An unfavorable lifestyle and recurrent headaches among adolescents : The HUNT Study

L. Robberstad, G. Dyb, K. Hagen, et al.

Neurology 2010;75;712; Published online before print August 18, 2010;
DOI 10.1212/WNL.0b013e3181eee244

An unfavorable lifestyle and recurrent headaches among adolescents

The HUNT Study

L. Robberstad, Stud.med
G. Dyb, MD, PhD
K. Hagen, MD, PhD
L.J. Stovner, MD, PhD
T.L. Holmen, MD, PhD
J.-A. Zwart, MD, PhD

Address correspondence and reprint requests to Dr. John-Anker Zwart, Department of Neurology, Oslo University Hospital, Ullevål, 0450 Oslo, Norway
j.a.zwart@medisin.uio.no

ABSTRACT

Objectives: To examine the relationship between recurrent headache disorders (i.e., migraine and tension-type headache) and lifestyle factors (overweight, low physical activity, and smoking) in an unselected population study among adolescents.

Methods: In this cross-sectional study from Norway, a total of 5,847 students were interviewed about headache complaints and completed a comprehensive questionnaire including items concerning physical activity and smoking. In addition, they underwent a clinical examination with height and weight measurements. Adolescents with high physical activity who were not current smokers and not overweight were classified as having a good lifestyle status. These students were compared to those with 1 or more of the negative lifestyle factors present in regard to headache diagnosis and headache frequency.

Results: In adjusted multivariate analyses, recurrent headache was associated with overweight (odds ratio [OR] = 1.4, 95% confidence interval [CI] 1.2–1.6, $p < 0.0001$), low physical activity (OR = 1.2, 95% CI 1.1–1.4, $p = 0.002$), and smoking (OR = 1.5, 95% CI 1.3–1.7, $p < 0.0001$). The prevalence of OR increased with more than 1 negative lifestyle factor present, evident for headache diagnoses and frequency.

Conclusion: The results from the present study show that overweight, smoking, or low physical activity are independently and in combination associated with recurrent headache among adolescents. The associations observed and the additive effect of these negative lifestyle factors on the prevalence of recurrent headache indicates possible targets for preventive measures. ***Neurology***® **2010;75:712–717**

GLOSSARY

BMI = body mass index; **CI** = confidence interval; **HUNT** = Helseundesøkelsen I Nord-Trøndelag; **OR** = odds ratio.

Headache, including migraine and tension-type headache, is one of the most frequently reported somatic complaints among children and adolescents.[1] Headache is associated with impairments in daily functioning, is associated with analgesic use, and has a negative impact on most aspects of health-related quality of life.[2-4]

For optimal treatment, nonpharmacologic interventions with changes in lifestyle are often recommended.[5] Studies among adults have shown that headache can be provoked by physical exercise,[6] but on the other hand, regular physical activity has been suggested as a method of migraine management, with a beneficial effect on attack frequency, intensity, and duration.[7,8] Smoking is a trigger for acute migraine attacks in adults,[6] and prevalence rates for headache are higher among smokers compared to nonsmokers.[9] Among adolescents, there is one population-based study that reported that headache was more prevalent among daily smokers, but no differentiation of the primary headache disorders was reported in this study.[10] Obesity is associated with chronic daily headache and frequent migraine in adults,[11-13] but this relationship

Editorial, page 680

e-Pub ahead of print on August 18, 2010, at www.neurology.org.

From the Faculty of Medicine (L.R., G.D., J.-A.Z.), University of Oslo; Department of Neurology (J.-A.Z.), Oslo University Hospital, Ullevål; Norwegian Centre for Violence and Traumatic Stress Studies (G.D.), Oslo; Department of Neuroscience (K.H., L.J.S., J.-A.Z.), HUNT Research Centre, Department of Public Health (T.L.H.), Faculty of Medicine, Norwegian University of Science and Technology, Trondheim; and Norwegian National Headache Centre, Section of Neurology (K.H., L.J.S.), and National Centre for Spinal Disorders (J.-A.Z.), St. Olavs Hospital, Trondheim, Norway.

Disclosure: Author disclosures are provided at the end of the article.

has not been established for other types of headache.[14] Only one study has addressed this relationship among adolescents, and reported that obesity was associated with headache frequency and disability.[15]

Lifestyle factors such as overweight, physical activity, and smoking are associated with headache in adults, but robust documentation about the importance of these factors among adolescents is scarce and no study has so far investigated the impact of the combination of these lifestyle factors in relation to headache among adolescents. Thus the main purpose of the present study was to evaluate this relationship in an unselected adolescent population.

METHODS

Participants. During a 2-year period from August 1995 to June 1997, all students in junior high schools (aged 12–15 years) and high schools (aged 16–19 years) in Nord-Trøndelag County in Norway were invited to participate in the youth part of the Nord-Trøndelag Health Study (Helseundesøkelsen I Nord-Trøndelag; HUNT).

A detailed description of the study population has been published previously.[16] In short, a total of 5,847 adolescents 13–18 years of age were subject to a headache interview in connection with a clinical examination performed at the schools during school hours. The clinical examination included spirometry, weight, height, and blood pressure measurements. The students also had to complete a comprehensive self-administered questionnaire, during 1 school hour, with several health-related questions, which included questions related to physical activity and smoking.

Headache diagnosis. Trained nurses performed the headache interviews and the students were asked whether they had experienced recurring headaches that were not related to cold, fever, or any other disease during the past 12 months. Two history descriptions of typical headache symptoms, one for migraine and one for tension-type headache, were then read for students reporting recurrent headaches, and they were asked to classify their headaches according to the descriptions. The students were also given a third alternative (nonclassifiable headache) in case none of the descriptions resembled their headache experiences. Subjects with a combination of migraine and tension-type headache were classified as migraine. The average number of days with headaches in the last 12 months was recorded as less than 1 day per month (less than monthly), 1–3 days per month (monthly), 1–5 days per week (weekly), or more than 5 days per week (daily). The recognition-based headache diagnoses obtained by the nurses have previously been validated against extensive semi-structured interviews by neurologists according to the diagnostic criteria from the International Headache Society.[17]

Physical activity, smoking, body mass index, and overall health (lifestyle factor) status. The question on physical activity—"Outside school, how many days per week do you perform sports or exercise until you get short of breath or sweaty?"—has been used in previous studies and involves frequency, endurance, and intensity.[18] Students who exercised less than twice a week were defined as having low physical activity. Current smoking was defined as reported daily or occasional smoking. Body mass index (BMI) was calculated according to the following formula: BMI = (weight [kilos]/height^2 [meters]). To define overweight and obesity, we used the International Obesity Task Force.[19] Each sex and age (by half year) has percentile cutoff points for overweight and obesity. At age 18, adult cutoff points were applied. The overweight group included all students with BMI scores above the cutoff points for overweight or obesity.

Students reporting a combination of high physical activity, not currently smoking, and normal weight were defined as having an overall good lifestyle status. The status was defined as intermediate if one of the negative lifestyle factors was present (overweight, low physical activity, or current smoking), poor if 2 factors were present, and very poor if all 3 factors were present. Among the total interviewed population of 5,847 adolescents, complete data on all 3 lifestyle factors were available for 5,588 in relation to headache diagnosis and for 5,529 with respect to headache frequency.

Ethics. Participation in the study was voluntary and each student signed a written statement of consent. For students younger than 16 years, a written consent was obtained from their parents. The HUNT study was approved by the Regional Committee for Ethics in Medical Research and by the Norwegian Data Inspectorate.

Statistical analyses. The associations between headache prevalence and health status, i.e., presence of 1 or more of the lifestyle factors (low physical activity, smoking, and overweight), were estimated using multiple logistic regression with odds ratio (OR) and 95% confidence interval (CI). The analyses were adjusted for gender, age, and the other independent variables. When appropriate, the independent variables were treated as single ordinal variables and incorporated in a 2-sided test for trend to evaluate the probability of a linear relationship between lifestyle factors and headache. Nonparametric tests were performed for between-group analyses. Data analysis was performed with the Statistical Package for the Social Sciences, version 16.0 (SPSS, Chicago, IL).

RESULTS

In unadjusted analyses, overweight, low physical activity, and current smoking were more prevalent among those with recurrent headache com-

Table 1 Prevalence of lifestyle factors in relation to recurrent headache diagnoses among boys and girls[a]

	Overweight	Low physical activity	Smoking
Boys (n = 2,680)	N = 421	N = 700	N = 440
No headache (n = 2,126)	314 (14.8)	527 (24.8)	329 (15.5)
Recurrent headache (n = 554)	107 (19.3)	173 (31.2)	111 (20.0)
Migraine (n = 126)	26 (20.6)	43 (34.1)	29 (23.0)
Tension-type headache (n = 320)	58 (18.1)	92 (28.8)	56 (17.5)
Nonclassifiable headache (n = 108)	23 (21.3)	38 (35.2)	26 (24.1)
Kruskal-Wallis test	$p = 0.034$	$p = 0.013$	$p = 0.019$
Girls (n = 2,908)	N = 470	N = 1,017	N = 629
No headache (n = 1,861)	264 (14.2)	591 (31.8)	342 (18.4)
Recurrent headache (n = 1,047)	206 (19.7)	388 (37.1)	287 (27.4)
Migraine (n = 266)	59 (22.2)	95 (35.7)	79 (29.7)
Tension-type headache (n = 630)	120 (19.0)	235 (37.3)	161 (25.6)
Nonclassifiable headache (n = 151)	27 (17.9)	58 (38.4)	47 (31.1)
Kruskal-Wallis test	$p < 0.001$	$p = 0.044$	$p < 0.001$

[a] Values are number of subjects in respective groups (percentage of total).

Table 2 Prevalence odds ratios for headache diagnoses in relation to lifestyle status

	Total (n = 5,588)	Recurrent headache (n = 1,601)		Migraine (n = 392)		Tension-type headache (n = 950)		Non-classifiable headache (n = 259)	
		%	OR (CI)	%	OR (CI)	%	OR (CI)	%	OR (CI)
Lifestyle status									
Good	2,856	24.5	1.0 (ref)	5.5	1.0 (ref)	15.3	1.0 (ref)	3.8	1.0 (ref)
Intermediate	1,920	30.2	1.3 (1.1-1.4)	7.9	1.5 (1.2-1.9)	17.3	1.2 (1.0-1.4)[b]	4.9	1.3 (1.0-1.8)[c]
Poor	717	37.4	1.8 (1.5-2.1)	9.8	2.1 (1.5-2.8)	21.5	1.6 (1.3-2.0)	6.1	1.8 (1.2-2.6)
Very poor	95	54.7	3.4 (2.2-5.2)	13.7	3.7 (1.9-7.1)	28.4	2.8 (1.7-4.7)	12.6	5.0 (2.6-9.9)
***p* for trend**			<0.0001		<0.0001		<0.0001		<0.0001

Abbreviations: CI = confidence interval; OR = odds ratio.
[a] The analyses were adjusted for age and gender.
[b] $p = 0.069$.
[c] $p = 0.039$.

pared to those without, evident for both sexes, as shown in table 1. In adjusted multivariate analyses, recurrent headache was associated with overweight (OR = 1.4, 95% CI 1.2–1.6, $p < 0.0001$), low physical activity (OR = 1.2, 95% CI 1.1–1.4, $p = 0.002$), and smoking (OR = 1.5, 95% CI 1.3–1.7, $p < 0.0001$). This was found for overweight both among girls (OR = 1.4, 95% CI 1.2–1.8, $p < 0.0001$) and boys (OR = 1.4, 95% CI 1.1–1.8, $p = 0.01$). Similarly for both genders, recurrent headache was associated with low physical activity (girls OR = 1.2, 95% CI 1.0–1.4, $p = 0.05$, boys OR = 1.3, 95% CI 1.1–1.7, $p = 0.006$) and smoking (girls OR = 1.6, 95% CI 1.3–1.9, $p < 0.0001$, boys OR = 1.3, 95% CI 1.0–1.7, $p = 0.02$).

The association between overweight and migraine (adjusted for age, gender, smoking, and physical activity) was 1.6 (95% CI 1.4–2.2, $p < 0.0001$), for tension-type headache 1.4 (95% CI 1.1–1.6, $p < 0.0001$), and for nonclassifiable headache 1.4 (95% CI 1.0–1.9, $p = 0.06$). The association between low physical activity and migraine (adjusted for age, gender, smoking, and overweight) was 1.5 (95% CI 1.0–2.2, $p = 0.09$), for tension-type headache 1.2 (95% CI 1.0–1.4, $p = 0.02$) and for nonclassifiable headache 1.3 (95% CI 1.0–1.7, $p < 0.05$). The association between smoking and migraine (adjusted for age, gender, overweight, and physical activity) was 1.8 (95% CI 1.4–2.2, $p < 0.0001$), for tension-type headache 1.4 (95% CI 1.1–1.6, $p = 0.001$) and for nonclassifiable headache 1.6 (95% CI 1.2–2.2, $p < 0.001$).

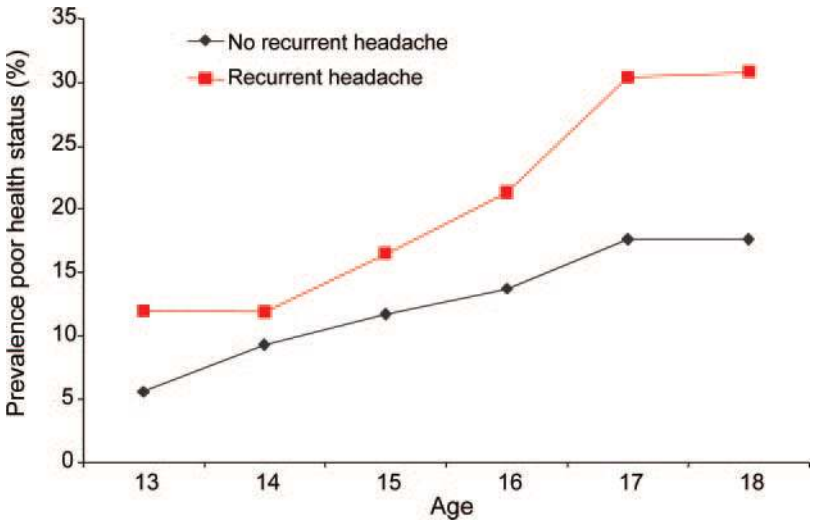
When considering lifestyle status based on the combination of overweight, level of physical activity, and smoking status, intermediate, poor, and very poor lifestyle status were all associated with higher prevalence of recurrent headache and the association was evident for all 3 headache diagnoses (table 2). There was a significant trend for stronger associations between the number of negative lifestyle factors present and the prevalence of the different headache diagnoses and headache frequencies. Regarding headache frequency, the strongest relationship was found between very poor lifestyle status and weekly or daily headache, as shown in table 3. The association between weekly and daily headache combined

Table 3 Headache frequency in relation to lifestyle status[a]

	Total (n = 5,529)	Headache < monthly (n = 306)		Headache monthly (n = 790)		Headache weekly or daily (n = 446)	
		%	OR (CI)	%	OR (CI)	%	OR (CI)
Lifestyle status							
Good	2,827	5.4	1.0 (ref)	12.0	1.0 (ref)	6.4	1.0 (ref)
Intermediate	1,897	5.4	1.0 (0.8-1.3)	15.4	1.3 (1.1-1.6)	8.5	1.3 (1.0-1.6)[c]
Poor	712	6.7	1.4 (1.0-2.0)[b]	18.7	1.9 (1.5-2.4)	11.5	2.0 (1.5-2.7)
Very poor	93	4.3	1.2 (0.4-3.4)	28.0	3.7 (2.2-6.1)	21.5	5.0 (2.8-8.9)
***p* for trend**			0.103		<0.0001		<0.0001

Abbreviations: CI = confidence interval; OR = odds ratio.
[a] The analyses were adjusted for age and gender.
[b] $p = 0.047$.
[c] $p = 0.019$.

Figure Prevalence of poor and very poor lifestyle status combined among subjects with and without recurrent headache in relation to age



and overweight was strongest for migraine (OR = 2.2, 95% CI 1.5–3.3, $p < 0.0001$), intermediate for tension-type headache (OR = 1.4, 95% CI 1.0–1.9, $p = 0.03$), and not significant for nonclassifiable headache (OR = 1.1, 95% CI 0.9–1.3, $p = 0.45$). The prevalence of poor and very poor lifestyle status combined increased with age and was higher among those with recurrent headache than among those with no headache (figure).

DISCUSSION In this cross-sectional study of 13- to 18-year-old adolescents, recurrent headache was associated with overweight, low physical activity, and smoking. There was a significant trend for stronger associations between the number of negative lifestyle factors that were present and the different headache diagnoses and headache frequency.

The strengths of the study are the large and unselected population, high participation rate, and the use of validated diagnoses. In addition, weight and height were measured by a nurse, and were not self-reported. As Young-HUNT is a cross-sectional survey that may be considered representative for the entire Norwegian population, selection bias often associated with studies of headache in children and adolescents were avoided.

The limitations to consider in this study are the change in lifestyle factors that might have occurred since the study was performed and the self-reported measurements of smoking habits and performed physical activity. The assessment of physical activity used in the present study has, however, proven to give reliable and acceptable measures of fitness.[20] The use of self-reported smoking habits has also proven to give reliable estimates.[10] Although one cannot exclude the possibility of an underestimation or overestimation of physical activity and tobacco consumption, it seems unlikely that this information bias should be differential, i.e., different for those with and without headache.

The association between low physical activity and recurrent headaches is in accordance with previous clinic- and population-based studies.[21,22] The finding supports the hypothesis that those with recurrent headache may avoid exercise because it tends to precipitate attacks, as many patients report.[6] On the other hand, these associations can also be explained by the converse hypothesis, that a low activity level leads to headache, and this is the rationale when physical exercise is mentioned as a method for migraine management. How exercise should be helpful for migraine is not well-understood, but it may be related to alterations in blood nitric oxide[7] or increase in β-endorphin levels,[8] or simply increase in well-being.[23]

Little physical activity can also contribute to overweight.[24] Obesity, which is highly prevalent in the population,[25] is associated with different chronic pain conditions,[26,27] and one prospective study has shown that obesity is a risk factor for developing chronic daily headache.[13] One recent study evaluated the relationship between headache and overweight among adolescents, and reported a significant association between obesity and headache frequency.[15] In the present study, the strongest association with overweight was found for those reporting frequent migraine, which has also been found in adults.[11] The mechanisms that link obesity with migraine attack frequency are uncertain, but they may be connected from a biochemical perspective.[28] It is known that obesity is a proinflammatory[29] and prothrombotic state[30] and neurovascular inflammation may be an important mechanism in migraine.[31] Additionally, calcitonin gene-related peptide levels are elevated in obese individuals,[32] and this transmitter is thought to play an important role in migraine pathophysiology.[33,34]

In a recent population-based study among adults, headache was significantly more prevalent among smokers compared to nonsmokers, most evident for those under 40 years smoking more than 10 cigarettes per day.[9] One population-based study also confirmed an association between headache and smoking among adolescents, but no differentiation of the primary headache disorders was reported in this study.[10] The question of a possible causal relationship between smoking and headache cannot be addressed in a cross-sectional study. However, cigarette smoking has several effects which may induce headache, such as alterations of nitric oxide levels in the brain,[35] decreased monoamine oxidase activity,[36] and accelerated metabolism of common headache

medications resulting in overall decreased clinical efficacy.[37] Also, the possibility of reversed causality, i.e., that headache may dispose to smoking, should be considered. Exposure to stressful stimuli such as headache may induce the craving to smoke.[38] Furthermore, nicotine has pain-inhibitory effects,[39] and as it induces strong addiction[35,39] and is used daily, one may speculate that smoking can lead to increased headache problems much in the same way that analgesics may produce medication overuse headache.[40]

The present study shows that overweight, low physical activity, or smoking are independently and in combination associated with recurrent headache among adolescents. There are, however, other possible mediating factors to consider, like socioeconomic status and psychiatric comorbidity.[4,13] Even though we were unable to adjust for all relevant confounders in the present study, and in spite of the fact that cross-sectional studies cannot adequately address the question of a causal relationship, we believe that the associations observed and the additive effect of these negative lifestyle factors on the prevalence of recurrent headache strongly indicates that these lifestyle factors are possible targets for headache preventive measures.

ACKNOWLEDGMENT

The Nord-Trøndelag Health Study (HUNT) is a collaboration between HUNT Research Centre, Faculty of Medicine, The Norwegian University of Science and Technology (NTNU), Norwegian Institute of Public Health, and Nord-Trøndelag County Council.

DISCLOSURE

L. Robberstad, Dr. Dyb, and Dr. Hagen report no disclosures. Dr. Stovner serves on scientific advisory boards for and has received honoraria from BTG plc, Minster Pharmaceuticals plc, and Pfizer Inc.; serves as Associate Editor of *The Journal of Headache and Pain* and on the editorial advisory board of the *Journal of the Norwegian Medical Association*; has received funding for travel and speaker honoraria from GlaxoSmithKline, Pfizer Inc., Merck & Co., Inc., AstraZeneca, Allergan, Inc., Nycomed, Desitin Pharmaceuticals, GmbH, and EMD Serono, Inc.; has received research support from GlaxoSmithKline, Pfizer Inc., Merck & Co., Inc., AstraZeneca, Allergan, Inc., Nycomed, Desitin Pharmaceuticals, GmbH, EMD Serono, Inc., and AstraZeneca; and has served as expert legal witness for Oslo Tingrett. Dr. Holmen receives research support from the Norwegian Research Council (NFR). Dr. Zwart reports no disclosures.

Received July 27, 2009. Accepted in final form March 10, 2010.

REFERENCES

1. Stovner LJ, Zwart JA, Hagen K, Terwindt GM, Pascual J. Epidemiology of headache in Europe. Eur J Neurol 2006; 13:333–345.
2. Roth-Isigkeit A, Thyen U, Stöven H, Schwarzenberger J, Schmucker P. Pain among children and adolescents: restrictions in daily living and triggering factors. Pediatrics 2005;115:152–162.
3. Dyb G, Holmen TL, Zwart JA. Analgesic overuse among adolescents with headache: the Head-HUNT-Youth Study. Neurology 2006;66:198–201.
4. Powers SW, Gilman DK, Hershey AD. Headache and psychological functioning in children and adolescents. Headache 2006;46:1404–1415.
5. Linde M. Migraine: a review and future directions for treatment. Acta Neurol Scand 2006;114:71–83.
6. Kelman L. The triggers or precipitants of the acute migraine attack. Cephalalgia 2007;27:394–402.
7. Narin OS, Pinar L, Erbas D, Ozturk V, Idiman F. The effects of exercise and exercise-related changes in blood nitric oxide level on migraine headache. Clin Rehabil 2003; 17:624–630.
8. Köseoglu E, Akboyraz A, Soyuer A, Ersoy AÖ. Aerobic exercise and plasma beta endorphin levels in patients with migrainous headache without aura. Cephalalgia 2003;23: 972–976.
9. Aamodt AH, Stovner LJ, Hagen K, Bråthen G, Zwart J-A. Headache prevalence related to smoking and alcohol use: the Head-HUNT Study. Eur J Neurol 2006;13:1233–1238.
10. Holmen TL, Barrett-Connor E, Holmen J, Bjermer L. Health problems in teenage daily smokers versus nonsmokers, Norway, 1995–1997: the Nord-Trøndelag Health Study. Am J Epidemiol 2000;151:148–155.
11. Bigal ME, Liberman JN, Lipton RB. Obesity and migraine: a population study. Neurology 2006;66:545–550.
12. Bigal ME, Lipton RB. Obesity is a risk factor for transformed migraine but not for chronic tension-type headache. Neurology 2006;67:252–257.
13. Scher AI, Stewart WF, Ricci JA, Lipton RB. Factors associated with the onset and remission of chronic daily headache in a population-based study. Pain 2003;106:81–89.
14. Bigal ME, Tsang A, Loder E, et al. Body mass index and episodic headaches: a population-based study. Arch Intern Med 2007;167:1964–1970.
15. Hershey AD, Powers SW, Nelson TD, et al. Obesity in the pediatric headache population: a multicenter study. Headache 2009;49:170–177.
16. Zwart JA, Dyb G, Holmen TL, Stovner LJ, Sand T. The prevalence of migraine and tension type headaches among adolescents in Norway: The Nord-Trøndelag Health Study (Head-HUNT-Youth), a large population based epidemiological study. Cephalalgia 2004;24:373–379.
17. Zwart JA, Dyb G, Stovner LJ, Sand T, Holmen TL. The validity of 'recognition-based' headache diagnoses in adolescents: data from the Nord-Trøndelag Health Study 1995–1997, Head-HUNT-Youth. Cephalalgia 2003;23: 223–229.
18. Holmen TL, Barrett-Connor E, Clausen J, Holmen J, Bjermer L. Physical exercise, sports, and lung function in smoking versus nonsmoking adolescents. Eur Respir J 2002;19:8–15.
19. Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition for child overweight and obesity worldwide: international survey. BMJ 2000;320:1240–1243.
20. Rangul V, Holmen TL, Kurtze N, Cuypers K, Midthjell K. Reliability and validity of two frequently used self-administered physical activity questionnaires in adolescents. BMC Med Res Methodol 2008;8:47.
21. Varkey E, Hagen K, Zwart JA, Linde M. Physical activity and headache: results from the Nord-Trøndelag Health Study (HUNT). Cephalalgia 2008;28:1292–1297.
22. Stronks DL, Tulen JH, Bussmann JB, Mulder LJ, Passchier J. Interictal daily functioning in migraine. Cephalalgia 2004;24:271–279.

23. Stubbe JH, de Moor MH, Boomsma DI, de Geus EJ. The association between exercise participation and well-being: a co-twin study. Prev Med 2007;44:148–152.
24. Fasting MH, Nilsen TI, Holmen TL, Vik T. Life style related to blood pressure and body weight in adolescence: cross sectional data from the Young-HUNT study, Norway. BMC Public Health 2008;8:111.
25. Ogden CL, Yanovski SZ, Carroll MD, Flegal KM. The epidemiology of obesity. Gastroenterology 2007;132:2087–2102.
26. Yunus MB, Arslan S, Aldag JC. Relationship between body mass index and fibromyalgia features. Scand J Rheumatol 2002;31:27–31.
27. Webb R, Brammah T, Lunt M, Urwin M, Allison T, Symmons D. Prevalence and predictors of intense, chronic, and disabling neck and back pain in the UK general population. Spine 2003;28:1195–1202.
28. Bigal ME, Lipton RB, Holland PR, Goadsby PJ. Obesity, migraine, and chronic migraine. Neurology 2007;68:1851–1861.
29. Lee YH, Pratley RE. The evolving role of inflammation in obesity and the metabolic syndrome. Curr Diab Rep 2005;5:70–75.
30. Alessi MC, Lijnen HR, Bastelica D, Juhan-Vague I. Adipose tissue and atherothrombosis. Pathophysiol Haemost Thromb 2004;33:290–297.
31. Moskowitz MA. Neurogenic inflammation in the pathophysiology and treatment of migraine. Neurology 1993;43:16–20.
32. Zelissen PM, Koppeschaar HP, Lips CJ, Hackeng WH. Calcitonin gene-related peptide in human obesity. Peptides 1991;12:861–863.
33. Storer RJ, Akerman S, Goadsby PJ. Calcitonin gene-related peptide (CGRP) modulates nociceptive trigeminovascular transmission in the cat. Br J Pharmacol 2004;142:1171–1181.
34. Petersen KA, Lassen LH, Birk S, Lesko L, Olesen J. BIBN4096BS antagonizes human alpha-calcitonin gene related peptide-induced headache and extracerebral artery dilatation. Clin Pharmacol Ther 2005;77:202–213.
35. Vleeming W, Rambali B, Opperhuizen A. The role of nitric oxide in cigarette smoking and nicotine addiction. Nicotine Tob Res 2002;4:341–348.
36. Littlewood JT, Glover V, Sandler M, Petty R, Peatfield R, Clifford RF. Migraine and cluster headache: links between platelet monoamine oxidase activity, smoking and personality. Headache 1984;24:30–34.
37. Zevin S, Benowitz NL. Drug interactions with tobacco smoking: an update. Clin Pharmacokinet 1999;36:425–438.
38. Balfour DJ, Ridley DL. The effects of nicotine on neural pathways implicated in depression: a factor in nicotine addiction? Pharmacol Biochem Behav 2000;66:79–85.
39. Jamner LD, Girdler SS, Shapiro D, Jarvik ME. Pain inhibition, nicotine, and gender. Exp Clin Psychopharmacol 1998;6:96–106.
40. Zwart JA, Dyb G, Hagen K, Svebak S, Holmen J. Analgesic use: a predictor of chronic pain and medication overuse headache: the Head-HUNT Study. Neurology 2003;61:160–164.