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Headache in Schoolchildren

Epidemiology, Pain Comorbidity and Psychosocial Factors

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Abstract
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Headache is the most frequently reported pain in children and is associated with missed schooldays, anxiety, depressive symptoms and various physical symptoms. A secular trend of increasing headache prevalence has been suggested. Few studies have focused on tension-type headache among children from the general population.

The aims of this thesis were to describe the prevalence, incidence and prognosis of tension-type headache, migraine and overall headache in schoolchildren, to identify medical, psychological and social factors associated with these headache types, and to determine whether the prevalence of headache has increased over the last decades.

In 1997, 1850 schoolchildren aged 7-15 years from the city of Uppsala participated in a questionnaire study and 1371 (74.1%) responded. Out of these, a randomly selected, stratified sample of 131 children and their parents were interviewed. Three years later, 122 children from the interview sample replied to an identical headache questionnaire.

Compared with a similar study in 1955, a significantly lower proportion of schoolchildren reported no headache. The prevalence of tension-type headache increased with age and was significantly higher in girls than boys after the age of twelve. Similar age and gender differences were obtained for migraine. A higher proportion of girls reported frequent headache than boys. Children with headache, especially those with migraine, as well as their first-degree relatives suffered from other pains and physical symptoms more frequently than headache-free children and their first-degree relatives. Although the likelihood of experiencing the same headache diagnosis and symptoms at follow-up was high, about one fifth of children with migraine developed tension-type headache and vice versa. Female gender was a predictor of migraine and frequent headache a predictor of overall headache at follow-up. The estimated annual incidence for tension-type headache, migraine and overall headache was 81, 65 and 131 per 1000 children, respectively.

In conclusion, the results indicate that headache has become increasingly common among schoolchildren over the last decades. Prevention and treatment of headache is particularly important for girls since they have high prevalence of headache, frequent headache episodes and a poor outcome. In children with headache, diagnoses and treatment should be reassessed regularly and other pains should be asked about and treated as well.

Keywords: Children, Headache, Tension-type headache, Migraine, Prevalence, Incidence, Prognosis, Pain, Psychosocial factors

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To Mats,
Ina, Adam and Filip

List of Papers

This thesis is based on the following papers, which will be referred to in the text by their Roman numerals.

I. Laurell, K., Larsson, B., Eeg-Olofsson, O. (2003) Headache in schoolchildren:agreement between different sources of information. *Cephalalgia*, 23: 420-428

II. Laurell, K., Larsson, B., Eeg-Olofsson, O. (2004) Prevalence of headache in Swedish schoolchildren, with a focus on tension-type headache. *Cephalalgia*, 24: 380-388

III. Laurell, K., Larsson, B., Eeg-Olofsson, O. Headache in schoolchildren: association with other pain, family history and psychosocial factors. (submitted)

IV. Laurell, K., Larsson, B., Mattsson, P., Eeg-Olofsson, O. A 3-year follow-up of headache diagnoses and symptoms in Swedish schoolchildren. (submitted)

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Abbreviations

ANOVA	Analyses of variance
CBCL	Child behaviour checklist
CI	Confidence interval
CGRP	Calcitonin gene-related peptide
CNS	Central nervous system
CTTH	Chronic tension-type headache
EEG	Electroencephalogram
FHM	Familial hemiplegic migraine
5-HT	5-hydroxytryptamine
IHS	International Headache Society
IHS 1.7	Probable migraine
IHS 2.3	Probable tension-type headache
MRI	Magnetic resonance imaging
OR	Odds ratio
PET	Positron emission tomography
PNS	Peripheral nervous system
Q	Questionnaire
SD	Standard deviation
SEI	Socio-economic index
tkr	Thousand Swedish crowns
TTH	Tension-type headache
VAS	Visual analogue scale
WHO	World Health Organisation

Introduction

Headache is the most frequently reported pain in children followed by abdominal and musculoskeletal pain (1-6). A secular trend of increasing headache prevalence has been reported (7).

As indicated by the definition of primary headache: "headache not attributed to an underlying disorder, trauma, substance or infection", such headache is rarely a life-threatening disorder. Yet, children with frequent headache report higher levels of anxiety and depressive symptoms, other physical symptoms and a lower quality of life (8, 9). Some individuals continue to have headache throughout childhood and grow up to become chronic headache patients, often disabled and with high consumption of medication and healthcare (10).

In this thesis, the following questions were raised: Is headache an increasing problem among children? What is the prognosis of headache in childhood? Which factors influence the occurrence and prognosis of headache?

Hopefully, the results of this thesis will be of value for the important goal of preventing chronic headache in children.

Background

History

Although headache was described in Egyptian texts already 5000 years ago, research interest for headache and other pain in children was low until the middle of the last century. In 1955 Bo Bille conducted his large, pioneering epidemiological study of migraine among children (11). Since then the literature on headache in children has increased rapidly (Table 1).

Compared with migraine the research interest for tension-type headache (TTH) has been considerably lower, reflected by vague definitions and variable denominations (tension headache, psychogenic headache, muscle contraction headache).

Table 1. *Reports found in Pub-Med database*

	1950-1969	**1970-1989**	**1990-2005[2]**
Headache and children	148	1443	3266
Migraine and children	99	770	1322
Tension-type headache and children	0[1]	23[1]	187

[1] Other search words; tension and psychogenic headache
[2] Until beginning of April 2005

Even less is published about cluster headache in children (12-14). It is important to recognise the characteristic symptoms of cluster headache, since the pain is nearly unbearable and treatment can be offered (15). In this thesis cluster headache will not be further discussed.

Epidemiology

Epidemiology is the systematic study of the factors that determine or influence the pattern and prevalence of a disease or a condition in populations (16).

Methodological aspects

Several methodological problems are associated with research on topics such as headache and pain, which lack precise measurement tools and involve the complexity of human beings. This is particularly complicated in children whose understanding and description of pain depend on cognitive level and previous pain experiences. Yet, many subjective aspects like relief of symptoms and well-being are important outcomes of care. As Feinstein (17) expressed it:

> "To avoid such soft data, the results of treatment are commonly restricted to laboratory information that can be objective, dimensional, and reliable-but it is also dehumanised. If we are told that the serum cholesterol is 230mg per 100ml, that the chest X-ray shows cardiac enlargement, and that the electrocardiogram has Q waves, we would not know whether the treated object was a dog or a person. If we were told that the abdominal pain disappeared, that functional capacity at work was restored, that the medicine tasted good and was easy to take, and that the family was happy about the results, we would recognise a human set of responses."

Reliability

Reliability is the extent to which repeated measurements of a stable phenomenon, by different people and instruments, at different times and places get similar results (16). Headache diagnoses may be unreliable because of variation in diagnostic criteria, in information obtained and in the interpretation of information (18). In particular, children younger than nine years of age may have difficulties in recalling and describing headache features (19), and the information is usually based on parents' reports. In a study involving children aged 10-15 years, discrepancies were found between children's and parents' interview reports of the child's headache features (20). However, in other studies, acceptable correlations have been found between children's and parents' reports (21-24).

Validity

Validity is the degree to which the data measure what they were intended to measure (16).

Internal validity is the degree to which the results of a study are correct for the sample being studied. The internal validity is distorted by unreliable measurements, selection bias and confounding factors (16).

External validity (or generalisability), is the degree to which the results of an observation hold true in another setting (16). The study population is important for the external validity of the results. For example, children from tertiary clinics are more likely to have severe and recurrent headache (25) and treatment may interact with the results. The observations from such samples are difficult to generalise to the general population, in which few children have been in contact with healthcare because of their headache (26).

Classification

Diagnosing headache can be complicated because no obvious clinical sign, easily accessible blood test or method to visualise headache exist. The best help is the anamnesis obtained from the children and their parents. A physical and neurological examination is also important and further investigations are only necessary when the anamnesis and/or the examination suggest that the headache is attributed to other disorders.

The differentiation between and definitions of different headache types have been discussed over many years. In previous prevalence studies different diagnostic criteria were used (27-29). To improve the reliability of headache classification and to decrease the variation between studies, the International Headache Society (IHS) classification was published in 1988 (30).

The IHS classification defines criteria for primary headaches such as migraine, TTH and cluster headache as well as secondary headaches, i.e. headache attributable to infections, trauma, substances or other diseases. According to the IHS classification, overlapping cases that fulfil both the criteria for TTH and migraine, should be diagnosed as migraine. Headache fulfilling all but one criterion for TTH, but not fulfilling the criteria of migraine with or without aura is classified as IHS 2.3. Similarly, IHS 1.7 is used for headache fulfilling all but one criteria for migraine, but not fulfilling the criteria for TTH. Overlapping cases should be diagnosed as IHS 1.7.

The IHS classification was primarily developed for adults, and in the first edition from 1988 the only modification for children was shortening the duration criterion for migraine without aura to a minimum of two hours. These IHS criteria were fairly reliable when diagnosing headache in adults (31), but their applicability in children has been questioned (32-35).

In comparison with adults, the reported duration of migraine is shorter (median 1.5-2.7 hours) in children (36). Children more often report bilateral headache (36) and younger children less often report visual aura compared with older children (37-39).

Several authors have suggested a further shortening of the minimum duration for migraine in children (19, 32, 33, 40-43), or to exclude this criterion (35, 37). The requirement of five earlier episodes of migraine has been questioned as well (32). In addition, some authors have proposed that bilateral location should be accepted and that only one of the symptoms phonophobia and photophobia should be required (44).

Revised IHS criteria have recently been published (45) (Table 2).

Table 2. Migraine and Tension-type headache according to the criteria of the International Headache Society (IHS). New revisions in bold.

Migraine without aura	**Tension-type headache**
A. At least 5 attacks fulfilling B-D	A. At least 10 episodes fulfilling B-D
B. Headache attacks lasting 4-72 h, children 2-72 **(1-72)** h	B. Headache lasting from 30 min to 7 d
C. Headache has ≥ 2 of the following: 1. unilateral location **(children may have bilateral)** 2. pulsating quality 3. moderate or severe pain intensity 4. aggravation by or causing avoidance of routine physical activity (e.g. walking, climbing stairs)	C. Headache has ≥ 2 of the following: 1. bilateral location 2. pressing/tightening quality 3. mild or moderate intensity 4. not aggravated by routine physical activity
D. At least one of the following: 1. nausea and/or vomiting 2. photophobia and phonophobia	D. Both of the following: 1. no nausea or vomiting 2. no more than one of photophobia or phonophobia
E. Not attributed to another disorder[1]	E. Not attributed to another disorder[1]

[1]History and physical and neurological examinations do not suggest that the headache is attributed to other disorders, or such disorders has been ruled out by appropriate investigations.

Data collection

The most appropriate method of data collection has been discussed (18, 46, 47). Most studies of headache prevalence have used questionnaires. Other commonly used methods are face-to-face or telephone interviews and headache diaries. It is considered better to use several methods to get a more complete answer to the research question.

Questionnaires are time and cost-effective for large populations but may give less reliable information. Further, low response rate is sometimes a problem (48).

Interviews are often regarded as the gold standard. However, for personal and psychological questions the validity may be lower than that of questionnaires because of underreporting of problems. In addition, interviews are more time consuming and costly (48).

Prospective registration of headache symptoms in diaries is considered to be more valid than retrospective information because of less recall-bias (49).

Prevalence

Prevalence is the proportion of a group of people possessing a clinical condition at a given point in time (16). The prevalence rates of headache, migraine and TTH vary (Table 3), not only due to differences between study populations, but also because different methods and diagnostic criteria have been used as discussed above.

Headache

In schoolchildren the prevalence of headache increases with age, especially for girls. Peaks in headache prevalence have been found at the age of about 7 and 12 years (50). The largest prevalence study of children was made by Bille in Uppsala, Sweden, 1955 (11). Among 8993 schoolchildren he found a total headache prevalence of 58.6%, whereas 41.4% reported no headache. In other Swedish studies the prevalence of headache in schoolchildren was 75% (26) and 48% (51).

In Turku, Finland, Sillanpää and Anttila found a nearly four-fold (14.4% to 51.5%) increase in prevalence of headache among 7-year-old children studied with 18 years interval, indicating an increase over time (7). Recently, in the same city, a slightly higher proportion of 8-year-old children reported frequent headache than 10 years ago (52).

Migraine

With the Vahlquist criteria, Bille found an overall prevalence of migraine of 3.9%. The prevalence rates in children aged 7 and 15 years were 1.4% and 5.3%, respectively. The prevalence of migraine increased with age, similarly for boys and girls until the age of about 12 and thereafter more in girls. Later studies have confirmed this age and gender pattern (44). In early school-ages a tendency of higher prevalence in boys has been described (44). The prevalence of migraine (Vahlquist) increased from 3.2% in 1974 (53) to 5.7% in 1992 (7) among 7-year-old children in Finland.

With the IHS criteria the prevalence of migraine in children has varied from 2.7% to 13.7% (Table 3). In Swedish adults, the one-year-prevalence of migraine (IHS) was 13.2% (54) and in women aged 40-74 years, 18.0% (55).

Tension-type headache

There is a paucity of population-based studies in children on TTH as defined by the IHS criteria, and the prevalence rates vary considerably (12.1% to 72.8%) (Table 3) (56-59). These variations in prevalence rates may be due to differences in study-populations and assessment methods employed, but probably also because the IHS criteria were applied differently.

The prevalence of chronic tension-type headache (CTTH), defined as TTH with a frequency of at least 15 days per month for 6 months or more, was reported to be 0.9% in Scottish schoolchildren (60) and 1.5% in Turkish schoolchildren (59). However, in a Finnish study of twelve-year-old children, no child fulfilled the criteria for CTTH (57).

Population-based prevalence studies using the IHS criteria are summarised in table 3.

Table 3. *Population-based prevalence studies using the IHS criteria*

Reference	Sample size	Age	Method	TTH	Migraine	Headache
Abu-Arafeh et al. (1994)(60)	1754	5-15	Q + I	(chronic 0.9%[1])	10.6%[1]	66%
Metsähonkala et al.(1994) (40)	3580	8-9	Q		2.7%[2]	36.6%
Pothmann et al. (1994) (56)	4835	8-9, 12-13, 15-16	Q[b]	48.5%[3]	11%[3]	88%
Raieli et al. (1995) (61)	1445	11-14	Q + I		3.0 %[1]	23.9%
Barea et al. (1996) (58)	538	10-18	I	72.8%[1]	9.9%[1]	82.9%
Bener et al. (1999) (62)	1159	6-14	Q + I		13.7%[1]	36.9%
Anttila et al. (2002) (57)	1135	12	Q	12.2%[3]	13.6%[3]	52.1%
Ayatollahi et al. (2002) (63)	1868[a]	11-18	I	12.1%[1]	6.1%[1]	27.2%
Özge et al. (2002) (59)	5562	8-16	Q + I[c]	24.7%[3]	10.4%[3]	49.2%
Laurell et al. (2004)(64)	1371	7-15	Q + I	9.8%[1]	11.0%[1]	44.8%
Zencir et al. (2004)(65)	2490	11-18	Q		8.8%[3]	

[1]One-year-prevalence, [2]Headache during the last 6 months, disturbing daily activities, [3]Lifetime prevalence or time period not defined

[a]Sample comprising girls only, [b]Modified IHS criteria, [c]Modified IHS criteria for migraine

Incidence

Incidence is the proportion of a group initially free of a condition that develops it over a given period of time. Cumulative incidence is the accumulation of new cases over time in a population of known and unchangeable size (16).

Headache

There are few prospective studies estimating incidence of headache. The incidence of headache among 7-year-old children starting school was 292/1000 (50) and the incidence of troublesome and frequent headache (at least once a week) among adolescents was 65/1000 (66).

Migraine

For migraine even less incidence data exist. The incidence of migraine without aura based on retrospective data of age at onset was estimated to peak in males at the age of 10-11 years (10.1/1000) and in females at the age of 14-17 years (18.9/1000) (67). Although the authors made mathematical corrections for recall-bias, retrospective incidence data are less reliable. Bille revealed such recall-bias for age at onset (11) and aura symptoms (68).

Tension-type headache

Incidence data are lacking for TTH.

Prognosis

Prognosis is the prediction of the future course of disease following its onset (16).

Migraine

The most extended longitudinal study was performed by Bille, who found that more than half of schoolchildren with pronounced migraine still had migraine after 40 years (68). In recent longitudinal studies using the IHS criteria, a considerable proportion of children changed their headache diagnosis or became free from headache after a few years (69-73).

Tension-type headache

Only three studies have described the outcome of TTH (69, 70, 72), none of them in a sample from the general population. Children at tertiary clinics have probably a different prognosis compared with the general population because they are more likely to have severe and recurrent headache (25). Further, treatment may affect the outcome. In the previous clinical studies including children with different age, sex distribution and follow-up time, 33-50% became headache-free and 8-12% changed into migraine at follow-

up (69, 70, 72). Guidetti and Galli (70) reported girls to become free from TTH less often than boys.

Demographic factors

Studies concerning socioeconomic background and headache prevalence among children show divergent results and no clear-cut associations have been found (74).

In a cohort of 5-year-old children, Sillanpää et al. (75) found an association of a lower housing standard and headache, which was not found in the same cohort at the age of 8-9. However, at that age headache in girls was significantly associated with mothers' but not fathers' educational level (76).

No systematic differences in headache prevalence rates have been found between different parts of the world (44) or between urban and rural residence (77-79).

Family history

The heredity for migraine is well established and involves both genetic and environmental factors (80-83). In about half of the families with the rare subtype of migraine called familial hemiplegic migraine (FHM), mutations have been described in a calcium ion channel gene (CACNA1A) linked to the chromosome 19p13. Recently, in about one fifth of the families with FHM, a mutation has been found in the ATP1A2 gene on chromosome 1q23 (84).

Heredity for TTH is difficult to study because of the high prevalence at least in adult populations. Low genetic effect was found for non-migrainous headache and TTH in twin studies (83, 85). Studies of CTTH showed a threefold increased risk for first-degree relatives to have the same disorder and the inheritance is suggested to be multifactorial (86).

Examples of environmental factors that may contribute to familial aggregation of headache are social-learning processes (modeling) and parental responses (87).

Medical factors and comorbidity

Few data exist concerning consultation rates and use of medication among children with headache. Comparisons between countries are difficult because of different organisation and availability of health care systems. Only 6% of 7, 11 and 15-year-old Swedish schoolchildren with headache had consulted a physician whereas 33% had taken analgesic for their headache (26). About half of Swedish adults with migraine had consulted a doctor for their headache (88). Among Finnish children with migraine persisting at 3-year follow-up, the consultation rate was 58.5% and correlated with a higher head-

ache frequency (25). Among children with weekly headache in Iceland, 47% had taken medication during the last month (79).

Although results differ between studies, epilepsy, allergy and diabetes mellitus seem to be overrepresented among children with migraine (44). Children with headache have been found to report other pains more often (4, 89-91) and according to parents, are more sensitive to pain experiences (e.g. vaccinations) than those without headache (91).

Psychological factors

Several studies report children with frequent headache to have more anxiety and depressive symptoms than those without headache (8, 89, 90, 92-95). In a few others, the levels of anxiety and depression did not differ from headache free controls (96, 97) or from children with other pain (98). A more consistent finding in these studies is that children with headache report more somatic symptoms.

Social factors

The association between headache in children and different social factors have been examined in a large number of studies, for review see Karwautz et al. (74). The most consistent association with headache, and especially with migraine, was found for school absence (60, 74, 89, 95).

Few studies have prospectively reported risk factors of headache in children. In a longitudinal study of children and their families, the following predictors of headache at the age of 6 were found: a history of frequent headache in mothers, poor health and feeding problems at the age of 9 months, depression and sleeping difficulties at the age of 3, travel sickness, nocturnal enuresis, long-term disease, concentration difficulties, behavioural problems and high sociability at the age of 5 (99).

In another prospective birth cohort study, frequent headache at age 7 and 11 years (as reported by parents) predicted headache, multiple physical symptoms and psychiatric comorbidity in adulthood (100).

Conversely, Waldie et al. (101) found in addition to maternal headache and childhood history of headache, anxiety symptoms during childhood and adolescence to be predictors of frequent migraine at the age of 26, whereas the only predictor of TTH was previous neck or back injury. Headache status at the age of 26 was unrelated to a history of perinatal complication, neurological disorder, or mild traumatic head injury.

Pain mechanisms

Some decades ago, pain in children often passed unrecognised or was undertreated. Since then understanding and treatment of pain in children has improved but still many children do not receive adequate treatment for their pain. One of the explanations is the difficulty to assess pain in children and for children to verbalize their pain experience (102).

Nociceptive input is transmitted through sensory nervous system and is modulated by facilitating and inhibiting mechanisms. The perception of pain includes subjective and emotional experiences. In newborn children, the nervous system is hypersensitive to sensory stimuli. Under the postnatal period the primary sensory neuronal function and modulation of inputs by spinal and descending mechanisms undergo large reorganisation. The plasticity continues to be considerable throughout childhood and long term effects of pain have been demonstrated (102).

Headache

The pathophysiology of headache is not fully clarified although great advances in research have been made during the last decades. Migraine has been more extensively studied than TTH. The knowledge of migraine pathophysiology is based on research in animals and adults (84, 103). Generalisation to children and adolescents may be hazardous because of the structural and functional changes in the PNS and CNS during the different stages of development. For example, myelinisation continues throughout childhood as well as arborisation and pruning of the neurons, the latter pronounced during the adolescence (104). Studies with MRI have shown that an adult dimension of the brain is reached around the age of 20 years (104) and somewhat earlier the EEG attains adult pattern (105). Research in children is limited because of human and ethical reasons, and few investigations about the pathophysiology of headache have been performed (106-112).

Recent theories of migraine pathophysiology are based on an extensive scientific background, nevertheless many questions are still unsolved (84, 103).

To summarize: Stress, light, sound or other triggering factors are thought to cause depolarisation of neurons located in the brainstem in predisposed individuals (perhaps dependent on altered calcium ion channels). This results in a wave of “cortical spreading depression” and cerebral hypoperfusion starting occipitally and spreading forward. The degree of vascular involvement in migraine has been debated. Hypoperfusion has been visualised with PET in individuals with aura (113-115). The vasoconstriction of cerebral vessels triggers the “trigeminovascular reflex”, mediated by sensory fibres with nociceptive function arising from the ophthalmic division of the trigeminal ganglion and from the upper cervical dorsal roots. The sensory

fibres release different neuropeptides (e.g. CGRP) locally at the vessel, which cause vasodilatation. The significance of a secondary neurogenic inflammation around the vessels has been discussed (116). Nociceptive signals are mediated centrally to nucleus trigemini caudalis in the brainstem and from there to the thalamus and cortical areas, which mediates the pain perception. As for other types of pain, facilitation or lack of inhibition of the afferent nociceptive signals may also be important.

The actions of the migraine drugs triptans (5-$HT_{1B/1D}$-receptor agonists) are probably as vasoconstrictors and pre-synaptic inhibitors of nociceptors, but a central effect is also likely. Triptans have been found to decrease the release of CGRP (117) and at present a CGRP-antagonist is tested for the treatment of migraine (118).

The pathophysiological mechanisms behind TTH are unclear. Lower pain pressure thresholds in neck and cranial musculature have been found in adults (119) but in children pressure tenderness has only been associated with migraine (112). In the more chronic forms, central sensitisation is probably important due to prolonged nociceptive input (120). Interestingly, in patients with chronic tension-type headache plasma levels of CGRP were low in those with non-pulsating headache and high in those with pulsating headache (120).

Aims

General aims

- Describe the prevalence, incidence and prognosis of TTH, migraine and overall headache in schoolchildren in Uppsala, identify medical, psychological and social factors associated with these headache types, and determine whether the prevalence of headache has increased compared with a similar study in 1955 (11).

Specific aims

- Estimate levels of agreement between different sources of information, i.e. questionnaires, interviews and diaries, concerning headache in schoolchildren and whether the agreement is related to age or gender of the child (Study I).
- Estimate the prevalence of TTH, migraine and other headaches by age and gender, using strict and modified IHS criteria (Study II).
- Compare the prevalence of headache in 1997 with the one reported by Bille in 1955 for schoolchildren from the same city (Study II).
- Determine whether children with TTH, migraine and headache-free differ in levels of other pain, physical symptoms, psychological and social problems (Study III).
- Determine whether first degrees relatives of children with TTH, migraine and headache-free, report pain and physical symptoms differently (Study III).
- Describe the outcome of TTH, migraine, overall headache and headache symptoms after three years (Study IV).
- Determine whether age, sex, heredity for migraine, frequency, intensity and duration of headache predict the outcome of TTH, migraine and overall headache (Study IV).
- Estimate the incidence of TTH, migraine and overall headache (Study IV).

Methods

Study population

The study population (Fig.1) consisted of 1850 schoolchildren, aged 7-15 years, from public comprehensive schools in the city of Uppsala in 1997. At that time, the total number of schoolchildren aged 7-15 years was 20 531, of which 93.2% attended public schools, 6.0% private schools and 0.8% schools for handicapped children (data from Uppsala municipal administration, January 1997).

In order to include a representative sample of schoolchildren, one class from every grade (1-9) was randomly selected from each of the eight districts of the city. Thus, altogether 72 classes distributed on 28 different schools participated in the study. The randomisation was performed with help of lists of classes in each district and random numbers generated by a computer.

The methods used were similar to those reported by Bille (11) in a study from the same city in 1955. The study populations were fairly comparable, Bille included all children aged 7-15 years attending public comprehensive schools (n = 9059), but not those attending schools for handicapped children or those aged 13-15 years, who had quit school or attended vocational schools.

A total of 1371 children (74.1%) returned acceptable questionnaires (Fig. 1) and a random sample of 131 children, stratified according to age, gender, and preliminary headache diagnosis were interviewed together with a parent. The reason for stratification was the intention to compare psychosocial variables between the diagnoses and keep background variables (i.e. age, sex and size of the groups) similar.

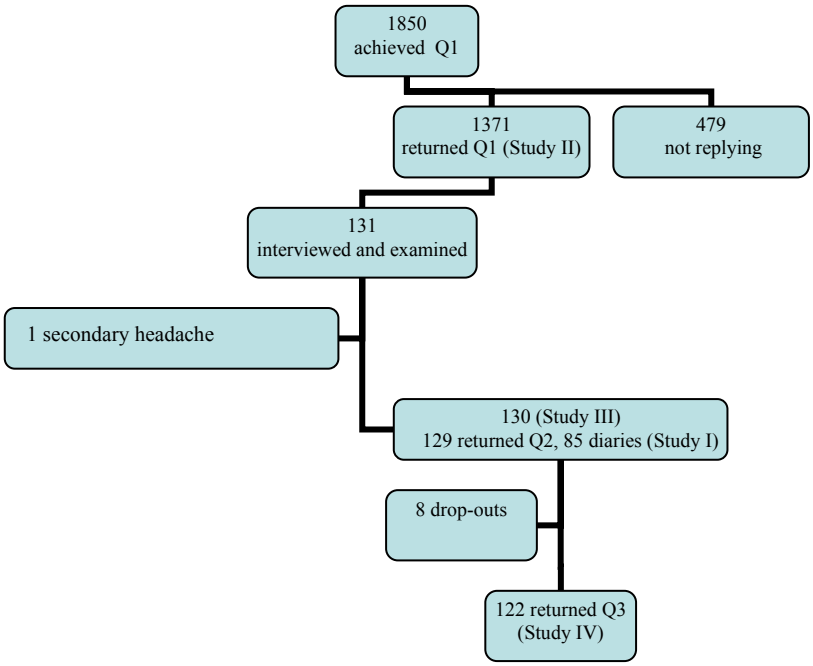
Children and parents who declined participation in interviews (17 with headache and 14 without) were replaced by new cases selected at random from the same stratum. Of those who did not participate, 19 gave no specific reason, 2 did not live in the catchment's area anymore, 5 did not have time and 5 gave late cancellations due to impediments. After interviews and examinations, one child was excluded because of secondary headache.

In 2000, the 130 children from the interview study were re-contacted by letter and asked to fill out an identical headache questionnaire about the situation during the preceding year. After one reminder a total of 122 chil-

dren (93.8%), 64 girls and 58 boys responded. Of the 8 children (6 girls, 2 boys) who did not respond, 1 had secret address and 1 rejected participation.

The ethical committee of Uppsala University approved the study and the children and their parents gave their informed consent to participate.

Figure 1. Study population



Case definition

The IHS classification (30) was applied for diagnosing the different headache-types in the questionnaire. For comparison with the study by Bille (11), in Study II we also used the Vahlquist criteria for migraine (paroxysmal headaches and at least two of the following: unilateral pain, nausea, visual aura and heredity). Against the background of findings in previous studies that a minimum duration of 2 hours for migraine is not appropriate for children, we used a minimum duration of 30 minutes for migraine in the stratification of preliminary headache diagnoses for interviews. This was also the duration of migraine used in the Swedish translation of the IHS classification.

Since the headache population consisted of migraine, TTH and other headaches we stratified into these three groups in addition to a control group with no primary headache (in the following denominated headache-free). The control group was about 1.7 times larger (the square-root out of number of comparing groups). Due to late cancellations the size of the strata differed slightly (Table 4).

Table 4. *Interview sample (n)*

	Migraine[1]	**TTH**[1]	**Other**	**Headache-free**	total
7-9	9	6	11	15	41
10-12	11	8	9	16	44
13-15	9	10	12	15	46
total	29 (15/14)[2]	24 (14/10)[2]	32 (20/12)[2]	46 (22/24)[2]	131 (71/60)[2]

[1]Minimum duration 30 minutes
[2](Girls/Boys)

In Study I, diagnoses in questionnaires and interviews showed a better agreement when the duration criterion was excluded, and in Study II the use of strict IHS criteria resulted in a high number of unclassified headaches. Therefore, in Study III and IV children with the headache-types IHS 1.7 and 2.3 were included in the migraine and TTH group, respectively.

Questionnaires

The teachers distributed questionnaires (Q1) to be filled out at home together with a parent. The non-responders were first reminded by the teacher and then by a letter sent home.

The questionnaire, which was developed and tested together with Bille, covered the Vahlquist as well as the IHS criteria. However, an important difference to the study by Bille (11) was that children with headache associated with infections or other diseases were asked to stop filling out the ques-

tionnaire after the initial questions concerning whether they had experienced headache during or previous to last year. The rest of the children were asked additional questions about different headache symptoms mainly answered by 'yes' or 'no', except for questions on the number of earlier episodes, duration, intensity and frequency of headache that were rated into categories.

Questionnaire answers were computerised and then the author used algorithms based on the IHS criteria to diagnose headache.

Interviews

Semi-structured, face-to-face interviews were conducted by the author between 5 and 18 months (median=12) after the initial survey. Because headache symptoms could have changed during this time, children and parents were asked to fill out a second questionnaire (Q2) at home a few days before the interview. This questionnaire was not assessed until after the interviews.

Parents attended the interview and supplemented information when needed. For adolescents aged 13 or older, parents participated only in the first part of the interview concerning demographic characteristics, family history, medical history and headache symptoms. Questions concerning psychological and social factors were first answered at home (children younger than 13 years with assistance of a parent) and then discussed and completed at the interview.

Measures

The questions were structured and originated mainly from a previous Swedish study on youth unemployment and ill-health. These questions have been used in several studies (121, 122) and found to discriminate well between children with and without headache (95). Some of the questions originated from the WHO Collaborative study conducted in 32 countries every fourth year since 1985 (123, 124). Psychological functioning was assessed with the Child Behavior Checklist (CBCL), a widely used questionnaire with well documented reliability and validity (125). The CBCL has been used in studies of children with headache (93, 95, 97, 98) and normative data on Swedish children and adolescents have been gathered (126).

Demographic characteristics

Demographic characteristics included information from parents on their occupation, residence, immigration, and housing conditions. For the parent with highest rated occupation a socio-economic index (SEI) (127) was calculated. We considered the child to have foreign background if he or she was

born abroad, entitled to home-language education or had a foreign citizenship.

Family history

Children and their parents were asked whether any first-degree relatives suffered from migraine, unspecified headache, abdominal, limb, back, shoulder and neck, jaw, and chest pain, sleeping disturbances, tiredness, vertigo or other diseases.

Medical history

The medical history covered previous diseases, accidents including head trauma, refraction problems, age of menarche or voice breaking, medication, and visits to a doctor or school nurse during the last year.

Headache symptoms

The interview questions on headache symptoms were similar as in the questionnaire with the following exceptions: 1. In the questionnaire, children were asked whether their headaches were unilateral or not, while during the interview they were asked for the localisation of the headache. 2. The duration of headache was estimated in intervals in the questionnaire, whereas during interviews, children and parents answered with a numeric value (minutes, hours and days). 3. In the questionnaire, questions concerning phonophobia, photophobia and aggravation by physical activity, were answered by “Yes” or “No”, but during interviews graded into: “None”, “Slight”, “Quite a lot” and “A lot”.

Pain and other physical symptoms

Children graded the occurrence of different pains (abdominal, limb, back, shoulder and neck, chest, face and jaw, and chewing pain) and other physical symptoms (sleeping disturbances, tiredness and vertigo) into “never”, “seldom”, “sometimes” or “often” (rank 0-3). The different pains and physical symptoms were added into a summary score ranging from 0-30. Any ongoing headache while answering the questions was assessed on a 0-100 mm VAS scale.

Psychological functioning

Parents answered the CBCL (125), a questionnaire to assesses social competence, emotional and behavioural problems in children and adolescents.

The CBCL includes different items, summarised into a "total behaviour problem score" and a "total competence score". The "internalizing syndrome scale" consists of the sum scores for the subscales "somatic complaints", "withdrawal", and "anxious-depressed" and the "externalizing syndrome scale" of the subscales "delinquent behaviour" and "aggressive behaviour". As headache is included as an item in the "somatic complaints" subscale it was excluded in comparisons between groups (migraine, TTH and no headache).

Social factors

Questions were asked about family situation (number of siblings, divorces, if the child stays with both or one of the parents, with other relatives, or with foster parents, and whether the family or the child experience lack of money), schooling conditions (number of pupils, satisfaction with school, teachers and own results, total time spent at school, and school absence because of headache), friends (whether the child has a close friend, feelings of loneliness, and experience of being bullied), leisure-time activities (number of sports and other activities, time spent outdoors, watching TV, using computers, doing homework or playing with friends) and lifestyle (sleeping and eating habits, use of alcohol or other drugs).

Physical examination

To exclude secondary headache, the author performed a physical and neurological examination of the 131 children. The examination covered weight and height, blood pressure, cardiac auscultation, skin examination, motor function, coordination and cranial nerves.

Diaries

The children were asked to keep a headache diary for 3 weeks following the interview. The diary has previously shown high inter-rater concordance between children and parents (24). The majority of discrepancies were found between no, slight and mild headache and the author suggested that these scale steps should be collapsed (24). In another study, good agreement was found between questionnaires and diaries for headache frequency and intensity (22). Other authors have found both overestimates as well as underestimates of headache symptoms in questionnaires or interviews preceding diary recordings (49). According to previous studies, the registration length of 3 weeks is adequate (128, 129). The diary has been used in several other epi-

demiological and treatment studies of headache in children and adolescents (130-134).

Children recorded headache episodes (including secondary headaches) and the intensity of each episode was estimated on a 0-5 rating scale; (0=”No headache”; 1=”Slight headache, notable only when paid attention to”; 2=”Mild headache that can be ignored”; 3=”Headache that cannot be ignored, but activities can be continued”; 4=”Severe headache disturbing concentration”; 5=”Severe incapacitating headache”). A mean value of the intensity levels reported during the 21 days was calculated for each subject.

Pilot studies

To test the questionnaire and methodology, pilot studies were performed in 1994 and 1996 in two different populations with different ages of the children. The first pilot study consisted of 266 schoolchildren aged 7-14 years from the city of Uppsala and a total of 190 (71.4%), 111 girls and 79 boys with a mean age of 10.9 years returned the questionnaire. Thirty-five children with migraine, TTH and unclassifiable headache were interviewed.

The second pilot study included 161 school- and preschool children 3-12 years old from a private school in Stockholm. Questionnaires were returned from 113 children (70.2%), 56 girls, 57 boys with a mean age of 7.6 years. No interviews were conducted.

Study I

The sample in Study I consisted of the 129 children who answered Q2 (Fig. 1), 69 girls and 60 boys, aged 7-17 years (mean 12.0, SD 2.6).

The headache diagnosis based on information from Q2 was compared with corresponding diagnosis based on information from interviews. In cases where two headache diagnoses were reported in the interview (n=10), agreement was considered when one of the interview-based diagnoses was similar to the questionnaire-based diagnosis. Reports of headache symptoms were also compared between questionnaires and interviews. Finally, the number of headache episodes and their mean intensity (0-5) reported in the diaries during the three weeks period following the interview were compared with the frequency and intensity (mild, moderate, severe) of headache reported in the questionnaires and interviews.

Study II

The sample in Study II consisted of the 1371 children (74.1%) responding to Q1 (Fig. 1), 686 girls and 685 boys, aged 7-15 years (mean 11.3, SD 2.6). In children aged 7-9, 10-12 and 13-15 years, the response rates were 69.4%, 79.9% and 72.9%. In the 8 different districts of the city the response rate ranged from 67.9% to 83.8%.

The prevalence of migraine and TTH was estimated with both strict and modified IHS criteria. We used the Vahlquist criteria to compare the prevalence of headache and migraine with the prevalence rates reported by Bille in 1955 in the same age group.

Study III

The sample in Study III consisted of the final interview sample of 130 children (Fig.1), 70 girls and 60 boys, aged 7-17 years (mean 12.1, SD 2.6). Interview data concerning demographic factors, medical history, other pain and physical symptoms, family history, and psychosocial factors were compared between children with migraine, tension-type headache and headache-free.

Study IV

The sample in Study IV consisted of the 122 children, 64 girls and 58 boys who answered Q3 (Fig.1). In 1997 they were aged 7-15 years (mean 11.2, SD 2.6). Headache diagnoses and symptoms at the initial evaluation 1997 were compared with those at follow-up 3 years later. Prognostic factors were analysed and the cumulative incidence of migraine, TTH and overall headache estimated.

Statistical methods

Agreement between variables was estimated by using Cohen's kappa coefficient and percentage agreement. Cohen's kappa coefficient (κ) corresponds to the following levels of agreement; 0-0.20: "slight", 0.21-0.40: "fair", 0.41-0.60: "moderate", 0.61-0.80: "good", 0.81-1.00: "excellent". To estimate whether the directions of disagreement were significantly different in questionnaires and interviews regarding headache symptoms, the Mc Nemar test was used. Differences in proportions of concordant answers between children younger than 13 years and older children and between boys and girls were tested using z statistics.

Chi-square and Fischer's exact tests were used to analyse relationships between categorical and dichotomous variables and Spearman rank coefficient was used for correlation analyses between ordinal and other variables. Differences between groups (migraine, TTH and headache-free) were analyzed with Kruskal-Wallis test for ordinal variables and ANOVA for continuous variables, with gender and age as covariates. When significant overall results were obtained we performed subsequent post hoc analyses with Mann-Whitney test (ordinal variables) and Bonferroni tests (continuous variables) to examine which of the groups that differed significantly from each other.

Logistic regression was used to analyze predictors of headache and to estimate the likelihood for persisting headache symptoms at follow-up. To estimate the cumulative incidence of headache, migraine and TTH, we used weighted calculations to correct for the different distribution of headache diagnoses in the follow-up sample and the original sample of 1371 children. Cumulative incidence was calculated by dividing the number of new cases deriving from other headache diagnoses and from the previously headache-free with the population at risk (children without the studied diagnosis at first evaluation). To achieve an annual average rate of cumulative incidence we divided by three.

In all analyses the level of significance was set to $p < 0.05$.

Results

Pilot studies

Although the sample in Pilot Study 1 was small and included more girls, the prevalence of headache during the last year (48.9%) was relatively similar to the main study (44.8%). Migraine (minimum duration of 30 minutes) occurred in 11.1% and TTH in 12.6%.

In Pilot Study 2 the prevalence of headache (35.4%) was lower, probably due to the younger age of the children. Migraine (minimum duration of 30 minutes) occurred in 9.0% and TTH in 9.7%. No child under the age of 6 reported headache.

In the first version of the questionnaire, answers could be given separately for two types of headaches. Although 27 children stated that they had more than one headache type, only 18 filled out the questionnaire for both types. However, only 2 children actually received two different diagnoses. Therefore, we did not use separate response alternatives for different headache types in the following studies.

The agreement between questionnaires and interviews concerning diagnoses of TTH, migraine and unclassified headache was high (85.3%), as was the inter-rater agreement between diagnoses based on the IHS criteria and clinical diagnoses set by two physicians (BL, OEO) after reviewing the interview responses (88.6%).

Study I

Headache diagnoses and headache features showed good agreement (κ=0.71, 82.5%) between Q2 and subsequent interviews. The concordance between questionnaires and interviews for headache diagnoses increased, and the number of unclassified headaches decreased, when the IHS duration criterion was excluded. When comparing headache frequency reported in questionnaires and interviews with diary recordings, the agreement was low (κ=0.15 and 0.27) and the frequency generally higher in the diaries. Overall, the agreement between questionnaires, interviews and diaries was not related to age or gender.

Figure 2. Agreement between questionnaires and interviews for IHS-diagnoses (without the duration criterion), (κ=0.71, 82.5%).

B	INTERVIEW (n)			
QUESTION-NAIRE (n)	Mi	TTH	UNC	Total
Mi	30	4	0	34
TTH	4	29	1	34
UNC	5	0	7	12
Total	39	33	8	80

Mi: Migraine; TTH: Tension-Type Headache; UNC: Unclassified Headache.
Concordant diagnoses in questionnaires and interviews (diagonal) are marked with grey colour.

The 49 children who reported no headache in Q2 were headache-free according to the interviews as well.

With all 129 children included and with the interview diagnosis as the gold standard, the sensitivity, specificity, positive predictive value and negative predictive value for the questionnaire (without duration criterion) was 76.9%, 95.6%, 88.2% and 90.5% for migraine, and 87.9%, 94.8%, 85.3% and 95.8% for TTH.

Study II

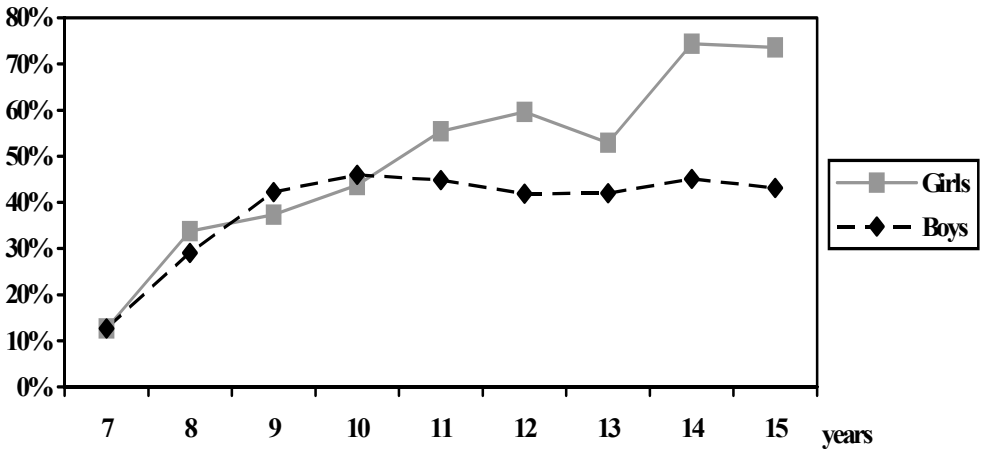
In the total sample of 1371 children, the one-year-prevalence of primary headache was 44.8%. The headache increased with age, similarly for boys and girls up to the age of 12. Thereafter the prevalence increased in girls but stayed unchanged in boys (Fig 3). The preponderance among teenaged girls was even more pronounced for TTH than for migraine.

Using the IHS criteria, the one-year-prevalence of TTH and migraine in the total sample was 9.8% and 11.0%, respectively. However, these prevalence rates increased considerably, to 23.0% and 17.0%, respectively, when excluding the criteria defining the number of earlier episodes and duration of headache.

The proportion of children who reported no headache at all during the last year was higher in 1955 (41.4%) than in 1997 (16.0%) indicating an overall increase in headache prevalence among today's schoolchildren. The preva-

lence rate of migraine according to the criteria of Vahlquist (6.6%) was also significantly higher than the one reported by Bille (3.9%) ($p<0.001$).

Figure 3. One-year-prevalence of headache among 7-15 year-old Swedish school-children



Study III

Children with headache, especially those with migraine, suffered from other pains and physical symptoms more frequently than headache-free children (Fig 4). The total sum scores of pain and other physical symptoms were significantly higher in children with migraine (mean rank 79.4) and TTH (mean rank 68.4) than in headache-free (mean rank 45.4) ($\chi 2 = 20.3$, df = 2, $p <0.001$). However, children with migraine and TTH did not differ significantly from each other.

First-degree relatives of children with headache suffered more often from migraine, other pains, and physical symptoms compared with relatives of headache-free children (Fig 5). Migraine among first-degree relatives was reported in 66.7% of the children with migraine, in 51.4% of those with TTH and in 29.8% of headache-free children ($p<0.01$). The total number of other symptoms than headache was significantly higher in first-degree relatives to children with migraine (mean 3.0) than in first-degree relatives to headache-free children (mean 1.9) ($p<0.01$).

Children with migraine visited a school nurse, used medication and were absent from school because of headache significantly more often than those with TTH. Migraine among first-degree relatives and the total sum of physical symptoms in children were the strongest predictors of headache in logistic regression analysis.

Figure 4. Proportions of children reporting pains and other symptoms (often or sometimes) in relation to headache diagnosis

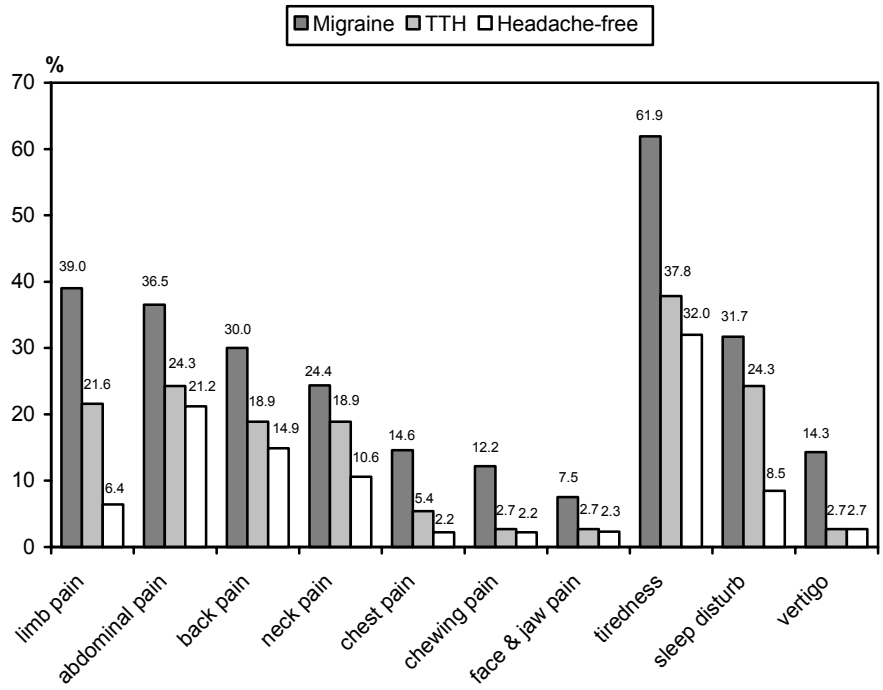
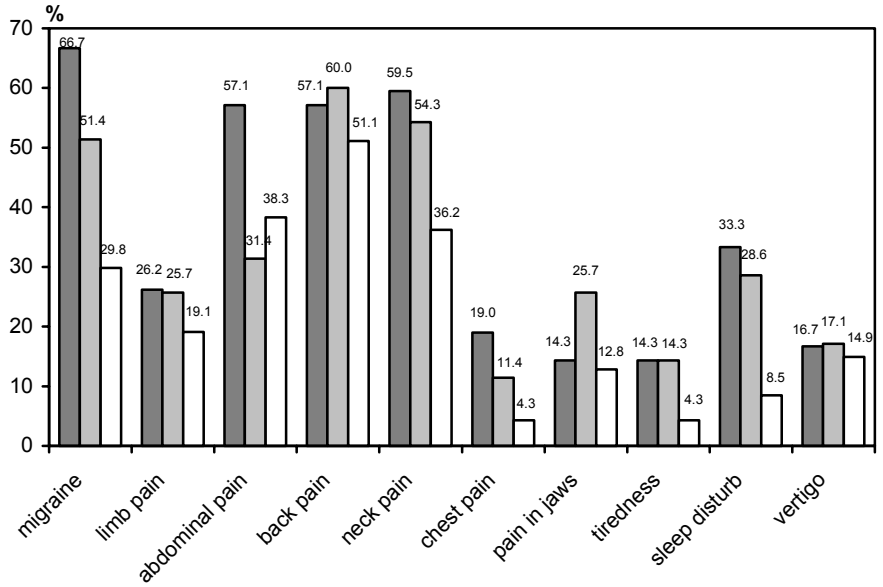


Figure 5. Proportions of first-degree relatives reporting pains and other symptoms (yes or no) in relation to children's headache diagnosis



Study IV

Nearly 80% of those with headache at first evaluation, still reported headache at follow-up after 3 years. Although the likelihood of experiencing the same headache diagnosis and headache symptoms at follow-up was high, about one fifth of children with migraine developed TTH and vice versa. In logistic regression analyses, female gender was a predictor of migraine and frequent headache a predictor of overall headache at follow-up. The annual incidence of headache was estimated to 131 per 1000, and that of TTH and migraine 81 and 65 per 1000, respectively. Because of the different populations at risk the incidence rates of TTH and migraine taken together was higher than the incidence of overall headache.

Discussion

In this sample of schoolchildren, the prevalence, incidence and prognosis of TTH, migraine and overall headache and the association with medical, psychological and social factors were studied. The prevalence of headache in 1997 was compared with the one reported by Bille in 1955 in the same city.

Few previous studies have focused on TTH among children from the general population.

Internal validity

Using the interview diagnosis as the gold standard, the questionnaire showed good validity when the IHS minimum duration criterion was excluded. The computerised method for diagnosing the different headache types minimised interpretation variation. Although headache symptoms vary over time, a test-retest of the questionnaire would have added valuable information about the short time reliability.

The inter-rater agreement of clinical diagnoses based on interview information was acceptable. The author interviewed children with structured questions on different headache symptoms and thereafter assessed the headache diagnosis with strict application of the IHS criteria (although later without criteria A and B) which probably diminished variation.

The large proportion of children with short duration of headache in this study suggests that the former IHS minimum duration criterion of 2 hours for migraine was inappropriate in children. This has previous been proposed by several other authors (19, 32, 33, 35, 37, 40-43). We may have obtained longer durations of headache if we had asked for the longest duration of untreated attacks or included the time of sleep at the end of attacks (38). Nevertheless, in epidemiological research of headache in children using duration as an obligate criterion is problematic because of the difficulties for children to estimate time during the attacks and for parents to judge when the pain starts and stops. In addition, the minimum requirement of 5 or 10 earlier headache episodes is unsuitable in children with a short history of headache. It is notable that in none of the previous classifications of migraine duration of headache was included and the required number of attacks was 3 at the most (27-29).

These problems are probably less prominent in clinical settings because of a selection of children with frequent and severe headache and because most clinicians would diagnose children with typical migraine symptoms as migraine even if either the length of the attacks were less than one hour or the number of attacks fewer than five or this information was uncertain. Yet, in epidemiological studies like this, the criteria considerably affect prevalence figures as shown in Study II.

External validity

The sample of schoolchildren was recruited from each of the 8 different districts in the city of Uppsala. In one of the districts (Eriksberg), the response rate was significantly higher. In 2004 this district had a similar mean income per capita and an unemployment rate as Uppsala on average, but a higher proportion (28.7% versus 19.0%) of inhabitants with a higher education. This may be because the district of Eriksberg includes the largest student residences in Uppsala. No clear association has been found for headache in children and socioeconomic background or parents' educational level (74). In this study we found no association between SEI and headache. In children aged 7-9 years the response rate was slightly lower and in children aged 10-12 slightly higher than for the total sample.

Otherwise no systematic sampling error was suspected, suggesting that the sample should be fairly representative of schoolchildren aged 7-15 years in Uppsala. The results should be possible to generalise to schoolchildren in Sweden because prevalence figures have not been found to vary between urban and rural populations (77-79). However, one limitation is that information is lacking about headache occurrence among the children who did not participate.

The prevalence rates of headache and migraine were in accordance with most previous reports (Table 3). For TTH, few and varying data exist. The prevalence rate of TTH in 12-year-old children in Finland (12.2%) was similar to that found in the present study for the same age group (14.8%).

The age and sex distribution of the interview sample was similar to the total sample of 1371 children, whereas the headache groups were randomly selected to about the same size and did not correspond to the distribution in the total sample.

Changes in prevalence

Compared with the study by Bille in 1955 (11), a significantly lower proportion of schoolchildren reported no headache at all. This comparison of headache-free children is most accurate because the inclusion of headache cases

was different in that we excluded headache due to infections or other diseases. The increasing headache prevalence over time found in this study is in accordance with reports of increased prevalence of headache among children aged 7 years (7) and recently in children aged 8 years (52) in Turku, Finland.

An increasing prevalence of headache among schoolchildren is worrying especially because frequent headache has been related to disability and a low quality of life (9). In this study we cannot measure whether there is a real increase in the occurrence of headache or an increased tendency to report such symptoms. Reports of subjective symptoms such as neck and back pain (135), psychosomatic symptoms (52) and perhaps depressive symptoms (136, 137) has increased among children. However, increased rates also of objective symptoms such as asthma and allergic diseases (138), overweight (139-141), type II diabetes (142), and decreased physical activity (143, 144) make a true increase in headache prevalence reasonable.

Changes in the society, family structure and lifestyle in western societies may be causal factors. For example, since the 1950s the number of divorces has increased, and both parents work longer days (145-147). Such societal changes, which affect children in particularly, could hypothetically cause an increase in emotional stress. Emotional stress is the most common self-reported trigger-factor for headache, and children with headache have been found to report stress more often than headache-free children (89, 95, 148). Although research evidence is sparse, children with headache may respond to stressful events with poorer coping strategies than those without headache (149). On the other hand, the lack of association of headache with social factors in this and most previous studies does not support this hypothesis.

Another contributing factor to the increase in headache prevalence among schoolchildren may be an earlier onset of puberty today than in the 1950s (150). However, this explanation is less likely since the gender differences in headache prevalence appeared at about the same age in this study and the study by Bille in 1955.

Sex differences

We found preponderance in girls aged 13-15 years for TTH as well as for migraine, and girls reported more frequent headache than boys, especially in the age group 13-15 years. It is well established that the prevalence of migraine after the age of 12 years differs between girls and boys. Menstruation may aggravate and pregnancy relieve migraine but more systematic studies of hormonal influence have shown conflicting results (77).

In the few studies of TTH in pubescent age groups, results have been contradictory (56, 58). Pothmann et al. (56) reported preponderance in boys whereas Barea et al. (58) found a higher prevalence in girls. In adults, TTH

is more prevalent among women than men (77) which concurs with the finding of increasing prevalence in girls in the present study.
Similar sex differences appear during adolescence for other chronic pain conditions (151) and depression (152). The adolescence is a period of biological, psychological and social changes with a different course for girls and boys. Each of these three areas probably contributes to sex differences in pain reports. Although many of the changes in behaviour and maturation of the brain during the adolescence cannot be related to levels of gonadal hormones, these hormones influence a wide variety of neuronal processes and interact with different neuropeptides, e.g. serotonin (153). In adults, higher pain thresholds have been measured in men than women, at least when pressure and electrical stimulation were used and in animals, males and females differ in stress-induced analgesia (154). Further, males and females (both humans and animals) differ in the response to opiates (154).

Comorbidity

The comorbidity of headache, pain and other physical symptoms found in this study, especially in children with migraine, is in agreement with previous reports (4, 89-91) and was confirmed by parent's in the CBCL. In addition, we found more migraine, other pain and physical symptoms among first-degree relatives to children with headache than among relatives to children without headache. An overrepresentation of multiple pains among relatives to children with pain has been suggested but not shown in epidemiological studies (4, 155, 156). In a Finnish study, parents of 6-year-old children with headache more often reported themselves to be sensitive to pain and they suffered from headache more frequently than controls, however the occurrence of other pain conditions was not assessed (91).

The mechanisms behind clustering of different pains and physical symptoms in some individuals are complex and the neurobiology is largely unknown (157). One explanation may be malfunctioning of the central pain transmission systems e.g. descending pain-modulating pathways. Further, psychological factors such as anxiety and depression have a modulating effect on pain perception (158). The serotonergic system has importance for mood, anxiety, sleep regulation and pain transmission, which may explain why these disorders often are connected. In addition, genetic factors, social-learning processes (modeling), and parental responses are important in the development and maintaining of pain symptoms (87).

In contrast to most previous studies (8, 89, 90, 92-95, 159) we did not find higher levels of anxiety and depressive symptoms in children with headache than in those without headache. Unlike these studies comprising children from tertiary clinics or from the general population with frequent or pronounced headache, the present headache sample mainly consisted of

children with infrequent or moderate headache and only a few had visited a doctor because of their headache. The selection of children with frequent or pronounced headache is likely to overestimate levels of psychological problems as compared with headache-free controls and may explain the discrepant results between previous studies and this study.

Incidence

We found a higher incidence of overall headache compared with incidence of troublesome and frequent headache (at least once a week) among children aged 12-14 years (66) but lower than that reported for 7-year-old children (50). Anttila et al. (50) suggested that the stressful event of starting school contributed to a high incidence. Their finding is in accordance with the considerably higher prevalence rates of headache reported for children aged 7 years than for preschool children (60, 75, 160, 161). The lower incidence rates reported for children aged 12-14 years may be explained by the inclusion of severe cases only (66).

To date, this is the first report of incidence of TTH based on prospective data. The incidence among schoolchildren was slightly higher for TTH than migraine, which is in accordance with TTH being less prevalent than migraine among children but considerably more frequent in adults. The incidence of TTH probably increases over a longer period of time and peaks later in life than migraine.

The estimates of incidence in this study were limited by the small number of children included and the follow-up period of three years. We presented annual mean values of the cumulative incidence but it is probable that the incidence rates differed during this time because the children in the sample became older. Preferably, incidence should be estimated annually in large cohorts from the general population.

Prognosis

The outcome of migraine in this study was similar to findings in most recent studies (69-72, 162). Children with TTH became headache-free less often compared with those at tertiary clinics (69, 70, 72). This may be because the clinic-based samples received treatment and because of the different age and sex distribution of the study populations, follow-up time and drop-out rates. To my knowledge, no previous study has described the outcome of TTH in a sample of children from the general population.

In logistic regression analyses, frequent headache predicted the occurrence of headache and female gender predicted migraine at follow-up. In accordance, Bille found a poorer outcome for girls with migraine (163) and

for those with high frequency of attacks (11). A higher frequency and intensity of headache has been associated with lower quality of life in adolescents (9) and frequency of headache correlated in this study significantly with other pain and physical symptoms as well as visits to healthcare because of headache. Thus, effective interventions in children with frequent headache are particularly important because of the associations with a poor prognosis as well as an increased impairment.

Only a few other studies have described the prognosis separately for boys and girls, mostly with a more favourable prognosis for boys (39, 70, 164). However, in one study the outcome was better for girls (73).

The high rates of transitions between migraine and TTH in this study and previous studies suggest that these diagnoses are closely related (165). Another possible explanation is co-occurring TTH and migraine with difficulties for children and parents to separate these two headache types. This is less likely in the present sample because none of the children who changed diagnosis at follow-up achieved two different diagnoses at the interview.

As long as the basic mechanisms of the different headache types are unclear and overlapping and co-occurring symptoms are frequent, the division into migraine or TTH may be difficult, especially in children from the general population with less pronounced symptoms. However, it is important to distinguish migraine from other headache types because of specific pharmacological treatment. Psychological treatments are useful for both migraine and TTH in children (166). In the future the interest should focus more on the frequency and intensity of headache.

Summary of main results

Headache diagnoses and headache features showed high agreement between questionnaires and subsequent interviews. The concordance increased, and the number of unclassified headaches decreased, when the IHS duration criterion was excluded.

The prevalence of TTH increased with age, and was significantly higher in girls than boys after the age of twelve. Similar age and gender differences were obtained for migraine. A higher proportion of girls than boys reported frequent headache, especially in the age group 13-15 years.

Compared with a similar study in 1955 (11), a significantly lower proportion of schoolchildren reported no headache.

Children with headache, especially those with migraine, suffered from other pains and physical symptoms more frequently than headache-free children. Few differences in psychosocial factors were found.

First-degree relatives of children with headache suffered more often from migraine, other pains, and physical symptoms compared with first-degree relatives of headache-free children.

Nearly 80% of children with headache still reported headache at a 3-year follow-up. About one fifth of children with migraine developed TTH and vice versa.

In logistic regression analyses, frequent headache was a predictor of headache and female gender a predictor of migraine at follow-up.

The estimated annual incidence of TTH, migraine and overall headache was 81, 65 and 131 per 1000 children, respectively.

Conclusions

The prevalence of headache among schoolchildren in Uppsala has increased over the last decades.

The prevalence of TTH increases with age and show a gender difference after the age of twelve with preponderance for girls.

There is a considerable risk of developing and maintaining headache during childhood. Prevention and treatment of headache is particularly important for girls since they have high prevalence of headache, frequent headache episodes and a poor outcome.

When dealing with children with headache, diagnoses and treatment should be reassessed regularly and other pains should be asked about and treated as well.

The IHS criterion for minimum duration of headache is too restricted in children.

Future directions

The results of this thesis suggest that research in children should address:

The reasons for the increasing prevalence of headache during the last decades. Prospective, longitudinal studies would be valuable to study causal factors of headache and differences over time.

The impact of frequency, intensity and diagnosis of headache on quality of life and daily life activities as well as coping mechanisms in children with and without headache.

Prospective measurements of headache features such as duration, intensity and frequency for example with electronic diaries.

Pathophysiological differences and similarities between headache types.

Mechanisms behind comorbidity of pain as well as age and gender differences in pain reports.

Svensk sammanfattning

Huvudvärk är den vanligaste smärtformen bland skolbarn. Barn med frekvent huvudvärk har ökad förekomst av skolfrånvaro, ångest, depressiva symtom samt olika kroppsliga symtom. Det är sannolikt att förekomsten av huvudvärk bland barn har ökat under de senaste decennierna.

Syftet med denna avhandling var att beskriva prevalensen, incidensen och prognosen för spänningshuvudvärk, migrän och total huvudvärk, att identifiera vilka medicinska, psykologiska och sociala faktorer som är förknippade med de olika huvudvärkstyperna och att klarlägga om huvudvärk har ökat i förekomst jämfört med en studie som utfördes av Bo Bille i Uppsala 1955.

Totalt ingick 1850 skolbarn i åldrarna 7-15 år från Uppsala i en enkätundersökning om huvudvärk 1997. Metoden liknade den som Bille använde i sin undersökning och studiepopulationen var jämförbar. Svar erhölls från 1371 (74.1%) skolbarn, 686 flickor och 685 pojkar. Ett slumpvist urval av 131 skolbarn, stratifierade efter kön, ålder och huvudvärkstyp, deltog tillsammans med en förälder i semistrukturerade intervjuer och en klinisk undersökning. Tre år senare besvarade 122 skolbarn på nytt en identisk huvudvärksenkät.

Andelen skolbarn som angav att de inte hade haft huvudvärk under det senaste året var signifikant lägre än 1955. Förekomsten av spänningshuvudvärk ökade med åldern och var högre hos flickor efter 12 års ålder. Liknande köns- och åldersskillnader sågs för migrän. En större andel flickor än pojkar rapporterade täta huvudvärksepisoder. Skolbarn med huvudvärk, särskilt de med migrän, och deras anhöriga rapporterade mer andra smärtor och fysiska symtom än huvudvärksfria barn och deras anhöriga.

Sannolikheten var stor att barnen hade samma huvudvärksdiagnos och symptom vid uppföljningen efter tre år, men ungefär en femtedel av dem med spänningshuvudvärk hade utvecklat migrän och vice versa. Kvinnligt kön predicerade förekomst av migrän och täta huvudvärksanfall predicerade huvudvärk vid uppföljningen. Den beräknade årliga incidensen för spänningshuvudvärk var 81/1000, migrän 65/1000 och total huvudvärk 131/1000.

Resultaten i denna avhandling tyder på att huvudvärk har blivit vanligare bland skolbarn under de senaste årtiondena. Förebyggande insatser och behandling är särskilt viktiga för flickor eftersom de har en hög förekomst av huvudvärk, täta anfall och en dålig prognos, åtminstone för migrän. Hos barn bör huvudvärksdiagnosen omprövas regelbundet och behandlingen justeras. Dessutom bör andra smärttillstånd efterfrågas och behandlas.

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