometer that looks like a wristwatch and is usually worn on the non-dominant wrist. The actigraph recognizes movement with piezoelectric beams and stores the information digitally. When connected to a computer thereafter, the recorded movement data can be analyzed. In this study the data were analyzed with the algorithm incorporated in the Actiwatch Activity & Sleep Analysis V 5.42 software [28], to determine whether the participant was asleep or awake during a certain epoch. High frequency of movement within an epoch is indicative of wakefulness, that is, if the activity count exceeds a predefined threshold value the epoch is scored as wake. If the activity level does not surpass the threshold during several consecutive epochs, the wearer is considered to be asleep. The threshold sensitivity can be further regulated within the program's sensitivity setting. The validity of actigraphy, as compared with the "gold standard" in sleep research – polysomnography – has been shown to be good in several studies, producing epoch-by-epoch sleep–wake agreement rates of >90% [29–32]. Despite the possible limitations of actigraphy when it comes to detection of sleep start [33], actigraphy is good at detecting activity changes, which suffices to be of interest when studying circadian phase changes.

The participants kept a sleep diary in which they reported when the actigraph was not worn (when showering, etc.) and when they