Sleep and Lipid Profile During Transition from Childhood to Adolescence

Liisa Kuula, MA[1], Anu-Katriina Pesonen, PhD[1], Eero Kajantie, MD, PhD[2,3,4], Jari Lahti, PhD[1,5,6], Sture Andersson, MD, PhD[2], Timo Strandberg, MD, PhD[7,8], and Katri Räikkönen, PhD[1]

Objectives To assess the longitudinal effects of sleep duration and quality on lipid profiles during the transition from childhood to early adolescence, over a 4-year-period.

Study design A cohort study of children born in 1998 examined at 8 years of age (SD, 0.3; n = 105) and 12 years of age (SD, 0.5; n = 190). Sleep duration, wake after sleep onset, sleep efficiency, and weekend catch-up sleep were measured with actigraphs for 7 (8 years of age) and 8 (12 years of age) nights. Fasting serum samples were collected at 12 years of age. Covariates included age, pubertal development, socioeconomic status, body mass index, and physical activity.

Results In girls, shorter sleep duration at 8 and 12 years of age was associated with lower high-density lipoprotein-cholesterol and higher triglycerides at 12 years of age. Poorer sleep quality at 8 years of age and longer weekend catch-up sleep at 12 years of age was associated with higher triglycerides at 12 years of age. From 8 to 12 years of age, improvement in sleep quality associated with higher total cholesterol, and a decrease in sleep duration with lower lipid levels. In boys, longer sleep duration at 8 years of age, and a larger decrease in sleep duration from 8 to 12 years of age was associated with higher levels of triglycerides at 12 years of age.

Conclusions Poorer sleep during transition to early adolescence is associated with an atherogenic lipid profile in early adolescent girls, and such effects are less prominent in boys. Poor sleep may have long-term associations with health, which are not mitigated by the amount of physical activity. *(J Pediatr 2016;177:173-8).*

Sleep and health are intertwined already in childhood. Short sleep and poor sleep quality are associated with overweight and obesity,[1,2] increased mental health problems,[3,4] and adverse neuroendocrine changes[5] in children, and toward adolescence, risks related to cardiometabolic disease begin to emerge.[6-9]

To understand the mechanisms underlying the relationships between sleep and somatic health outcomes, more information is needed to clarify the developmental trajectories of these associations from childhood to adolescence. In particular, it is not yet well-known how sleep quantity and sleep quality over the transition from childhood to adolescence are associated with metabolic risk factors.

With regard to cross-sectional findings, one study reported that longer sleep duration as measured objectively with actigraphy had a beneficial effect on overall lipid metabolism in a community cohort of children aged 4-10 years, one-half of whom were overweight or obese.[10] Shorter sleep duration, especially in the presence of irregular sleep patterns, was associated with higher plasma fasting insulin, low-density lipoprotein cholesterol (LDL-C), and C-reactive protein concentrations. Some studies including children and adolescents with more healthy body mass indices (BMI), have not found associations between objectively measured sleep and lipids.[11,12] Conclusions of the existing cross-sectional studies are, however, unclear because many studies have not measured sleep objectively[13-15] or include a large age variation between the participants.[10]

The few longitudinal studies have indicated that sleep patterns in childhood have far-reaching effects on other indicators of metabolic risks: one study reported that persistently short sleep duration during childhood increased the risk to become obese or overweight by up to 4.2-fold,[2] and another reported that children with continuously insufficient sleep duration from infancy to school age had higher metabolic risk scores.[16] However, to our knowledge no previous study has reported the longitudinal impact of sleep on lipid metabolism using objectively measured sleep in this age group.

BMI	Body mass index
HDL-C	High-density lipoprotein cholesterol
WASO	Wake after sleep onset
LDL-C	Low-density lipoprotein cholesterol
TC	Total cholesterol
TGs	Triglycerides

From the [1]Institute of Behavioral Sciences, University of Helsinki, Finland; [2]Children's Hospital, Helsinki University Hospital, University of Helsinki, Helsinki, Finland; [3]Chronic Disease Prevention Unit, National Institute for Health and Welfare, Helsinki, Finland; [4]Department of Obstetrics and Gynecology, MRC Oulu, Oulu University Hospital, University of Oulu, Oulu, Finland; [5]Helsinki Collegium for Advanced Studies, University of Helsinki, Helsinki, Finland; [6]Folkhälsan Research Centre, Helsinki, Finland; [7]University of Helsinki, Helsinki University Central Hospital, Helsinki, Finland; and [8]Center for Life Course Epidemiology and Systems Medicine, University of Oulu, Oulu, Finland

Supported by Academy of Finland (1287174), PsyCo Doctoral Programme, Päivikki and Sakari Sohlberg Foundation, Finska Läkaresällskapet, University of Helsinki, Emil Aaltonen Foundation, Foundation for Pediatric Research, Juho Vainio Foundation, Novo Nordisk Foundation, Signe and Ane Gyllenberg Foundation, Sigrid Juselius Foundation, The Paulo Foundation, Helsinki University Central Hospital. The authors declare no conflicts of interest.

Portions of the study were presented at the Congress of the European Sleep Research Society, Bologna, Italy, September 13-16, 2016.

http://dx.doi.org10.1016/j.jpeds.2016.06.026

We investigated the longitudinal effects of actigraphy-measured sleep duration and quality on lipid profiles during the transition from childhood to early adolescence over a 4-year period. Additionally, we examined the associations between irregular sleep patterns and lipid profiles; previous studies have reported that sleep irregularity increases risks related to health outcomes.[10,17]

Methods

Participants came from an urban community-based cohort composed of 1049 healthy singletons born between March and November 1998 in Helsinki, Finland.[18] Details are described in previous reports.[19,20] In 2006 (at 8 years of age), we invited a subsample of the initial cohort members who had given permission to be included in a follow-up and who were traceable (n = 413 invited, n = 321 participated [77%]; 164 girls and 157 boys; mean age, 8.1 years [SD, 0.3; range, 7.4-8.9]). This subsample was weighted on mothers who in pregnancy consumed more glycyrrhizin (which inhibits placental 11β-HSD2 function) in the form of licorice.[20] Of the 321 participants, 297 (92.5%) took part in the sleep measurement, of whom 296 had valid sleep measurements on a minimum of 3 nights, and of them, valid fasting blood serum samples at 12 years of age were available from 105 participants (35%). The Ethics Committees of the City of Helsinki Health Department and Children's Hospital in Helsinki University Central Hospital approved the study protocol. Each child and her or his parent(s) provided their written informed consent at both follow-up visits.

In 2009-2011 (at 12 years of age), all the initial cohort members (n = 1049) who had given permission to be contacted and whose addresses were traceable (n = 920; 87.7% of the original cohort) were invited to a follow-up, of which 692 (75.2%) could be contacted by phone (mothers of the adolescents). Of them, 451 (234 girls and 217 boys; 49% of the invited; 65.2% of the contacted) participated in a follow-up at a mean age of 12.3 years (SD, 0.5; range, 11.0-13.2). Of the 451 participants, 362 (80%) took part in the sleep measurement, of whom 358 (79%) had valid sleep measurement on a minimum of 3 nights. Of them, valid fasting blood serum samples were available from 190 participants (53%).

Complete sleep actigraphy data from both the 8 and 12 years of age measurement points were available for 188 adolescents (99 girls, 89 boys; 64% of those with valid actigraphy data from 8 years of age), and of these, fasting serum sample data from 95 (50 girls, 45 boys). Thus, our analytical sample consisted of 190 in cross-sectional analyses at 12 years of age and 105 in longitudinal analyses associating sleep at 8 years of age and lipids at 12 years of age (note that 10 of these participants in the longitudinal sample did not have complete sleep data at both ages 8 and 12 years of age and lipids at 12 years of age, allowing the analyses of change in sleep).

The cross-sectional sample (n = 190) did not differ (all $P \geq .06$) from the rest of the participants at 12 years of age in BMI, age, mother's BMI, mother's age at birth, gestation age, maternal alcohol consumption, length at birth, birthweight, physical activity, pubertal development, socioeconomic status, or maternal licorice consumption. With regard to the initial cohort, there were no differences (all $P \geq 0.11$) in mother's BMI, mother's age at birth, maternal licorice consumption, maternal alcohol consumption, gestation age, length at birth, and birthweight.

The longitudinal sample with sleep measurements and lipid profiles available did not differ (all $P \geq .09$) from the rest of the sample at 8 years of age in age, mother's age at birth, mother's BMI, gestation age, length at birth, birth weight, physical activity, and maternal licorice consumption. They differed in 4 respects: the current sample had higher BMI ($P = .035$), higher socioeconomic status ($P = .03$), more advanced pubertal status ($P = .04$), and had mothers who reported lower levels of alcohol consumption ($P = .04$) than the rest of the sample at 8 years of age. With regard to the initial cohort there were no differences (all $P \geq .07$) in BMI, mother's age at birth, maternal licorice consumption, gestation age, length at birth, and birthweight, but differed in that their mothers reported lower levels of alcohol consumption ($P = .04$).

Sleep duration and quality were objectively measured using actigraphs (Actiwatch AW4 and AW7, CamNtech Ltd, Cambridge, United Kingdom). During the sleep registration period some of the participants took part in a very low dose overnight dexamethasone suppression test[21]; the night after dexamethasone intake at bedtime was excluded from sleep analysis, and serum samples were not collected at this time. Sleep was measured for an average of 7 nights at 8 years of age (SD, 1.2; range, 3-14) and 8 nights at 12 years of age (SD, 1.8; range 3-10). The measurement periods included both weekday nights (8 years of age: mean, 5.1 nights [SD, 1.0; range, 1-10]; 12 years of age: mean, 5.9 nights [SD, 1.5; range, 1-9]) and weekend nights (8 years of age: mean, 2 nights [SD, 0.4; range, 1-4]; 12 years of age: mean, 2 nights [SD, 1.0; range, 0-4]).

Sleep duration refers to actual sleep time and was determined by the actigraph algorithm. Wake after sleep onset (WASO) time was defined as the amount of minutes when actual sleep time is subtracted from the assumed sleep. Sleep efficiency was defined as the ratio between actual sleep time and time in bed. Irregular sleep patterns were operationalized as the amount of catch-up sleep (calculated as the subtraction of weekday nights' sleep duration from weekend nights' sleep duration) during the weekend. Longer catch-up sleep is assumed to be an indicator of cumulative sleep debt from weekdays. The scoring was carried out as reported previously.[19] Additionally, change variables were calculated as the subtraction of sleep variables at 12 years of age from 8 years of age, resulting in units that directly reflect the size of decrease of either sleep duration, or sleep quality as measured by WASO over time: the larger the change in duration, the more sleep duration decreases, and, the greater the change in WASO the more sleep quality improves.

Blood samples were collected at a clinical visit between 8:00 a.m. and 10:00 a.m. after an overnight fast. Serum total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C) and LDL-C, and triglycerides (TGs) were analyzed in the clinical laboratory of Helsinki University Hospital.

Covariates measured in conjunction with sleep measurements and the clinical visit at 12 years of age include age, BMI