TURUN YLIOPISTON JULKAISUJA
ANNALES UNIVERSITATIS TURKUENSIS

SARJA-SER. D OSA – TOM. 757
MEDICA – ODONTOLOGICA

Neck pain in adolescent headache sufferers

A cohort study of schoolchildren

by

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TURUN YLIOPISTO
Turku 2007

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ISBN 978-951-29-3311-2 (Print)
ISBN 978-951-29-3312-9 (PDF/Electronic)
ISSN 0355-9483
Painosalama Oy – Turku, Finland 2007

To my dear family

ABSTRACT

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Neck pain in adolescent headache sufferers - a cohort study of schoolchildren

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Annales Universitatis Turkuensis
Series D Medica – Odontologica
Painosalama Oy, Turku, Finland, 2007

Although neck pain (NP) and headache (HA) are often concomitant in adolescents, few data exist on the association of NP with HA in this age group.

The aim of the study was to examine the association of concomitant NP with adolescent HA and with the outcome of HA. The associations of self-reported NP, physical findings of the neck and disc degeneration of the cervical spine with adolescent HA were studied.

This study is part of a population-based follow-up study of 12-year-old children (N 1135/1409) with and without HA. A sample of adolescents (N = 304) was followed to the age of 16 years. At the age of 17 years, 69 of them participated in a magnetic resonance imaging (MRI) study of the cervical spine.

During the follow-up from 13 to 16 years of age, changes in both HA type and frequency were common. A poor outcome of HA was associated with NP interfering with daily activities at the age of 13 years. The changes in HA type were not predictable by NP. At the age of 16 years, local and referred palpation pain of the neck muscles, self-reported NP and NP intensity were associated with HA, and especially with disturbing HA unresponsive to analgesics. The association of NP with HA was not determined by HA type. Mild degenerative changes of the cervical spine were common but did not contribute to headache.

HA in adolescence is often episodic, and prevention and treatment of NP could be important in the prevention of future chronic adult HA.

Keywords: Adolescent, chronicization, disc degeneration, headache, migraine, MRI, muscle, myofascial pain, neck pain, outcome, palpation, tension-type headache, visual analogue scale

TIIVISTELMÄ

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Niskakipu päänsärkyisillä nuorilla – koululaisten seurantatutkimus

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Annales Universitatis Turkuensis
Series D Medica – Odontologica
Painosalama Oy, Turku, Suomi, 2007

Vaikka niskakipu ja päänsärky esiintyvät nuorilla usein samanaikaisesti, tutkimustietoa niiden yhteydestä on vähän. Tutkimuksen tarkoituksena oli selvittää niskakivun yhteyttä nuoren päänsärkyyn ja päänsäryn ennusteeseen. Tutkittiin niskaoireiden, mitatun niskakivun ja kaularangan välilevyrappeuman yhteyttä nuoren päänsärkyyn.

Tämä tutkimus on osa väestöpohjaista 12-vuotiaiden päänsärkyisten ja päänsäryttömien lasten (N 1135/1409) seurantatutkimusta. Osaa nuorista (N = 304) seurattiin 16 vuoden ikään. 17-vuotiaina heistä 69 osallistui kaularangan magneettitutkimukseen.

Päänsärkytyypin ja esiintymistiheyden muutos oli yleistä 13-16-vuotiaana. Päänsäryn paheneminen oli todennäköisempää, jos 13-vuotiaan päänsärkyyn liittyi päivittäistä toimintaa haittaava niskakipu. Niskakipu ei selittänyt päänsärkytyypin muutosta. 16-vuotiaana niskalihasten paikallisella ja päähän säteilevällä painoarkuudella, nuoren raportoimalla niskakivulla ja niskakivun voimakkuudella oli yhteys päänsärkyyn, erityisesti haittaavaan päänsärkyyn, joka ei helpottunut särkylääkkeiden avulla. Niskakivulla ei ollut yhteyttä päänsärkytyyppiin. Lievät kaularangan rappeumamuutokset olivat yleisiä, mutta ne eivät liittyneet päänsärkyyn. Nuoren päänsärky on usein ajoittaista, ja nuoren niskakivun ehkäisy ja hoito saattaa olla tärkeää ehkäistäessä tulevaa aikuisen kroonista päänsärkyä.

Avainsanat: ennuste, kroonistuminen, lihas, migreeni, MRI, myofaskiaalinen kipu, niskakipu, nuori, palpaatio, päänsärky, tensiotyyppinen päänsärky, VAS, välilevyrappeuma

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ABBREVIATIONS

CTTH	chronic tension-type headache
DD	disc degeneration
EMG	electromyography
ETTH	episodic tension-type headache
HA	headache
ICHD 1	Headache Classification Committee of the International Headache Society. Classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain. 1st edition at 1988
ICHD 2	Headache Classification Subcommittee of the International Headache Society. The International Classification of Headache Disorders, 2nd edition at 2004
IHS	International Headache Society
IHS 1	migraine, M
IHS 1.7	migrainous disorder (subtype of migraine), M1.7
IHS 2	tension-type headache, TTH
IHS 2.3	tension-type headache not fulfilling criteria (subtype of tension-type headache), TTH2.3
IHS 13	non-classifiable HA, major group nr 13 in ICHD 1
M	migraine
M1.7	migrainous disorder (subtype of migraine)
MRI	magnetic resonance imaging
MwA	migraine with aura
MwoA	migraine without aura
NP	neck pain
OR	odds ratio
P	significance level, p-value
ROM	range of motion
SD	standard deviation
TTH	tension-type headache
TTH2.3	tension-type headache not fulfilling criteria (subtype of tension-type headache)
VAS	visual analogue scale

LIST OF ORIGINAL PUBLICATIONS

The thesis is based on the following original articles, referred to in the text by their Roman numerals I to IV. In addition, some unpublished data are presented.

I **Katri Laimi**, Liisa Metsähonkala, Pirjo Anttila, Minna Aromaa, Tero Vahlberg, Jouko J. Salminen, Matti Sillanpää. Outcome of headache frequency in adolescence. Cephalalgia 2005; 26:604-12.

II **Katri Laimi**, Tero Vahlberg, Jouko J. Salminen, Liisa Metsähonkala, Marja Mikkelsson, Pirjo Anttila, Minna Aromaa, Matti Sillanpää. Does neck pain determine the outcome of adolescent headache? Cephalalgia 2007; 27:244-53.

III **Katri Laimi**, Minna Erkintalo, Liisa Metsähonkala, Tero Vahlberg, Marja Mikkelsson, Pirkko Sonninen, Riitta Parkkola, Minna Aromaa, Matti Sillanpää, Päivi Rautava, Pirjo Anttila, Jouko J. Salminen. Adolescent disc degeneration – no headache association. Cephalalgia 2006; 27:14-21.

IV **Katri Laimi**, Jouko J. Salminen, Liisa Metsähonkala, Marja Mikkelsson, Pirjo Anttila, Minna Aromaa, Tero Vahlberg, Sakari Suominen, Marjo-Riitta Liljeström, Matti Sillanpää. Characteristics of neck pain associated with adolescent headache. Accepted to Cephalalgia 16.06.2007.

1. INTRODUCTION

In adults, different features of neck pain (NP) such as self-reported NP, pericranial muscle tenderness, myofascial referred pain from neck muscles, and the dysfunction of the joints of the upper cervical spine have been associated with headache (HA) (Aprill et al 2002, Sjaastad and Fredriksen 2000, Jensen 1999, Travell and Simons 1999, Davidoff 1998, Lipchik et al 1996). In adolescents, NP and HA are often concomitant, but few data are available on various features of NP associated with HA, and it is not known if NP can influence on the incidence or the persistence of HA in adolescence (Ståhl et al 2004, Anttila et al 2002a, 2002b, 2001, Mikkelsson et al 1997).

As HA in adolescence is often episodic and may be a pecursor to potentially severe HA syndromes later in life, it is important to seek for treatable components of adolescent HA (Bandell-Hoekstra et al 2001, Aromaa et al 2000, Spierings et al 1998). NP could be one of the treatable components contributing to the chronicization of HA (Bendtsen 2000, Jensen 1999). Persistent unaddressed headache triggers, such as NP, may also limit the effectiveness of headache treatment (Holroyd 2002).

Degeneration of the cervical spine could be a pathological finding associated with HA in adolescence. While degenerative changes of the cervical spine, increasing with age, are common in asymptomatic adults, the clinical significance of the degeneration is obscure (Petren-Mallmin and Linder 1999, Matsumoto et al 1998, Lehto et al 1994, Boden et al 1990). The study presented in this dissertation is the first population-based MRI study of the adolescent cervical spine. As age-dependent physiologic degeneration of the cervical spine is thought to have its onset in adulthood, it is possible that the possible degenerative changes found in adolescents are more clearly associated with pain than in adults (Matsumoto et al 1998, Lehto et al 1994, Boden et al 1990).

2. REVIEW OF LITERATURE

2.1. Headache in adolescence

Adolescence is defined by the WHO as a period of 10 to 19 years of age (Goodburn and Ross 1995).

2.1.1. IHS classification of headache

The first edition of the International Classification of Headache Disorders (ICHD 1) was published by the International Headache Society (IHS) in 1988, and the second edition in 2004 (ICHD 2). All new clinic- and population-based HA studies of primary HA are based on these IHS criteria. As the major principles of the classification of primary HA disorders were not changed in the second edition, using the first edition remains valid for most HA diagnoses (ICHD 2, 2004).

HA disorders are classified into 13 (ICHD 1) or 14 (ICHD 2) major groups. These first digit major groups (IHS 1-13/14) are then subdivided into subtypes. The diagnostic criteria are etiological for secondary headaches and symptom-based for primary headaches such as migraine (M) and tension-type HA (TTH). These symptom-based clinically-defined HA:s are probably heterogeneous (ICHD 2, 2004). Table 1 shows the IHS criteria of M, TTH, HA associated with disorder of neck, and occipital HA.

Migraine and tension-type headache

The criteria of M and TTH are virtually the same from 1988 and 2004. When HA diagnoses according to ICHD 1 and ICHD 2 were compared in children and adolescents with M and TTH, the number of children with migrainous disorder (IHS 1.7) was reduced by 60% without any change in the total amount of children with migraine, IHS 1 (Kienbacher et al 2006, Lima et al 2005, ICHD 2, ICHD 1). Patients coded for TTH are believed to include some with migraine without aura (MwoA). When a HA patient is suspected of having more than one HA type, the use of a diagnostic HA diary has been shown to improve diagnostic accuracy. (ICHD 2, 2004).

The precise etiology of M and TTH is not known. The continuum theory for headaches, on the other hand, suggests that there may be a common mechanism for most HA types (Graff-Radford and Newman 2002). ICHD2 describes the current concepts of the pathophysiology of M and TTH. A migraine attack with aura (MwA) starts with decreased blood flow in the cortex, followed by gradual transition into hyperaemia in the same region. Cortical spreading depression has been implicated. MwoA shows no changes suggestive of cortical spreading depression, although blood flow changes in the brainstem may occur, as may cortical changes secondary to pain activation. While MwoA was previously regarded as primarily vascular, the importance of sensitization of perivascular nerve terminals and the possibility that the attacks may originate in the central nervous system have gained attention over the last decades (ICHD 2, 2004). Peripheral pain mechanisms are likely to play role in episodic TTH (ETTH), whereas central pain mechanisms play a more important role in chronic TTH (CTTH) (ICHD2, 2004).

Table 1. IHS-classification of headache disorders (ICHD 1 and ICHD 2)

	Diagnostic criteria, ICHD 1 (IHS 1988)	**Changes in ICHD 2 (IHS 2004)**
Migraine (M) IHS 1	A. at least 5 attacks fulfilling criteria B. attacks lasting untreated 4-72 hours in adults, 2-48 hours in children below age 15, C. at least two of the following characteristics: 1. unilateral position, 2. pulsating quality, 3. moderate or severe pain intensity, 4. aggravation by walking or similar routine physical activity D. during HA at least one of the following: 1. nausea and/or vomiting 2. photophobia and phonophobia E. not attributed to another disorder	B. 1-72 hours in children C4: or causing avoidance of routine physical activity (eg, walking or climbing stairs)
Migrainous disorder not fulfilling criteria IHS 1.7, M1.7	HA fulfils all criteria but one for migraine and does not fulfil criteria for tension-type HA	Name: Probable migraine, Code: IHS 1.6
Tension-type HA (TTH) IHS 2	A. at least 10 episodes B. lasting from 30 minutes to 7 days C.at least two of the following characteristics: 1. bilateral location, 2. pressing/tightening (non-pulsating) quality, 3. mild or moderate intensity, 4. not aggravated by routine physical activity 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.	HA associated with cervical myofascial tender spots is coded as tension-type HA.
TTH not fulfilling criteria IHS 2.3, TTH 2.3	HA fulfils all criteria but one for TTH and does not fulfil criteria for migraine without aura (MwoA)	Name: probable TTH, code: IHS 2.4

HA associated with disorder of neck IHS 11.2	11.2.1. HA associated with cervical spine A. pain localized to neck and occipital region B. precipitated or aggravated by special neck movements or sustained neck posture, C. at least one of the following: 1. resistance to or limitation of passive neck movements, 2. changes in neck muscle contour, texture, tone or response to active and passive stretching and contraction, 3. abnormal tenderness of neck muscles D. Radiological examination reveals at least one of the following: 1. movement abnormalities in flexion/extension, 2. abnormal posture, 3. fractures, congenital abnormalities, bone tumours, rheumatoid arthritis or other distinct pathology (not spondylosis or osteo-chondrosis). 11.2.2. HA associated with retropharyngeal tendinitis diagnosed in X-ray.	11.2.1 Cervicogenic HA: A. Pain, referred from a source in the neck and perceived in one or more regions of the head and/or face B. Clinical, laboratory and/or imaging evidence of a disorder or lesion within the cervical spine or soft tissues of the neck known to be, or generally accepted as, a valid cause of headache. C. Evidence that the pain can be attributed to the neck disorder or lesion based on at least one of the following: 1. demonstration of clinical signs that implicate a source of pain in the neck 2. abolition of HA following diagnostic blockade of a cervical structure or its nerve supply using placebo- or other adequate controls. D. Pain resolves within 3 months after successful treatment of the causative disorder or lesion.
Occipital neuralgia IHS 12.6	A. Pain is felt in the distribution of greater or lesser occipital nerves B. Paroxysmal stabbing pain, aching may persist between paroxysms C. Tenderness over the affected nerve D. Pain is eased temporarily by local anaesthetic block of the nerve.	Code: IHS 13.8 A. …in the distribution(s) of the greater, lesser and / or third occipital nerves.

In the examination of the peripheral pain mechanisms of ETTH, the IHS recommends manual palpation of the frontal, temporal, masseter, pterygoid, sternocleidomastoid, splenius and trapezius muscles. NP associating with HA can be diagnosed as TTH, if myofascial tender points occur in the neck muscles (ICHD 2, 2004).

Cervicogenic headache

The criteria of HA associated with disorder of neck have greatly changed from 1988 to 2004. HA disorder associated with (ICHD 1) or attributed to (ICHD 2) disorder of neck can not be diagnosed without radiological examination (ICHD 1) or without successful treatment of the causative disorder (ICHD 2). Also the diagnosis of occipital neuralgia requires local anaesthetic block of the nerve. These strict IHS -criteria do not allow the diagnosis of cervicogenic HA or occipital neuralgia in population-based epidemiologic studies (ICHD 2, 2004).

The concept of cervicogenic HA in adults is controversial with different authors using different diagnostic criteria. There are also other types of HA clearly of cervical origin, and descriptions of cervicogenic HA overlap with those of M, TTH and myofascial pain (Sjaastad et al 2006, ICHD 2). Primary HA disorders may present with coexisting neck pain (NP), and thus NP is not pathognomonic for cervicogenic HA. Some define cervicogenic HA consisting only of HA originating from the cervical spine (ICHD 1, 1988), while others include HA originating from other structures innervated by the upper three cervical nerves (Biondi 2005, ICHD 2 2004). In some studies, cervicogenic HA is unilateral without sideshift (Biondi 2005, Sjaastad and Fredriksen 2000), in others also bilateral HA is included (ICHD 1, 1988 and ICHD 2, 2004). Occipital neuralgia, meaning pain produced or aggravated by trauma or entrapment of the greater occipital nerve, is considered by some authors as a distinctive disorder, while others regard it as a part of cervicogenic HA. Occipital neuralgia is also difficult to be distincted from myofascial pain or from pain of the zygapophyseal joints or spinal roots (Biondi 2005, Packard 2002). Originally, the term "cervicogenic HA" referred to unilateral HA triggered by neck movement and/or position, generally starting from the neck and "spreading" forwards with signs pertaining to the neck (Sjaastad and Fredriksen 2000). The lack of specificity of the cervical blocks used in the treatment of cervicogenic HA further clouds this picture (Graff-Radford and Newman 2002).

The pathophysiology and source of pain in cervicogenic HA have been debated, but the pain is probably referred from one or more muscular, neurogenic, osseous, articular, or vascular structures in the neck through the convergence of the upper spinal nerves with the trigeminal nucleus (Biondi 2005, ICHD2, Graff-Radford and Newman 2002).

2.1.2. Epidemiology of headache in adolescence

2.1.2.1. Prevalence

HA is the most common pain in adolescents (Roth-Isigkeit et al 2004, Haugland et al 2001, Perquin et al 2000). Table 2 shows population-based studies of HA prevalence in adolescence. HA is rare before the age of four years, and its prevalence increases throughout childhood with female predominance after the age of 13 years (Russell et al 2006, Boardman et al 2003, Fichtel and Larsson 2002, Bandell-Hoekstra et al 2001, Fearon and Hotopf 2001, Haugland et al 2001, Aromaa et al 2000, Perquin et al 2000, Bille 1997). A marked increase in HA has been demonstrated in the early teenage years, followed by a decrease in middle adolescence, then a steady rise occurs into late adolescence, especially in girls (Aromaa et al 2000, Sillanpää and Aro 2000). The prevalence of overall HA in previous 6-12 months varies from 46 to 92% in

adolescent years (Karli et al 2006, Zwart et al 2004, Anttila et al 2002a, Bandell-Hoekstra et al 2001, Aromaa et al 2000). Weekly HA occurs in 9-33% of adolescents, twice as often in adolescent girls than in boys (Dooley et al 2005, Larsson and Sund 2005, Stakes 2005, Zwart et al 2004, Fichtel and Larsson 2002, Bandell-Hoekstra et al 2001, Haugland et al 2001, Rhee 2000, Kristjánsdóttir and Wahlberg 1993). There is little increase in overall HA from adolescence to adulthood, and from middle age overall HA prevalence declines with advancing age (Stovner et al 2006, Hagen et al 2000).

The prevalence of M is somewhat higher among boys than girls under the age of 10 years, but after this age higher rates are seen among girls and women in all age groups. M prevalence increases gradually, peaks during middle age and declines thereafter (Russell et al 2006, Stovner et al 2006). Studies applying the IHS criteria (ICHD 1 or ICHD 2) report prevalence rates of adolescent migraine between 3 and 22% (Laurell et al 2006, Russell et al 2006, Wang et al 2005, Zwart et al 2004, Anttila et al 2002a, Lu et al 2000, Split and Neuman 1999, Raieli et al 1995, Pothmann et al 1994).

Epidemiological data on TTH in adolescents have become available in recent years and suggest prevalence rates between 10 and 25%, higher in girls than in boys (Laurell et al 2006, Zwart et al 2004, Özge et al 2003, Anttila et al 2002a). When modified criteria of TTH were used, its prevalence was as high as 49%, higher in adolescent boys than in girls (Pothmann et al 1994). In a Danish twin study, the prevalence of adolescent TTH was even higher (81-91% among girls, 79% among boys) (Russell et al 2006). When 13-15-year-olds were compared with 7-9- and 10-12-year-old schoolchildren, the frequency of HA and the prevalence of TTH increased in both genders with age (Laurell et al 2004). No changes were found in the prevalence of TTH from adolescence to the age of 41 years, but an increase of frequent and chronic TTH was seen in both genders from 12 to 39 years of age (Russell et al 2006).

About half of the adolescent HA sufferers have HA attacks less frequently than once a month (Bandell-Hoekstra et al 2001, Aromaa et al 2000). Frequent HA seems to be more common in girls than in boys, and in M sufferers when compared with TTH sufferers (Laurell et al 2006, Zwart et al 2004, Anttila et al 2002a, Bandell-Hoekstra et al 2001, Rhee 2000).

The wide variation of reported prevalences depends on methodological differences in factors such as representativeness, age and gender of participants, the diagnostic criteria used as well as geographical, sociocultural and ethnical differences among study populations. The differences do not seem to be large between 1-year and 3-month prevalence rates (Stovner et al 2006). Interviews are recommended as the golden standard (Stovner et al 2006, Rasmussen et al 1991). Higher prevalences are found in answers to neutral questions (e.g. ‘Do you have HA?’) than to questions involving some specification of the degree of HA (e.g. ‘Do you have repeated HA’, ‘Do you suffer from HA?’) (Stovner et al 2006). Among Norwegian adolescents the 1-year prevalence of ‘any HA’ was 77%, while ‘recurrent HA’ was only reported by 29% (Zwart et al 2004).

The prevalence of childhood and adolescent HA has increased from 1974 to 2002 in Finland, from 1983 to 1995 in the Netherlands, and from 1955 to 1997 in Sweden (Anttila et al 2006, Laurell et al 2004, Bandell-Hoekstra et al 2001).

Table 2. Population-based headache prevalence studies

Author	population (response rate), recall period	Headache, HA %,	Migraine, M %	TTH %	Assessment method
Anttila et al 2002a Finland (study population of present thesis)	12-y schoolchildren N=1135 (81%), RP 6mo	overall HA: 52 HA≥ 15 d/mo: 2	14	12	Q
Aromaa et al 2000 Finland	Follow-up of 7-y schoolchildren N =1205 (Baseline 87%, Follow-up 51%), RP 6mo	7-y: 27 (♂27♀28) 13-y: 63 (♂60♀67) 14-y: 64 (♂58♀70) 22-y: 66 (♂52♀79)	7-y: ♂4, ♀4 13-y: ♂7,♀15 14-y: ♂3,♀7 22-y: ♂3,♀11		Q + I
Bandell-Hoekstra et al 2001 the Netherlands	10-17-y schoolchildren N=2358 (85%) RP 1y + lifetime 1. elementary school-aged N = 943 2. high school-aged N= 1415	Lifetime 97, previous year 92, previous week 47. Monthly:elementary ♂44♀59 high school ♂36♀58 Weekly: elementary ♂21♀26 high school ♂14♀28			Q
Barea et al 1996 Brazil	10-18-y schoolchildren N =538 (?%) RP 1y.	Lifetime 93 (♂92♀94) Previous year 83 (♂78 ♀88) Previous week 31 point prevalence 9	Previous year 10 (♂10♀10)	Non-M: previous year 73 (♂68♀77)	Q + I
Dooley et al 2005 Canada	general population (?%) RP 6mo 12-13-y N=1694 14-15-y N=1764	Weekly: 12-13-y 26 14-15-y: 31			Q
Fichtel and Larsson 2002 Sweden	13-19-y schoolchildren. N = 793 (84%), RP 6mo	Weekly 33 (♂24♀42)			Q
Haugland et al 2001 Finland (F) Norway (N) Poland (P) Scotland (S)	11-15-y schoolchildren N = 20,324 F:93%, N:82%, P:91%, S:78%. RP?	Weekly: 11-y: F:♂25♀36, N:♂14♀24, P:♂14♀29, S:♂22♀27. 13-y: F:♂ 27♀42, N:♂17♀21, P:♂14♀26, S:♂26♀35. 15-y: F:♂ 24♀47, N:♂17♀31, P:♂14♀33, S:♂22♀44.			Q

Karli et al 2006 Turkey	12-17-y public secondary school N=2387 (?%) RP 1y Interview N=1064	52: 12-y:42 (♂39♀45), 13-y:46 (♂41♀51), 14-y:53 (♂44♀61), 15-y:54 (♂49♀61), 16-y:61 (♂52,♀71), 17-y:58 (♂46♀71)	interview: 32% of recurrent HA sufferers	interview: 58% of recurrent HA sufferers	Q + I
Kristjánsdóttir and Wahlberg 1993 Iceland	Schoolchildren (89%) RP? 11-12-y N=1016 15-16-y N=1124	Monthly 11-12-y:♂28♀26, 15-16-y:♂30♀33, weekly 22:11-12-y: ♂22♀28 15-16-y: ♂12♀27.			Q
Larsson and Sund 2005 Norway	12-15-y schoolchildren N=2465 (88%), RP?	Weekly: 12-13-y:8 (♂5 ♀12) 14-15-y:9 (♂5 ♀13)			Q
Laurell et al 2006 Sweden	7-15-y schoolchildren N=1371 (74%), RP 1y	lifetime 45 previous year 45 (♂39♀50)	11(♂10♀12) (modified criteria 17) IHS 1.7: 7 (♂6♀8)	10 (♂8♀12) (modified crit 23) IHS 2.3:10(♂9♀10)	Q
Lu et al 2000 Taiwan	13-15-y schoolchildren N=4064 (92%) RP 6mo + lifetime	85 (♂81♀88). 13-y:83 (♂80♀86) 14-y:84 (♂80♀88) 15-y:87 (♂84 ♀90)	7 (♂6, ♀8):13-y: 5: ♂4♀6, 14-y: 7: ♂6♀8 15-y: 8: ♂7♀9		Q I (N=201)
Perquin et al 2000 the Netherlands	0-18-y: schoolchildren, 0-3-y: general population N=5423 (82%), RP?	Chronic (weekly >3 mo): 0-3-y: 0.2, 4-7-y:2, 8-11-y:2, 12-15-y:5, 16-18-y:4			Q
Pothmann et al 1994 Germany	8-16-y schoolchildren N = 4835 (61%) RP lifetime	88 8-9-y: 83 12-13-y:90 15-16-y:93	11 (♂8♀14) 8-9-y: ♂9♀15 12-13-y: ♂8♀13 15-16-y: ♂7♀14	modified criteria 49 (♂52♀45) 8-9-y: ♂44♀40 12-13-y: ♂55♀50 15-16-y: ♂57♀47	Q
Raieli et al 1995 Italy	11-14-y schoolchildren N=1445 (?%), RP 1y	recurrent 24 (♂20♀28). Of these 80% ≥1/mo	3(♂3♀3):13-y:3 (♂2♀4) 14-y:3 (♂2♀5)		Q + I
Roth-Isigkeit et al 2004 Germany	10-18-y schoolchildren N = 715 (89%) RP 3mo	66 (♂60♀72), 10-12-y: 55 (♂52♀59) 13-15-y: 75 (♂70♀82) 16-18-y: 68 (♂54♀80)			Q

Russell et al 2006 Denmark	12-41-y twins N=28,195 (84%) RP 1y		12-14-y: ♂7♀8 15-19-y: ♂11♀14 20-24-y: ♂14♀23 25-29-y: ♂14♀26 30-34-y: ♂17♀31 35-39-y: ♂16♀30 40-41-y: ♂17♀29	12-14-y: ♂79♀81 15-19-y: ♂79♀91 20-24-y: ♂78♀94 25-29-y: ♂79♀95 30-34-y: ♂81♀94 35-39-y: ♂78♀93 40-41-y: ♂78♀91	Q
Split and Neuman 1999. Poland	15-19-y schoolchildren N=2351 (?%) RP 1y		22(MwA9,MwoA19): ♂10(MwA3,MwoA7) ♀28(MwA9,MwoA19) 15-y♂6♀13,16-y♂9♀26, 17-y♂8♀28,18-y ♂14♀35,19-y:♂14♀28		Q + CE
Stakes 2005 Finland	14-17-y schoolchildren (?%), RP 6mo. 14-15-y N=48,585 16-17-y N=23,646.	14-15-y: at least monthly 65, at least weekly 30 (♂21♀38), daily 8 16-17-y: at least monthly 63, at least weekly 27 (♂16♀35), daily 6			Q
Wang et al 2005 Taiwan	13-15-y schoolchildren N= 2414 (?%) RP 1y		13-y:MwoA4(♂3♀4), M(=MwoA/M1.7) 19(♂15♀23) 14-y:MwoA 6(♂4♀8) M 18(♂14♀23) 15-y: MwoA 8 (♂6♀11) M 22(♂16♀29)		Q
Zwart et al 2004 Norway	13-18-y schoolchildren + nonstudent adolescents (88%), RP 1y. .Q:N=8255,I:N=5847	77 (♂69♀84) Recurrent 29 (♂21♀37): <1/mo: 6, 1-3/mo: 14, 1-5/w: 8, >5/w: 1	recurrent:7 (♂5♀9)	18 (♂13♀23)	Q + nurse I, self- diagnosis.
Özge et al 2003 Turkey	8-16-y schoolchildren N=5562 (96%), RP?	recurrent: 49 current: 31	10	25, CTTH: 6	Q + I

RP = recall period, mo = previous month, y = previous year, ?= not stated, ?% = participation rate not stated, ♂ = male, ♀ = female, CE = clinical examination, CTTH = chronic TTH, mo = month, MwA = migraine with aura, MwoA = migraine without aura, M1.7 = IHS1.7 = migrainous disorder, non-M = HA, but not migraine, Q = questionnaire, TTH = tension-type headache

Factors associated with adolescent headache in cross-sectional studies

The cross-sectional nature of HA prevalence studies limits conclusions about causal relationships between HA and associated factors. In a Canadian adolescent HA study, however, 15 of the found 16 associated factors of weekly HA in 12-13-year-olds remained associated with weekly HA in the same adolescents after two years, and 14/16 of these factors were also associated with weekly HA in a new group of 12-13-year-olds (Dooley et al 2005).

HA is more common in adolescent girls than boys. In pain studies, several mechanisms have been suggested as explanations for gender differences in overall pain sensitivity: Sex hormones, biological differences in processing noxious stimuli and psychosocial factors such as gender role beliefs, pain coping strategies, moods, pain-related expectations and familial factors may affect pain responses (Roth-Isigkeit et al 2004, Fichtel and Larsson 2002, Marcus 2001, Dao and LeResche 2000, Fillingim and Ness 2000).

In children and adolescents, HA has been associated with the HA and other health complaints of family members (Laurell et al 2005, Grøholt et al 2003, Özge et al 2003, Bandell-Hoekstra et al 2001, Fearon and Hotopf 2001, Leonardsson-Hellgren et al 2001, Aromaa et al 1998). Relatives of children with HA and M, but not with TTH reported other types of pain more often than relatives of children without HA (Laurell et al 2005). A genetic risk for M is evident and exists for other HA as well, but other family factors such as coping methods and social functions of the family also contribute to HA (Svensson et al 2002, Gervil et al 1999).

Children and adolescents with HA have more non-headache pains than HA-free controls (Larsson and Sund 2005, Laurell et al 2005, Anttila et al 2004, Ghandour et al 2004, Grøholt et al 2003, Perquin et al 2000, Anttila et al 2001, Fichtel and Larsson 2002). The difference in the levels of somatic complaints has been reported to be greater between HA sufferers and controls than between children with M and those with TTH (Laurell et al 2005, Anttila et al 2004). At the age of 8-9 years, children with M had higher co-morbidity with other types of pain than those with non-migrainous HA (Anttila et al 2001). Co-occurrence of various types of pain in the same child suggests that certain children might have increased suspectibility to pain. Genetic factors, psychological burden, stress, disturbances in pain modification and central sensitization have been suggested to play role in the origin of multiple pains (Grøholt et al 2003, Alfvén 2001, Woolf and Decosterd 1999). Anxiety and depressive symptoms are also associated with HA in this age group and may predict onset of HA (Dooley et al 2005, Larsson and Sund 2005, Anttila et al 2004, Gordon et al 2004, Waldie and Poulton 2002, Fearon and Hotopf 2001, Fichtel and Larsson 2002, Rhee 2000, Guidetti et al 1998).

In children and adolescents varying associations of stress factors with HA have been reported (Dooley et al 2005, Galli et al 2004, Gordon et al 2004, Virtanen et al 2002, Bandell-Hoekstra et al 2001, Lanzi et al 2001, Waldie 2001, Rhee 2000, Metsähonkala et al 1998). It has been suggested that children with HA may be more sensitive to everyday life stressors and daily hassles than those without HA. Recent studies from Sweden and of our study population, however, have found few differences in psychosocial factors between children with M, TTH and without HA (Laurell et al 2005, Anttila et al 2004). Associations between socio-economic factors and adolescent HA are also controversial (Virtanen et al 2004, Grøholt et al 2003, Virtanen et al 2002, Fearon and Hotopf 2001). In a German study, the prevalence of HA and TTH but not M was higher in urban children than in their rural peers (Pothmann et al 1994).

In adolescents, the association of HA with physical exercise is controversial (Gordon et al 2004, Leonardsson-Hellgren et al 2001, Kujala et al 1999). In our study population at the age of 13 years, frequent sport activities were associated with M, and HA sufferers reported computer use more often than HA-free children (Oksanen et al 2005).

2.1.2.2. Prospective follow-up studies

As primary HA may have a marked effect on the quality of life of adolescents, information on the prognosis of HA is essential. Table 3 shows follow-up studies of HA in adolescence. Population-based follow-up studies have shown that both the frequency and type of HA change substantially during adolescence (Laurell et al 2006, Larsson and Sund 2005, Wang et al 2005, Camarda et al 2002, Fearon and Hotopf 2001, Aromaa et al 2000, Bille 1997, Sillanpää 1983). Most of these studies have focused on the subgroup of children with migraine or on overall HA (Larsson and Sund 2005, Wang et al 2005, Camarda et al 2002, Fearon and Hotopf 2001, Aromaa et al 2000, Rhee 2000, Bille 1997, Sillanpää 1983).

Only a few follow-up studies with IHS criteria include over 200 participants or cover a follow-up period of more than 2 years (Kienbacher et al 2006, Wang et al 2005). As far as we know, only one population-based study has followed both children with TTH and those with M (Laurell et al 2006). The outcome of HA and outcome predictors are different in HA patients seen in tertiary clinics from those in HA sufferers in the general adolescent population. Few children of the general population contact healthcare providers because of their HA (Wang et al 2006, Bandell-Hoekstra et al 2001). In clinic samples, children are more likely to have severe and recurrent HA, and the treatment of HA also influences the natural course of HA.

Changes in headache type

Changes in HA type are common in adolescent years (Laurell et al 2006, Wang et al 2005, Camarda et al 2002). Population-based follow-up studies show that 48-83% of schoolchildren with migraine still have migraine after 2-7 years of follow-up, 13-18% of migraine change to ETTH, and 49% to non-migrainous HA (Laurell et al 2006, Wang et al 2005, Camarda et al 2002, Bille 1997, Metsähonkala et al 1997, Sillanpää 1983). After 40 years of follow-up, half of children with pronounced migraine (N = 73) still had migraine (Bille 1997). TTH in 7-15-year-old schoolchildren was shown to persist as TTH in 49% and to change to M in 26% in a 3-year follow-up study (Laurell et al 2006).

In clinical studies of children and adolescents, M has been found to change to TTH more often than vice versa (Kienbacher et al 2006, Brna et al 2005, Guidetti and Galli 1998). Of HA not quite fulfilling IHS criteria for either M or TTH about one fourth disappeared, 1/3 met full criteria and 20% changed from M to TTH or vice versa, in a 2-5-year follow-up (Zebenholzer et al 2000). In a 20-year-follow-up of child patients, the initial HA diagnosis was not a useful predictor of HA type at follow-up (Brna et al 2005).

The high rates of transition between M and TTH in adolescence suggest that these diagnoses are related, as explained by the continuum model of HA (Graff-Radford and Newman 2002). Another explanation may be concurrent TTH and M and the difficulty of separating between these HA types. However, a persistent change from M to TTH cannot be excluded (Kienbacher et al 2006, Laurell et al 2006).

Table 3. Follow-up studies on adolescent headache

Author, country	Population, assessment method, recall period	HA type during follow-up	HA frequency during follow-up	predictors
1. Clinical studies				
Brna et al 2005 Canada	Child HA patients 20-y follow up N = 60 (B:?%, F:63%). B: I, F: TI, RP?	TTH→TTH 40%, M 7%. M →TTH33%, M+TTH24%	R: 27% (TTH 53%, mild HA 45%, moderate or severe 18%), IM: 66%	TTH predicted remission. HA type did not predict HA type.
Galli et al 2004 Italy	7-17-y chronic daily HA patients >15d/mo,>3mo. N=59 (?%). B:I+CE, F:I. 4-y follow up, RP 2y.		R: 29%, IM: 59%, 12% remained	Psychiatric disorder predicted persistence, sleep disorder or analgesic overuse not.
Guidetti and Galli 1998 Italy	100 child HA patients. B:I+CE, F:I. 8-y follow up (?%) RP 2y.	M → M 40%, TTH 27%, TTH →TTH47%, M 8%. MwoA→MwoA44,ETTH26%, ETTH→ETTH26, MwoA 11%	R: 34% (M 28, TTH 44) IM: 45%	Psychiatric comorbidity predicted worsening or persisting of HA. Higher remission rate for boys.
Kienbacher et al 2006 Austria	Young HA patients (M or TTH) N=227 (B:?%, F:56%). Q + I. 5-8-y follow-up, age at the end 11-26 yrs. RP 1y.	M →M49,TTH26% TTH→TTH 41, M 21%. M1.7→MwoA35,TTH35%. TTH2.3→TTH 53, M 7%. CTTH →EM 15, ETTH 45%. CM→TTH > MwoA→TTH. CM→ETTH 38%. Frequent ETTH→M > CTTH→M.,	Favourable prognosis (= frequency decreased $\geq$ 50%): 70% (in chronic daily 91) R: M 26%, TTH 38%, M1.7 30%, TTH2.3 40%.	The long time between the onset of HA and the visit in HA clinic, female gender, M and a changing HA location predicted persistence. Not predictive: age and HA frequency.
Zebenholzer et al 2000 Austria	Child-adolescent patients: M1.7 or TTH2.3. N=84 (B:?%, F:68%). B:I, F:I/ TI 2-5-y follow-up. RP?	1/3 meet full IHS criteria M →TTH: 1/5 TTH→ M: 1/5	R: 29%	
2. Population-based studies				
Aromaa et al 2000 Tampere, Finland	7-y schoolchildren. N=1205 (B:87%, F:58%) 15-y F. B:I+Q+CE, F:Q, RP 6mo.		R: 27%	HA at 7 yrs predicted frequent HA and M at 22 yrs

Bille 1962, 1997 Sweden	7-15-y schoolchildren (B:?%,F:100%). 6-y F N=254, 40-y F:N=73 (pronounced M). B:Q, F:I/ TI, RP 1y.	6-y: 66% still had M. 40-y:51% had M.	6-y: R: 34% IM: 51%	
Camarda et al 2002 Italy	11-14-y schoolchildren N = 64 (B:?%, F:80%) 5-y F, B:I, F:I. RP?	MwoA→MwoA 56, ETTH 13, M1.7 or HnC 13%. M1.7 →M1.7:11, ETTH 11, MwoA 28, HnC 6%. HnC→HnC 14, M1.7:21, MwoA 14, ETTH 14%	R: 30%: MwoA 19 M1.7: 45 HnC: 36	
Fearon and Hotopf 2001 UK	7-y general population N = 9841 (57%). 26-y F: I. RP?		HA →HA21% RecurrentHA→HA24% no HA →HA12%	
Larsson and Sund 2005 Norway	12-14-y schoolchildren. 1-y F. N=2355 (B:88%, F:96%). Q. RP?		weekly HA→weekly HA 38% (♂22♀45), IM: 62% (♀56♂78).	HA frequency, reduction of leisure time activities, depressive symptoms, gender and older age predicted weekly HA.
Laurell et al 2006 Sweden	7-15-y schoolchildren. N = 122 (B:74%, F:94%). 3-y F. B: Q+I, F:Q. RP 1y.	M →M 61%, TTH 18% TTH→TTH49%, M26%. Incidence of HA: 39% (TTH 26, M 13)	R: M 21%, TTH 23%	Female gender predicted M. Frequent and intensive HA predicted persistance of HA
Metsähonkala et al 1997, 1999 Finland	8-9-y general population N=3580 (B:67%, 8-y F:56%). 3-y F (N=218: I + diary), 8-y F of M (N=53,TI) B:Q, F:I+diary, TI. RP 6mo.	3-y: M→M63%, M1.7 20%, ETTH 8%, other HA 4%. 8-y: M→M 70%	3-y F: R: 5% of M.	Poor outcome of M associated with male gender, with frequent M and having divorced parents
Rhee 2000 USA	11-21-y students at 7th -12th grades. 1-y F. B:I,F:I. N=4591, B:80%, F:76%, RP 1y.			Depression and low self-esteem predicted frequent HA in girls. Insomnia did not predict HA

Sillanpää 1983 Finland	7-y schoolchildren N = 2921 (B:88%, F:69%), 7-y F. B:Q, F:Q. RP 1y.	M→M (♂74%,♀83%).	R: M 22%, IM: M 37 %	M onset before school age predicted persistence
Virtanen et al 2002 Finland	6-y first-born-children, 6-y F,N=798 (B:86%,F:80%).Q. RP 6mo.		HA→HA 41%, R: 59%, incidence 15%.	Maternal HA predicted HA, a worse prognosis in boys.
Wang et al 2005 Taiwan	13-y schoolchildren. 1-y and 2-y F. N=2414 (B:?, F:91%). B:Q, F:Q. RP 1y.	M (1.1. and 1.7) →M 1y 43%, 2y 48%, to other HA 49 (1 y) and 37% (2 y).	R: M (1.1 and 1.7): 8% (1 y) 16% (2 y)	greater frequency and pulsatile HA predicted persistence of M

RP = recall period, 6 mo =previous 6 months, y =previous year, ious 2 years, ?= not stated, ?% = participation rate not stated, ♂ = male, ♀ = female, B = baseline, CE = clinical examination, F = follow-up, HA = headache, I = interview, TI = telephone I, mo = month, M = migraine, MwoA = M1.1 = migraine without aura, MwA = migraine with aura, EM = episodic M, CM = chronic M, M1.7 = migrainous disorder, TTH = tension-type HA, TTH2.3 =TTH not fulfilling criteria, ETTH = episodic TTH, CTTH = chronic TTH, HnC = headache not classifiable, R = total remission, IM = improvement, Q = questionnaire.

Changes in headache frequency

A remarkable tendency for improvement of HA during adolescence has been found especially in boys (Kienbacher et al 2006, Larsson and Sund 2005, Guidetti and Galli 1998). The outcome of M and HA in boys before adolescent years, on the other hand, is poor compared with that in girls (Virtanen et al 2002, Metsähonkala et al 1997). In 2-26-year follow-ups of schoolchildren, 27-71% of overall HA, 16-30% of M and 23% of TTH remitted (Laurell et al 2006, Wang et al 2005, Camarda et al 2002, Fearon and Hotopf 2001, Aromaa et al 2000, Sillanpää 1983). Of weekly HA in 12-14-year-old children, 62% improved in one year's follow-up. HA at the age of 14 years was more persistent than at the age of 12 years (Larsson and Sund 2005).

When the results of population- and clinic-based studies are compared, the remission rates of migraine are about the same but in a population-based TTH study, TTH remitted less often than in clinical studies (Kienbacher et al 2006, Laurell et al 2006, Brna et al 2005, Guidetti and Galli 1998).

The prognosis of HA also seems to be good in adult HA sufferers,. In a 13-year follow-up of adults, 45% of subjects with frequent or chronic TTH, and 42% of migraine sufferers experienced remission (Lyngberg et al 2005).

Determinants of headache outcome in follow-up studies

Little is known about the determinants of the outcome of adolescent HA, although most adult patients with chronic HA report that their HA already started in adolescence (Spierings et al 1998). To prevent the worsening of adolescent HA, it is important to determine the predictors of outcome. Various factors transform episodic HA into a more chronic form. One simple etiology and a simple pathophysiological mechanism, however, cannot be expected (Scher et al 2002). In adults, the aggravating role of overconsumption of analgesics, peripheral and central sensitization of nociceptors, muscle tenderness, psychosocial stress and genetic factors have been associated with chronic HA (Cady et al 2005, Zwart et al 2003, Lu et al 2001, Burstein and Woolf 2000, Russell et al 1999, Davidoff 1998, De Benedittis and Lorenzetti 1992). However, it is uncertain whether these same predictors are important for the worsening of childhood or adolescent HA (McGrath 2001).

In previous population-based studies, HA frequency, HA type, gender, age at onset of HA, anxiety, depressive disorders, leisure time activities, and maternal HA have been associated with the outcome of childhood or adolescent HA (Laurell et al 2006, Larsson and Sund 2005, Wang et al 2005, Virtanen et al 2002, Waldie and Poulton 2002, Fearon and Hotopf 2001, Waldie 2001, Aromaa et al 2000, Rhee 2000, Metsähonkala et al 1997, Sillanpää 1983). In clinical studies, HA frequency, HA type, HA severity, psychiatric disorders, gender, and the time between the onset of HA and a visit to a HA clinic have been associated with the outcome of childhood or adolescent HA (Kienbacher et al 2006, Brna et al 2005, Galli et al 2004, Guidetti and Galli 1998).

It is not known if NP affects the outcome of adolescent HA.

2.2. Neck pain in adolescence

NP refers to a subjective unpleasant sensory experience in the neck. It may be manifested as fatigue, tension, or pain radiating to the upper extremities or the head (Merskey and Bogduk 2004). The neck is defined as the area between the occiput and the third thoracic vertebra and between the medial borders of the scapulae (Fejer et al 2005) or as including the cervical spine,

occiput region, cervicothoracic junction and muscles originating from the cervical region acting on the head and shoulders (Borghouts et al 1998).

2.2.1. Classification of neck pain

No generally-accepted classification of NP is used throughout the world. NP has been classified on the basis of the etiology, duration, findings of clinical status, location and type, radiological findings or dysfunction of the cervical joints. NP is not a uniform symptom resulting from one source of pain with a single uniform etiology (Siivola et al 2004, Andersen et al 2002). On the contrary, NP is a symptom with multifactorial and often unknown etiology without pathoanatomically well-defined diseases. In most cases, NP is mainly associated with mechanical or functional disorders (Ylinen 2004, Ariëns et al 2001, Travell and Simons 1999, Borghouts et al 1998).

Many structures in the neck are capable of inducing pain. The exact source of NP is not revealed by the location of pain. Potential structures causing NP include the facet joints, ligaments, muscles, nerves, nerve roots, discs, dura and vertebrae, or NP can be referred from other areas of the body (Bogduk 2004, Travell and Simons 1999). The pain can be nociceptive, neuropathic, idiopathic or psychosomatic. In the current care guidelines for NP in Finland, adult NP has been divided into acute (with duration less than 3 months) or chronic, to local or radiating NP, to non-specific or specific NP including traumatic NP after whiplash injury, myelopathy and NP associated with other diseases (Hoitosuositustyöryhmä 2002).

No studies have been carried out of non-traumatic adolescent NP associated with physical findings of the neck such as local muscle pain, myofascial pain, or disc degeneration of the cervical spine.

2.2.1.1. Muscle pain

Muscle pain is defined as pain caused by excitation of muscle nociceptors by mechanical stimuli or chemical stimulants (Mense et al 2001). In addition to their role in movement and support, the cervical and neck muscles are related with stabilization of the head and the eyes, vestibular function and proprioseptive systems serving postural orientation (Falla and Farina 2006). Muscle pain may be associated with muscle contraction, increased muscle activation or with a poor motor control of postural muscular activity (Westgaard 1999b). Measurable sources of muscle stiffness or muscle tension include viscoelastic tone, physiologic contracture, voluntary contraction, and muscle spasm, which is defined as involuntary muscle contraction. Muscle tension depends on the viscoelastic properties and the degree of activation of the contractile apparatus of the muscle (Mense et al 2001). In addition of muscle activation, individual differences in motor coordination, physical strength, and working techniques influence muscle pain (Westgaard 1999a, 1999b). Muscle imbalance and poor posture are often combined (Mense et al 2001).

Recent studies of the role of cervical muscles in NP support the hypothesis of an inhibitory effect of pain on motor neurons (Falla and Farina 2006). Nociception alters the load sharing within and between muscles, which leads to muscle overuse or disuse in functional activities in an attempt to minimize the use of the painful muscle with minimal disruption to the task. Pain-induced alterations of the motor strategy may be viewed as a compensatory mechanism to allow similar motor outputs in painful and non-painful conditions. NP has been associated with inhibition of deep muscle activation concomitant with increased activation of the superficial muscles with reduced ability to relax these muscles following activation. Alterations in motor

control and in the level of muscle activity are sufficient to produce chronic changes in muscle properties in the long term, and muscle biopsies of ventral and dorsal neck muscles have demonstrated specific morphological changes in NP (Falla and Farina 2006).

Stress, physical and psychosocial stressors can be risk factors for muscle pain (Westgaard 1999a), and an etiological model explaining muscular NP could be based on interaction between mechanical and psychosocial factors (Östergren et al 2005). Heavy manual handling, sustained posture, repetitive movements, extreme postures, and mental stressors have been associated with adult occupational muscular NP (Östergren et al 2005, Ming et al 2004). Muscle loads higher than 8-10% of maximal voluntary contraction cannot be sustained, and a static activity level above 2% represents a risk of muscle pain (Dalenbring et al 1999, Westgaard 1999a, 1999b). The probable sources of pain in maintained awkward positions are the ligaments and joint capsules that are under continuous tension (Mense et al 2001). Extreme postures of the spine are maintained passively or by active muscle work (Dalenbring et al 1999).

Psychological factors can be associated with NP through an increase in perceived muscle tension or less muscle control due to poor concentration (Ylinen 2004). Muscles often react to psychosocial strain with increased tension and subjects with stress may have a lowered threshold of reporting pain. Emotional state may also influence posture, affecting NP through physical factors. Stress may activate the central nervous system, resulting in muscle activation. Increased muscle tone can lead to painful tensional syndromes (Westgaard 1999b, Simons and Mense 1998, Alfvén 1997).

2.2.1.2. Myofascial pain

Myofascial pain has been used as a term to describe a common regional muscular disorder characterized by the presence of myofascial trigger points and production of referred pain and/or autonomic phenomena referred from active trigger points, with associated dysfunction (Packard 2002, Graff-Radford and Newman 2002, Gerwin 2001, Mense et al 2001, Travell and Simons 1999). The trigger point is a focus of hyperirritability in the muscle, which when compressed is locally tender and if sensitized causes referred pain and tenderness. Spontaneous electrical activity occurs in the trigger points, which can be powerful sources of muscle spasms (Gerwin 2001, Mense et al 2001, Travell and Simons 1999). Trigger point referral shows a characteristic pattern not following strict neuroanatomic dermatomes or myotomes. The muscle pain guide of Travell and Simons shows maps of referred patterns of different muscles (Travell and Simons 1999).

Pathophysiologic theories about referred pain suggest that nociceptive dorsal horn and brain stem neurons receive convergent inputs from various tissues; higher centres cannot therefore correctly identify the actual input source. Somatic pain can cause rapid central sensitization, changes in the central nervous system, as a manifestation of neuroplasticity, or the remodelling of central processes in response to peripheral stimulation. Central hyperexcitability of dorsal horn and brainstem neurons initiated by nociceptive activity from muscles may explain the expansion of pain with referral to other areas. In animal studies, also dysregulation of the descending endogenous pain control system has been involved in the central perception of muscle pain (Graff-Radford and Newman 2002, Arendt-Nielsen and Svensson 2001, Gerwin 2001, Travell and Simons 1999, Davidoff 1998).

Myofascial NP is produced by factors damaging or stressing muscles, such as direct overload, muscle imbalance, excessive neck muscle contraction and overwork fatigue. Postural stresses, especially forward head posture, are among the most common causes of myofascial NP (Fernández-de-las-Peñas et al 2006, Gerwin 2001, Davidoff 1998). The head in the upright

position is usually maintained with minimal or no muscle activity. Deviated postures lead to compensatory muscle activity predisposing to the development of trigger points (Davidoff 1998). When one muscle in a functional unit develops trigger points, that muscle ceases to work effectively as it is weakened and loses its ability to lengthen. Other muscles must compensate for the impaired function and are thereby exposed to overuse or are shortened (Gerwin 2001).

2.2.1.3. Discogenic pain

The cervical spine is a dynamic structure protecting the spinal cord, supporting and orienting the head in space and transmitting forces from the trunk influencing the position of the head (Falla and Farina 2006). Degenerative changes of the cervical spine are common in asymptomatic adults, and degeneration is thought to have its onset in adulthood (Ishikawa et al 2003, Petren-Mallmin and Linder 1999, Matsumoto et al 1998, Lehto et al 1994, van der Donk et al 1991, Boden et al 1990). In a recent Finnish study, at the age of 24-26 years, disc degeneration (DD) of the cervical spine was common in both asymptomatic subjects and those with NP (Siivola et al 2002). In another study, the prevalence of DD in asymptomatic 20-year-olds was 17% for men and 12% for women (Matsumoto et al 1998). Degeneration of the cervical spine in adolescents could be a pathological finding associated with pain or only an unpreventable normal process of the ageing body without severe consequences. On the other hand, early degenerative changes of the cervical spine may lead to pain later in adult years as has been shown in subjects with early degeneration of the lumbar spine (Salminen et al 1999, Erkintalo et al 1995). In a 10-year follow-up of healthy adults, degeneration at level C6/7 predicted the incidence of NP (Gore 2001).

There are no MRI studies of adolescent cervical spine, but in MRI studies of the lumbar spine, degeneration was more common in adolescents with back pain (Paajanen et al 1997, Erkintalo et al 1995). In population-based studies in adults, degenerative changes have been most common at level C5/6 (Krasny et al 2005, Dai 1998, Matsumoto et al 1998, Jäger et al 1997, Lehto et al 1994). At this level, the extension-flexion motion is considerable and it has been thought that the large extent of motion could induce degeneration (Bogduk and Mercer 2000). Degeneration at this level has also been associated with compression loading of the spine (Jäger et al 1997). Under axial compression loading, the dural sac has been shown to narrow in asymptomatic individuals, especially at the C5/6 interspace (Kimura et al 2005). In previous adult studies, pathophysiological changes of the cervical spine have, however, explained only a small proportion of pain, and no clear association has been found between self-reported NP and DD (MacGregor et al 2004, Siivola et al 2002, Van der Donk et al 1991).

2.2.1.4. Neck pain associated with trauma

In adults, over one quarter of chronic NP sufferers have a history of head or neck trauma (Guez et al 2002). In adult whiplash patients, pain mechanisms include structural damage of the neck, development of myofascial pain, interaction of the trigeminal nociceptive system with the upper cervical nerves also inducing cervicogenic HA as well as psychologic and emotional factors (Biondi 2005, Miettinen et al 2004, Packard 2002). Of whiplash patients, 15-40% have symptoms for more than 6 months (Packard 2002), and after one year as many as 66% report at least slight health problems (Miettinen et al 2004). Myofascial NP and fear of movement have been associated with a poor outcome of posttraumatic NP (Nederhand et al 2004, Gerwin 2001). Of chronic whiplash pain patients, 75% respond to the treatment of myofascial pain (Gerwin 2001).

Table 4. Prevalence of adolescent neck pain (NP) in population-based studies

Author	Population (response rate), assessment method, recall period	NP %	Associated factors
Diepenmaat et al 2006 the Netherlands	12-16-y schoolchildren N=3485 (92%). Q. RP 1mo.	NP ≥ 4 d/month: 12 (♀14♂9).	Female gender, depressive symptoms, stress, and not living with 2 parents. No association: computer use, physical activity
Ehrmann-Feldman et al 2002 Canada	high school students (7^{th}-9^{th} grade). N=502, 1-y F, (B:85%, F:62%). Q. RP 2y.	weekly NP/upper limb pain: Prevalence: 32. Incidence: 28, only NP 10	With the incidence: Working and lower mental health score. No association: sports or music participation
Hakala et al 2006 Finland	14-, 16- and 18-y general population N=6003 (68%). mail Q. RP 6mo.	NP seldom/not at all 44%: 14-y:♂61♀47, 16-y:♂53♀30, 18-y:♂51♀23 About once a month 30%: 14-y:♂28♀30, 16-y:♂30♀32, 18-y:♂29♀32 About once a week 16%: 14-y:♂8♀14, 16-y:♂12♀22, 18-y:♂14♀25 Almost daily 10%: 14-y:♂3♀9, 16-y:♂5♀16, 18-y:♂ 6♀20	Using computer > 2-3h/day. No association: viewing television, time spent on digital gaming or using mobile phones
Hertzberg 1985 Norway	16-y schoolchildren N=302, 9-12-y F (B:?%, F:98%). B: CE, F:Q. RP?	Weekly NP: ♂12♀33 NP+muscular tension+tenderness: ♂3♀16	cervical pain in the follow-up: subjective muscle pain + measured muscular tension and tenderness at baseline
Mikkelsson et al 1997, 1999 Finland El-Metwally et al 2004 Ståhl et al 2004	9-12-y schoolchildren N=1756 (867 at 3^{rd}, 889 at 5^{th} grade) (B:83%, 4-y F:of pain-free 72%, of children with weekly musculoskeletal pain 76%). 1-y- and 4-y F. B:Q+hypermobility+cardiorespiratory fitness test, F:Q. RP 3mo.	Weekly NP: 15 (♂14 ♀16) NP > once a week: 6. Persistence in F: 1-y: 48 (♂37♀58), 4-y: 52. Incidence in F: 1-y: ≥ monthly 21 (19♂24♀), weekly 6 4-y: ≥ monthly 43 (29♂57♀), weekly:19	13-16-y: The intensity of NP with the frequency of NP. The frequency of NP with disability. NP with other musculoskeletal pains. 28% of NP sufferers had used analgesics for NP. Fluctuation of NP in follow-ups.

Murphy et al 2006 UK	11-14-y schoolchildren N=679 (97%). Q+measurement for height, weight and weight of the school bag. RP 1mo.	27 (♂26♀27). 2% of all sought treatment for NP, 1% had been absent from school for NP.	HA, school chair height too low, emotional and conduct problems, previous treatment for musculoskeletal disorders, family history of low back pain. No association: age, gender, physical activity, school bag weight.
Niemi et al 1996, 1997 Siivola et al 2003, 2004 Finland	15-18-y high school students (1st, 2nd and 3rd grade) N=714 (B:86%, F:55%, MRI: 47%). RP 6mo. B:Q, F:Q, F:MRI. 7-y F: N=394. 8-9-y F MRI: N=31 (no NP/weekly NP)	at 15-18-y: Weekly NP: 17: ♂10: 1st:8, 2nd:14, 3rd:8 ♀21:1st:16,2nd:20,3rd:29 occasional NP 55: ♂52♀57 no NP 28: ♂37♀22. 42% with NP (♂15♀48) sought for care At 22-25-y: weekly NP 28 (♂19♀34), occational 54 (♂55♀53), no 18: ♂26♀13 Incidence in 7-y F: 59.	High NP frequency: Gender, age, low physical activity, static loading of the upper limbs (playing piano, using computer), psychosomatic, depressive symptoms. Low NP frequency: Sports dynamically loading the upper extremities At 22-25-y: baseline NP, seeking for care, psychosomatic symptoms, gender. Sports dynamically loading upper limbs protected from NP. No: BMI, height, school achievement. MRI: only disc protrusion
Poussa et al 2005 Finland	11-y schoolchildren, N=430, 11-y F (B:?%, F:41%), Q+ CE. RP 1y + lifetime.	At 22-y: lifetime 78: NP< 8 d/y: 41, NP 8-30d/y: 23, NP > 30 d/y: 15.	Short stature, female gender No association: spinal posture or asymmetry at 22-y
Smedbråten et al 1998 Norway	10-15-y schoolchildren N=569 (86%). Q. RP?	Usually NP: 17 (12♂, 23♀). 1/3 several days a week	NP and HA affected the concentration the most.
Stakes 2005 Finland	14-15-y and 16-17-y schoolchildren N=48648 (?%), Q. RP 6mo.	14-15-y: NP ≥ monthly 60, NP ≥ weekly 27, NP almost daily 9 16-17-y: NP ≥ monthly 69, NP ≥ weekly 35, NP almost daily 12	
Straker et al Australia 2007	14-y general population (cohort from pregnancy) N=884 (44%).Q+a lateral photography of usual sitting posture. RP 1mo + lifetime	Lifetime: 47 previous mo: 28 NP today: 5 NP > 3 mo 8	No use or high use (>21 h/w) of computer (NP twice as often as with moderate use).
van Gent et al 2003 the Netherlands	12-14-y schoolchildren N=745 (?%). Q, measurement of weight, length, weight of school bag. RP 3mo.	NP: 44 (♂34♀53): 12-y:49, 13-y: 45, 14-y: 35 severe NP: ♂5, ♀7: 12-y:4, 13-y:8, 14-y:4.	Young age, female gender, psychosomatic score. No association: sports activities, smoking, watching TV, using computer, weight of bag or way of carrying.

Vikat et al 2000 Finland	12-, 14-, 16- and 18-y schoolchildren N=11095 (77%), mail Q. RP 6mo.	almost daily: 5: 12-y:♂1♀2, 14-y:♂2♀4, 16-y:♂1♀9, 18-y:♂4♀14 > weekly: 15: 12-y: ♂5♀7, 14-y:♂7♀14, 16-y:♂8♀26, 18-y:♂15♀36 > once a month: 40: 12-y:♂23♀26, 14-y:♂28♀41 16-y:♂34♀57, 18-y:♂40♀65	NP: Female gender, higher age. Weekly NP: gender, age, psychosomatic symptoms, long-term illness, number of times catching cold, wearing glasses or lenses, early timing of puberty, smoking, low BMI, panting or sweating a lot in physical exercise, LBP
Wedderkopp et al 2001 Denmark	schoolchildren N=806 (75%): 8-10-y N=481, 14-16-y N=325. Q+I. RP 1mo.	Spinal NP without back pain 7 (♂5♀9): 8-10-y: 9 (♂6♀11), 14-16-y: 5 (♂3♀6)	

RP = recall period, mo =previous month, y = previous year, ?= not stated, ?% = participation rate not stated, ♂ = male, ♀ = female, B = baseline, BMI = body mass index, CE = clinical examination, F = follow-up, HA = headache, I = interview, LBP = low back pain, Q = questionnaire.

2.2.2. Epidemiology of neck pain in adolescence

2.2.2.1. Prevalence of neck pain

The epidemiology of NP in adolescence has not been studied as much as that of HA. Table 4 shows prevalence studies of adolescent NP. Most studies of NP in this age group are cross-sectional relying solely on questionnaires. Few studies have separated NP from other musculoskeletal pains, although that would be important because of potentially different epidemiological patterns and assumedly different risk factors (Östergren et al 2005, Wedderkopp et al 2001). Many studies have found NP to be more common than low back pain (Hakala et al 2006, El-Metwally et al 2004, Hertzberg 1985), whereas HA, limb pain, backache and abdominal pain have been more common in others (Borge and Nordhagen 2000).

The prevalence of NP in adolescence has increased from 1991 to 2001 in both genders, suggesting a new disease burden of musculoskeletal disorders in future adults (Hakala et al 2002). In adolescence, the prevalence of NP in preceding 1-12 months has been 27-72% (Straker et al 2007, Hakala et al 2006, Murphy et al 2006, van Gent et al 2003, Vikat et al 2000, Niemi et al 1997). O adolescents, 12-30% suffer from weekly NP (Diepenmaat et al 2006, Hakala et al 2006, Palmer et al 2001, Vikat et al 2000, Niemi et al 1997). The prevalence of NP in adolescence increases with age and is more common in girls than in boys (Diepenmaat et al 2006, Hakala et al 2006 and 2002, Ståhl et al 2004, Ehrmann-Feldman et al 2002, Palmer et al 2001, Vikat et al 2000, Smedbråten et al 1998, Niemi et al 1997).

Of adults, 14-71% have experienced NP during their lifetime (Fejer et al 2006b). The prevalence of NP increases until 35 years of age, remaining stable until age 50 years, and decreasing slightly thereafter (Fejer et al 2006b, Guez et al 2002, van der Donk et al 1991). At one point in time, 6-22% of adults have been estimated to have NP. Scandinavian countries report more NP than the rest of Europe and Asia. The prevalence of chronic NP in adults is 2-17%. Most NP sufferers report having NP for a long time (Fejer et al 2006b).

2.2.2.2. Factors associated with neck pain

Computer use has been associated with adolescent NP, with daily use of computers exceeding 2-3h as a threshold for NP (Straker et al 2007, Hakala et al 2006, Niemi et al 1996). In Australian adolescents, the high use of computer has also been associated with increased flexion posture of the head, neck and thorax in usual sitting position suggesting that temporary postural changes lead to changes in habitual postures (Straker et al 2007). Fixed and unergonomic sitting postures, on the other hand, have been associated with NP in schoolchildren (Murphy et al 2006). However, some studies found no association between computer use and adolescent NP (Diepenmaat et al 2006, van Gent et al 2003). So far, no association has been found between NP and the relative weight of schoolbags (Murphy et al 2006, Steele et al 2003, van Gent et al 2003).

NP in adolescence has been associated with other musculoskeletal pains, and the frequency of NP has been associated with the frequency of other pains, with the higher dissability index of combined pain (Murphy et al 2006, El-Metwally et al 2004, Vikat et al 2000, Mikkelsson et al 1997).

The association of physical exercise with adolescent NP is controversial. Epidemiologic studies of NP in adolescence have associated it with static loading of the upper extremities. Both high intensity of physical exercise and low physical activity have been associated with a high

frequency of NP, whereas moderately intense physical exercise and sports dynamically loading the upper extremities have been associated with a low frequency of NP (Vikat et al 2000, Barnekow-Bergkvist et al 1998, Niemi et al 1997, Niemi et al 1996). Some other studies have found no association of physical activity with NP (Diepenmaat et al 2006, Murphy et al 2006, van Gent et al 2003, Ehrmann-Feldman et al 2002).

NP has been shown to have strong familiar clustering (Borge and Nordhagen 2000). Stress as well as depressive and emotional symptoms have been associated with adolescent overall or weekly NP (Diepenmaat et al 2006, Murphy et al 2006, van Gent et al 2003, Ehrmann-Feldman et al 2002, Härmä et al 2002, Niemi et al 1997). Other factors associated with adolescent NP include early timing of puberty, smoking, long-term illness or wearing glasses (Vikat et al 2000). Good flexibility of the trunk in adolescent boys and good endurance strength in adolescent girls have been associated with a decreased risk of tension neck syndrome in adulthood (Mikkelsson et al 2006).

In an adult twin study, genes seemed to play a significant role in adult NP in both genders, particularly in women. However, the genetic influence became less evident with increasing age, and environmental factors dominated almost completely in an older age group (Fejer et al 2006a). In population-based studies of adults, female gender, number of children, poor self-assessed health, poor psychological status, history of low back pain, neck injury and degenerative changes at level C6-7 have predicted the incidence of NP (Croft et al 2001, Gore 2001). Job-related mechanical exposure in both genders and psychosocial factors in women, independently of each other seemed to play a part in the development of NP (Östergren et al 2005). Adult NP has also been associated with certain occupations (Sjaastad et al 2006). Chronic NP has been more common in communities with a small than in those with a large population (Guez et al 2002). In adult epidemiological studies, NP has also been associated with overweight, smoking and sitting position when working. It is not known whether driving or leisure time physical activities affect NP (Hoitosuositustyöryhmä 2002).

2.2.2.3. Outcome of neck pain

Although NP fluctuates in adolescent years, it has been shown to be the most persistent of adolescent pains, more persistent in girls than in boys (El-Metwally et al 2004, Siivola et al 2004, Ståhl et al 2004, Mikkelsson et al 1999, Mikkelsson et al 1997, Hertzberg 1985). NP and muscle tenderness in 15-18-year-old adolescents has been shown to predict NP in young adults (Siivola et al 2004, Hertzberg 1985). In a follow-up of adolescents with and without NP, of base line factors at the age of 15-18 years of age, NP, seeking for care, psychosomatic symptoms, and female gender were associated with unfavourable outcome of NP from adolescence to early adulthood; sports dynamically loading the upper limbs were reported to protect from NP (Siivola et al 2004). In a 22-24-year follow-up of 13-year old adolescents, baseline psychosocial factors were not associated with NP in adults (Viikari-Juntura et al 1991).

In a 1-year follow-up of Canadian adults, NP persisted or aggravated in 47% of NP sufferers, and one third of adult NP patients still had moderate or severe NP after 10 years of follow-up. Individuals with NP do not seem to experience complete resolution of NP and related disability (Côté et al 2004, Guez et al 2002, Gore et al 1987).

2.3. Neck pain in adolescent headache

The co-occurrence of adolescent HA with other pains is high. In girls, a marked increase occurs in reporting chronic, intensive and multiple pains between 12 and 14 years of age. On the other

hand, the prevalence of intensive chronic pains in boys is highest at the age of 8-11 years (Fearon and Hotopf 2001). However, scanty epidemiological data have been obtained on the co-occurrence of NP and HA in adolescence. Muscular changes or degenerative changes of the cervical spine in adolescent HA sufferers have not been studied. Figure 1 shows a conceptual model describing associations of various individual, physical and psychosocial factors with NP and HA in adolescence.

2.3.1. Epidemiology of neck pain in adolescent headache

2.3.1.1. Self-reported neck pain

Adolescent NP and HA co-occur and have similar epidemiological features: increasing prevalence with age in girls and recent increases in prevalence (Anttila et al 2006, Laurell et al 2005, Ståhl et al 2004, Hakala et al 2002, Anttila et al 2001, Bandell-Hoekstra et al 2001, Aromaa et al 2000, Vikat et al 2000, Smedbråten et al 1998, Mikkelsson et al 1997, Niemi et al 1996).

Table 5 shows studies of NP in adolescent HA. In 10-year-old Finnish children NP has been found associated with migraine (Anttila et al 2001). In a Swedish study of 7-17-year-old children, and in our study population aged 12-13 years, self-reported NP was more common in M and TTH sufferers than in HA-free children. NP was equally common in children with M and in those with TTH (Laurell et al 2005, Anttila et al 2002a, 2002b). Of first-degree relatives of Swedish children with M 60%, with TTH 54%, and with no HA 36% reported having NP (Laurell et al 2005). In a Finnish follow-up study of 9-11-year-old schoolchildren, HA was co-occurring with self-reported NP more often than with other musculoskeletal pains. Of children with weekly NP, 62% also reported weekly HA (Mikkelsson et al 1997). When these children were followed for 4 years, weekly HA at baseline predicted persistent musculoskeletal pain at follow-up (El Metwally et al 2004). At the age of 13-16 years, the frequency of NP was associated with that of HA (Ståhl et al 2004).

A 4-year follow-up of 13-year-old Australian schoolchildren (N=436) showed a decreasing prevalence of HA, while NP increased with age in both genders. HA reported at baseline did not increase the risk of experiencing HA or NP at the age of 17 years (Grimmer et al 2006).

2.3.1.2. Physical findings of the neck

At the age of 7 years, tenderness on palpation of occipital muscle insertion areas was more common in HA sufferers than in controls (Aromaa et al 1998). In a study of 18-27-year-old female students, pericranial muscle tenderness was associated with frequent HA but not with HA type (Lipchik et al 1997). In our study population at the age of 12 and 13 years, muscle tenderness on palpation of the neck muscles was associated with migraine (Anttila et al 2002a, 2002b). Low muscle strength of the upper extremities was associated with ETTH in girls. Migraine or ETTH were not associated with changes of the mobility of the cervical spine (Oksanen et al 2006).

In a population-based study of Danish adults (N=735), muscle tenderness on palpation was associated with HA in men and with TTH in both genders, but not with migraine. Muscle tenderness was highest in CTTH sufferers. In males, the tenderness of splenius muscles and in females tenderness of temporal, masseter, sternocleidomastoid, frontal, trapezius muscles and posterior neck muscle insertions was associated with frequent TTH. Study groups could not be

differentiated by pressure threshold measurement, and EMG could only differentiate CTTH sufferers from those with other types of HA and from HA-free participants (Jensen 1999).

The prevalence of cervicogenic HA in adults has been estimated at 0.4-3%, and at about 20% in chronic HA patients (Biondi 2005). The prevalence of cervicogenic HA by modified IHS criteria was reported to be 18% in adults with a HA frequency over 4 times a month (Nilsson 1995). In a Norwegian study, 7% of adults had bilateral HA originating in the neck, provoked by awkward neck positions but not fulfilling the strict criteria of cervicogenic HA. Usually NP had preceded HA by years (Sjaastad et al 2006). In an interview of 94 Norwegian tractor drivers, 17% reported combined NP and HA at work during protracted head turning, while NP without HA was found in 71%. No HA of this type occurred without NP (Sjaastad and Bakketeig 2002). In Australian non-injured adults (N=427), the monthly prevalence of frequent HA reported to be associated with the cervical spine was 28%, and another 35% of subjects had these HAs occasionally (Grimmer et al 1999).

2.3.2. Development of co-occurring neck pain and headache in adolescence

The association of NP and HA may result from various pathophysiological mechanisms. No studies have been carried out of the possible causal association of NP and HA in adolescence. Neither is it known whether a reciprocal association occurs between NP and HA; if these two pain symptoms contribute to each other but are only a part of a widespread pain with other causal factors; or if these symptoms co-occur only because both pains are common but do not interact. The structures of the neck innervated by the first three cervical nerves can be associated with HA through the convergence of nociceptive afferents at the level of the caudal part of the trigeminal nucleus in the brainstem and sensitization of trigeminocervical neurones (Busch et al 2006, Bartsch 2005, Biondi 2005, Bogduk 2004, Bartsch and Goadsby 2003, Packard 2002, Piovesan et al 2001, Davidoff 1998). NP could initiate or maintain HA, or NP could be a consequence of HA extended from the head to other parts of the body (ICHD 2 2004, Graff-Radford and Newman 2002, Davidoff 1998, Jensen et al 1998).

According to the first current hypothesis, NP has been regarded as a peripheral cause of adult HA or HA becoming more chronic (Fernández-de-las-Peñas et al 2006, Bogduk 2004, Shevel and Spierings 2004, Jensen 2001, Piovesan et al 2001, Sjaastad and Fredriksen 2000, Jensen 1999, Davidoff 1998, Jensen and Olesen 1996). Epidemiological studies of adolescents support this hypothesis, as NP is persistent pain with a high tendency to convert to widespread pain on follow-up (El-Metwally et al 2004, Mikkelsson et al 1999, Mikkelsson et al 1997, Hertzberg 1985). Although episodic TTH has been regarded as a multifactorial disorder with several pathophysiological mechanisms, muscular factors seem to play an important role in ETTH (Jensen 2001, Jensen 1999, Jensen and Olesen 1996, Jensen et al 1993). In chronic TTH, secondary, segmental central sensitization and/or impaired supraspinal modulation of incoming stimuli seems to be involved, but prolonged nociceptive stimuli from the neck muscles could also be important for the conversion of episodic HA into chronic HA by producing continuous afferent bombardment of the trigeminal nerve nucleus caudalis, and, thence, activation of the trigeminovascular system (Fernández-de-las-Peñas et al 2006, Bendtsen 2000, Jensen 1999). As the pathogenesis of migraine is linked to the trigeminal innervation of the cranial blood vessels, noxious stimuli from the cervical muscles may also play a role in this pathogenesis by facilitating central sensitization (Shevel and Spierings 2004).

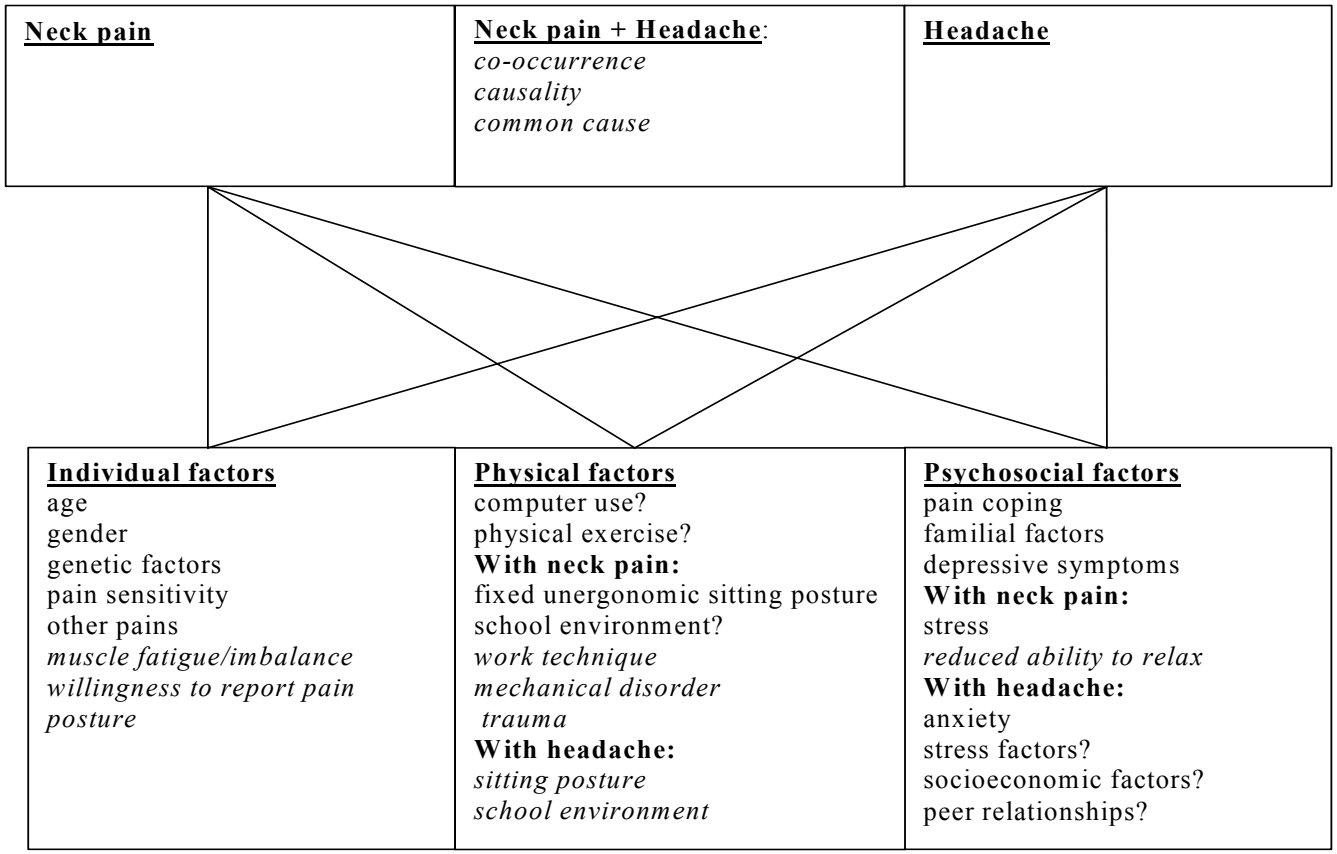

Figure 1. Conceptual model describing associations of various individual, physical and psychosocial factors with neck pain and headache in adolescence. *Italic fonts* describe factors not studied in adolescence, ? = factors with contradictory results in adolescence

Table 5. Neck pain (NP) in adolescent headache (HA)

Author	Population (participation rate), assessment method of NP and HA, recall period.	Found associations of NP and HA
Anttila et al 2002b Metsähonkala et al 2006 Oksanen et al 2006 Finland*	12-13-y schoolchildren: 12-y: N=1135 (81%):Q, 13-y:N=311 (95%): Q+I+CE, physiotherapist (N=183): manual palpation, dolorimeter, muscle endurance strength, cervical ROM. RP 6mo.	NP during daily activities in 73% of M, 51% of TTH and 54% of no HA. Neck muscle tenderness with M, but not with TTH. Lower endurance strength of the upper extremities with ETTH in girls. No association: cervical ROM with HA type,or muscle tenderness outside the neck region with HA, M or TTH.
Laurell et al 2005 Sweden	7-15-y schoolchildren, N=130 (M 42, TTH 37, no HA 49) (74%): Q + I. RP 1y.	NP in 24% of M, 19% of TTH, 11% of no HA. NP with HA, no difference between M and TTH. Intensity of HA (VAS) was not correlated with other pains.
Lipchik et al 1996, 1997 USA	17-26-y female students with recurrent HA N=112 (?%) (ETTH 31, CTTH 31, MwoA 33, MwA 17, no HA 31). Q+I+EMG, manual palpation of pericranial muscles (suboccipital, posterior cervical, upper trapezius, masseter, sternocleidomastoid, temporalis muscles. RP?	Higher pericranial tenderness in CTTH than other HA or no HA. Tenderness was not associated with frequency of M or TTH. Independently of HA intensity CTTH was most often associated with upper trapezius (84%), cervical (74%), suboccipital (71%), sternocleidomastoid (65%) tenderness. 90% of CTTH and 32% of controls had tenderness in at least 2 muscle groups. Suboccipital and cervical muscle tenderness best distinguished HA from controls, temporalis and masseter were the least likely to be tender in HA. No differences in EMG between HA groups.
Mikkelsson et al 1997 El Metwally et al 2004 Ståhl et al 2004 Finland	9-12-y schoolchildren N=1756 (B: 83%, F:72% of pain-free, 76% of weekly musculoskeletal pain) B: Q, 4-y F: Q. RP 3mo.	62% of 9-12-y with weekly NP reported weekly HA. 8% of adolescents with weekly NP had visited doctor because of HA. At 4-y F: Weekly HA at baseline was associated with persistent musculoskeletal pain. Incidence of monthly HA was 65%, and of weekly HA 25%. NP frequency was associated with HA frequency.

= the same study sample as in present study. RP = recall period, mo =previous month, y = previous year, ?= not stated, ?% = participation rate not stated, B = baseline, CE = clinical examination, F = follow-up, ROM = range of motion. M = migraine, TTH = tension-= the same study sample as in present study. ROM = range of motion, M = migraine, TTH = tension-type HA, CTTH = chronic TTH, ETTH = episodic TTH, MwoA = M without aura, MwA = M with aura, B = baseline, CE = clinical examination, F = follow-up, I = interview, VAS = visual analoque scale, Q = questionnaire.

In the second hypothesis of the association of HA and NP, HA has been thought to precede NP. NP has been found to be a common part of migraine attacks (Kaniecki 2002, Blau and MacGregor 1994) improving with the treatment of HA. NP could partly be a consequence of pain extended from the head to other parts of the body. Central neuroplastic changes in HA could affect the regulation of peripheral mechanisms and lead to increased pericranial muscle activity (Bartsch 2005, Holroyd 2002, Bendtsen 2000). Both hypotheses may be partly true, and NP could be a peripheral cause of HA but also a manifestation of central mechanisms. This theory is supported by studies showing that nociceptive afferents from the meninges and the upper three cervical nerves from cervical structures converge to the same second-order neurons in the trigeminovascular complex (Bogduk 2004, Bartsch and Goadsby 2003, Graff-Radford and Newman 2002), and thus inputs from the periphery and from central nerve structures may modify the experience of pain. Regularly experienced HA may also predispose adolescents to experiencing NP through changes of posture (Grimmer et al 2006, Nilsson 1995). It has been hypothesized that early adolescent HA progresses to mid-adolescent NP by sensitization of pain structures (Grimmer et al 2006).

In the third hypothesis of the association of NP and HA, both pain syndromes are regarded as due to a common risk factor, such as individual, physical, psychosocial, familial and genetic risk factors, which could predispose to general pain "proneness" and to a more refractory pain condition. NP and HA would thus be part of a widespread pain syndrome. Complex mechanisms underlie the clustering of various pains in some individuals (Scher et al 2006, Laurell et al 2005). One explanation for them may be malfunctioning of central pain transmission. Further, psychological factors such as anxiety and depression have modulating effects on pain perception (Scher et al 2006). In addition, genetic inheritance, social learning processes, mechanical factors and parental responses are important in the development and maintanance of pain symptoms (Fichtel and Larsson 2002). Further, the subject's willingness to report symptoms cannot be ruled out as a contributing factor (Scher et al 2006).

2.3.3. Characteristics of co-occurring headache and neck pain

2.3.3.1. Muscle pain

Muscle tenderness has been found in association of M at the age of 13 years and with different kinds of adult HA (Sjaastad et al 2006, Anttila et al 2002b, Aprill et al 2002, Ashina et al 2002, Hagen et al 2002, Piovesan et al 2001, Sjaastad and Fredriksen 2000, Ashina et al 1999, Jensen 1999, Westgaard 1999b, Davidoff 1998). In adults, pericranial muscle tenderness has been shown to increase with increasing HA frequency (Graff-Radford and Newman 2002, Jensen 1999, Lipchik et al 1996). The results of muscle tenderness in distinguishing adult TTH sufferers from migraineurs are controversial (Jensen 1999, Lipchik et al 1996). In a recent adult study of Sjaastad and colleques (2006), HA associated with muscle tenderness was mostly in the occipital region.

2.3.3.2. Myofascial muscle pain

Myofascial pain has been associated with intense and disabling HA in adults and is diagnosed when the palpation of trigger points in the neck or face muscles refers pain to the head (Fernández-de-las-Peñas et al 2006, Biondi 2005, Merskey and Bogduk 2004, Mense et al 2001, Marcus et al 1999, Travell and Simons 1999, Davidoff 1998). Myofascial pain has been more common in adult TTH and M sufferers than in HA-free controls (Fernández-de-las-Peñas et al 2006, Gerwin 2001, Jensen 1999). In adults, the myofascial pain of the sternocleidomastoid,

upper trapezius and posterior nuchal muscles is important in HA (Gerwin 2001, Marcus et al 1999, Travell and Simons 1999, Davidoff 1998). Stimulation of trigger points can induce HA and their inactivation can eliminate HA (Fernández-de-las-Peñas et al 2006, Hou et al 2002). In one study, 100% of chronic HA sufferers had active trigger points, with the trapezius involved in 93% of cases (Gerwin 2001). In another study of chronic HA patients and HA-free controls, nuchal myofascial pain was associated with HA without differentiating type of HA (Marcus et al 1999).

2.3.3.3. Degenerative changes of the cervical spine

Provided that HA can be caused by degeneration in the cervical spine, convergence between the trigeminal afferents and the upper three cervical nerves suggests that degenerative changes in the upper neck may be more likely to cause HA than degeneration in the lower cervical spine (Bogduk 2004). In adult HA patients, dynamic spinal X-rays have shown joint dysfunction and changes in posture both in migraine and tension-type HA (Vernon et al 1992). In a MRI study of the spine, no difference was seen in disc bulging between adult patients with cervicogenic HA and healthy controls (Coskun et al 2003). When radiological changes in TTH were compared with those in other types of HA or with those in spondylogenic pain in adults, TTH was not found to be associated with changes in the cervical spine (Wöber-Bingöl et al 1992). In healthy adults, extreme positions of the cervical spine have been shown to lead to NP referring to the head (Dalenbring et al 1999, Harms-Ringdahl and Ekholm 1986). As the cervical spine of adolescents is more flexible than that of adults (Kumaresan et al 2000), it could be thought that in extreme spine positions in sedentary hobbies the neck muscles and the spine in this age group are even more prone to become loaded than in adults.

2.3.3.4. Characteristics of headache with concomitant neck pain

Adult HA with concomitant NP has been thought to be frequent or continuous with fluctuation in severity (Davidoff 1998). NP in adults is more clearly associated with HA frequency than with HA type (Hagen et al 2002, Lipchik et al 1996), although pericranial tenderness and NP have traditionally been associated with adult TTH (ICHD 2 2004, Jensen et al 1998). In Norway chronic NP preceded mainly mild or moderate posterior HA in 7% of the adult population (Sjaastad et al 2006). HA associated with NP during protracted head turning was mainly bilateral and occipital, rarely with anterior spread (Sjaastad and Bakketeig 2002).

2.3.4. Common determinants of neck pain and headache in adolescence

Associating factors have been studied separately for adolescent NP and adolescent HA, but no studies have addressed associating factors of concomitant NP in adolescent HA sufferers. If NP does not induce HA, and if HA is not predictive of NP, there have to be some underlying environmental, individual or genetic factors shared in the pathogenesis of both HA and NP (Scher et al 2006, Silber and Pao 2003).

One potential common cause of the recent increase in NP and HA prevalence among adolescents is the use of information and communication technology. Sitting in a static position often in ergonomically unfavourable conditions while using computers could be a determinant of both NP and HA. During adolescence, the growth of spinal structures is rapid and thus exposure to flexed static postures may be of increased significance in adolescent years (Straker et al 2007). Computer use can induce excessive loading of the neck region and irritate the muscle-nerve system of the upper neck owing to unfavourable positions and difficulty of relaxing muscles (Grimmer et al 2006). The forward head position has been associated with

adult M and CTTH, and, on the other hand, in healthy adults, extreme flexion of the cervical spine has been found to induce pain in 15 minutes (Fernández-de-las-Peñas et al 2006, Harms-Ringdahl and Ekholm 1986). In children, laxity of the transverse ligament has been suggested as one cause of HA in the posture with the head bent forward. In flexion, the dens-atlas distance increases, inducing stretching of the transverse ligament, which, on the other hand, is associated with a reversible blockage of the atlanto-occipital joint and a painful spasm of the extensor muscles (Ormos 2003).

As both NP and HA are more common in adolescent girls than in boys, the gender also has to be regarded as a modifying factor of concomitant NP in adolescent HA sufferers. In adults, women have been shown to have a higher level of pericranial muscle tenderness than men with equally frequent HA (Chesterton et al 2003, Lipchik et al 2000).

Psychological factors such as anxiety and depression have modulating effects on pain perception. The presence of comorbid depression or anxiety – whether a cause or consequence of pain may increase the likelihood of the development of an additional pain condition (Scher et al 2006). Depressive and stress symptoms have been associated with both NP and HA in adolescence. In adult M patients, the presence of anxiety and depression has also been found to increase muscle tenderness (Mongini et al 2004, Virtanen et al 2004, Anttila et al 2002a, Härmä et al 2002, Niemi et al 1997).

3. AIMS OF THE STUDY

The aims of the study were to investigate:

1. outcome of headache frequency and of headache type and factors associating with the outcome (I-II).
2. effect of concomitant neck pain on the outcome of headache frequency and HA type (II).
3. what characteristics of NP are associated with HA (IV).
4. associations between degenerative changes in the cervical spine and HA in adolescence (III).

4. STUDY POPULATION AND METHODS

4.1. Study population

The present study is part of a population-based follow-up study of HA in schoolchildren. This study is based on the data derived from the follow-up from 13 to 16 years of age (Papers I-II), from the cross-sectional data at the age of 16 years (Paper IV) and from the magnetic resonance imaging (MRI) study of the cervical spine at the age of 17 years (Paper III). Figure 2 shows the flow chart of the study population with participation rates of the follow-up studies.

The original source population covered all 12-year-old schoolchildren (6^{th} grade in the primary school) in the city of Turku (total population 170 931) in south-western Finland. The questionnaire on HA was completed acceptably by 1135 (81%) of the 1409 eligible children. The details of the study design at the age of 12 years and part of the study design at the age of 13 years have been published previously (Anttila et al 2002a, 2002b, 2004).

At the age of 13 years, 70 children were randomly selected by computer from each of the HA groups (ICHD 1, 1988) included in the study (Figure 2). If a child was unable to participate (24% of children), another child of the same sex, randomly selected in advance, was recruited. The total number of participants was 311. Their HA type was reclassified at a face-to-face interview and a clinical examination between 12th October 1998 and the end of February 1999. As part of the clinical examination, manual palpation, measurement of the pressure pain threshold of neck muscles, and stomatognathic examination were carried out. All examiners were blinded to the participants' pain history. Participants reporting HA at least once a month at the interview were given a headache diary for making notes over the following two months. Sixty-four percent of the diaries (98/154) were returned acceptably completed. All participants with HA occurring at least twice a month according to the HA diary (N=43) were offered participation in a relaxation training given by a nurse in the Department of Child Neurology. Nineteen (15 girls and 4 boys) children participated in relaxation training.

At the age of 16 years, the adolescents examined at the age of 13 years were re-examined. In addition, as the main study interest was in the association of neck pain (NP) with HA, adolescents reporting at the age of 12 years HA associated with head or neck trauma, or a refractive disorder of the eyes, and adolescents with non-classifiable headache (IHS 13) were invited to the study (Fig. 2). The number of drop-outs varied from 20 to 27% in the HA groups IHS 1-2 (migraine, tension-type HA, migrainous disorder, and tension-type HA not fulfilling the criteria at the age of 13 years), was 31% in the healthy controls, 33% in HA secondary to trauma or refractive error, and 38% in HA not classifiable. At the age of 16 years, all the examinations of 13-year-olds were repeated. In addition, a thorough physical examination of the neck was performed by a trained specialist in physical medicine and rehabilitation (KL) blinded to the participants' pain history.

Adolescents with HA at least 3 times a month and adolescents with no HA at the age of 16 years were invited to undergo MRI of the cervical spine 1 year later. Of participants with HA (N=47/59, participation rate 80%), 17 had weekly NP (>3 times/month) and 30 had infrequent NP (<1/month). In adolescents with no HA (N=22/37, participation rate 59%), the frequency of NP was <1/month (infrequent NP). HA sufferers with NP 1-3 times/month and HA-free participants with NP at least once a month were excluded from the MRI study.

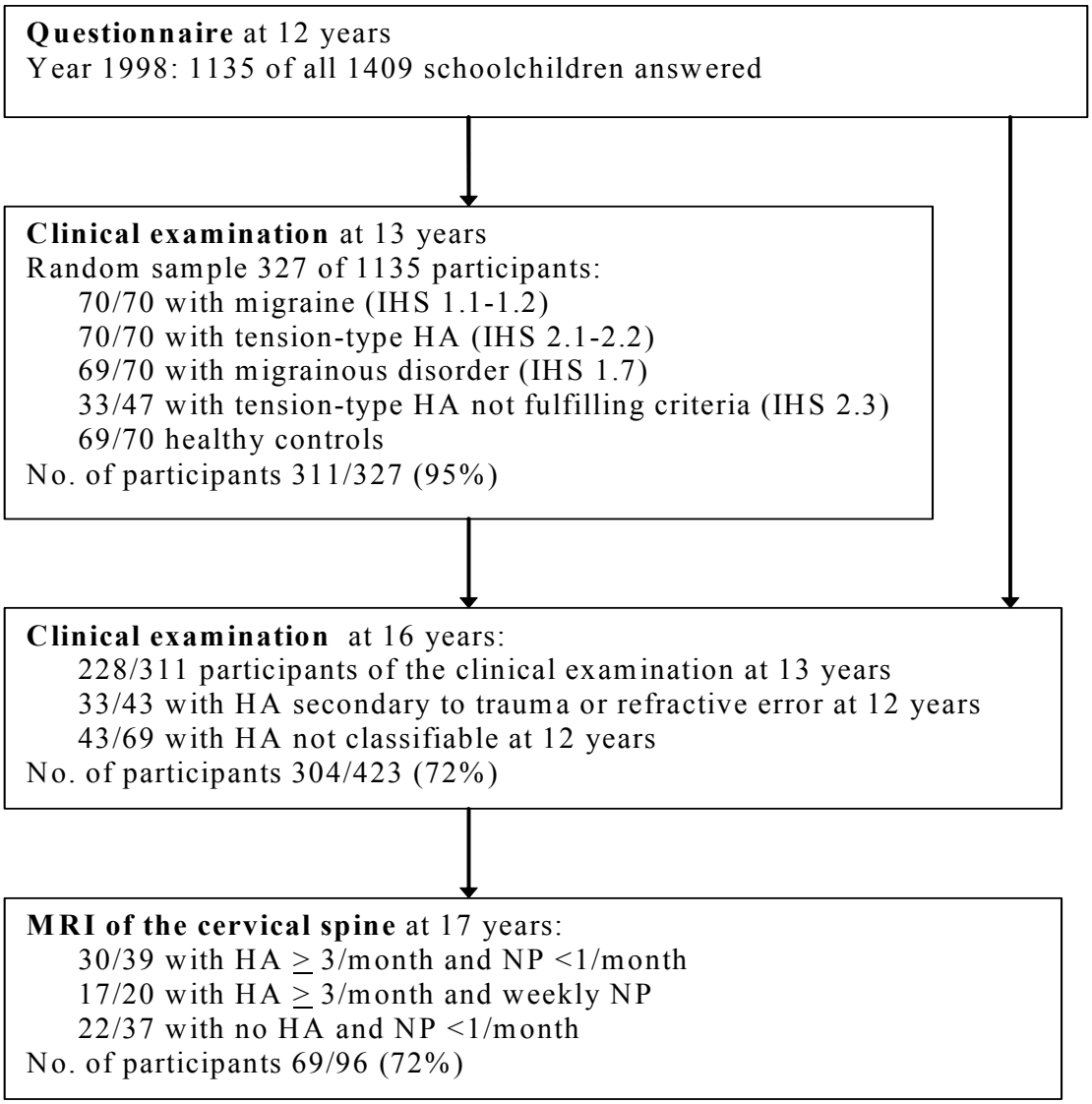

Figure 2. Flow chart of the study population. HA, headache; NP, neck pain. Published in Paper III, Laimi et al. Adolescent disc degeneration – no headache association. Cephalalgia 2006; 27:14-21, and has been reproduced with the permission of the copyright holder Blackwell Publishing Ltd *Cephalalgia*.

Table 6. Study design and analysed variables

PAPER	I	II	III	IV
QUESTIONNAIRES	7,12 and 13 years of age	12 and 13 years of age	16 years of age	16 years of age
CLINICAL EXAMINATION	13 and 16 years of age	13 and 16 years of age	16 years of age and MRI at 17 years of age	16 years of age
STUDY SETTING	prospective follow-up	prospective follow-up	cross-sectional	cross-sectional
STUDY POPULATION	N = 228	N = 228	N = 69	N = 304
OUTCOME VARIABLES	outcome of 1. monthly HA 2. non-frequent HA	outcome of 1. HA frequency 2. HA type	1. HA / no HA 2. HA with and without NP	7 HA variables
PREDICTIVE VARIABLES	<u>variables associated with HA in cross-sectional studies:</u> 1. individual variables: a. gender b. pain: HA at 7 years of age, HA type, use of analgesics for HA, and non-HA pains at 12 and 13 years, change in HA type from 13 to 16 years of age c. diseases 2. familial and social factors: bereavements, familial HA, parents' education	NP variables at the age of 12 and 13 years	degenerative changes of the cervical spine	NP variables: 5 self-reported NP variables and 12 measured NP variables (physical findings of the neck)
CONFOUNDING VARIABLES		1.significant predictive variables of the first article 2.possible determinants of both NP and HA in adolescence: relaxation training, temporo-mandibular disorder, leisure sport activities, using the Internet, stress and depressive symptoms	HA type: migraine / tension-type HA	

4.2. Methods

Table 6 shows the study design and analysed variables.

4.2.1. Follow-up study from 13 to 16 years of age *(I, II)*

Figures 3-4 show outcome variables, predictive and confounding factors of the follow-up study.

4.2.1.1. Outcome variables (I, II)

From 13 to 16 years of age, the outcome of HA was measured using two end variables, outcome of HA frequency and outcome of HA type. In analysing the outcome of HA frequency, improved HA (decrease in headache frequency from >1/month to 0-1/month) was compared with persistent monthly HA (>1/month both at the age of 13 and 16 years). Unchanged non-frequent HA (0-1/month) was compared with incident monthly HA (increase in frequency from 0-1/month to >1/month). The cut-off point of HA frequency (>1/month, ≤1/month) was chosen partly because of clinical relevance and partly because of statistical needs. Appendix 1 shows the questions of HA in detail.

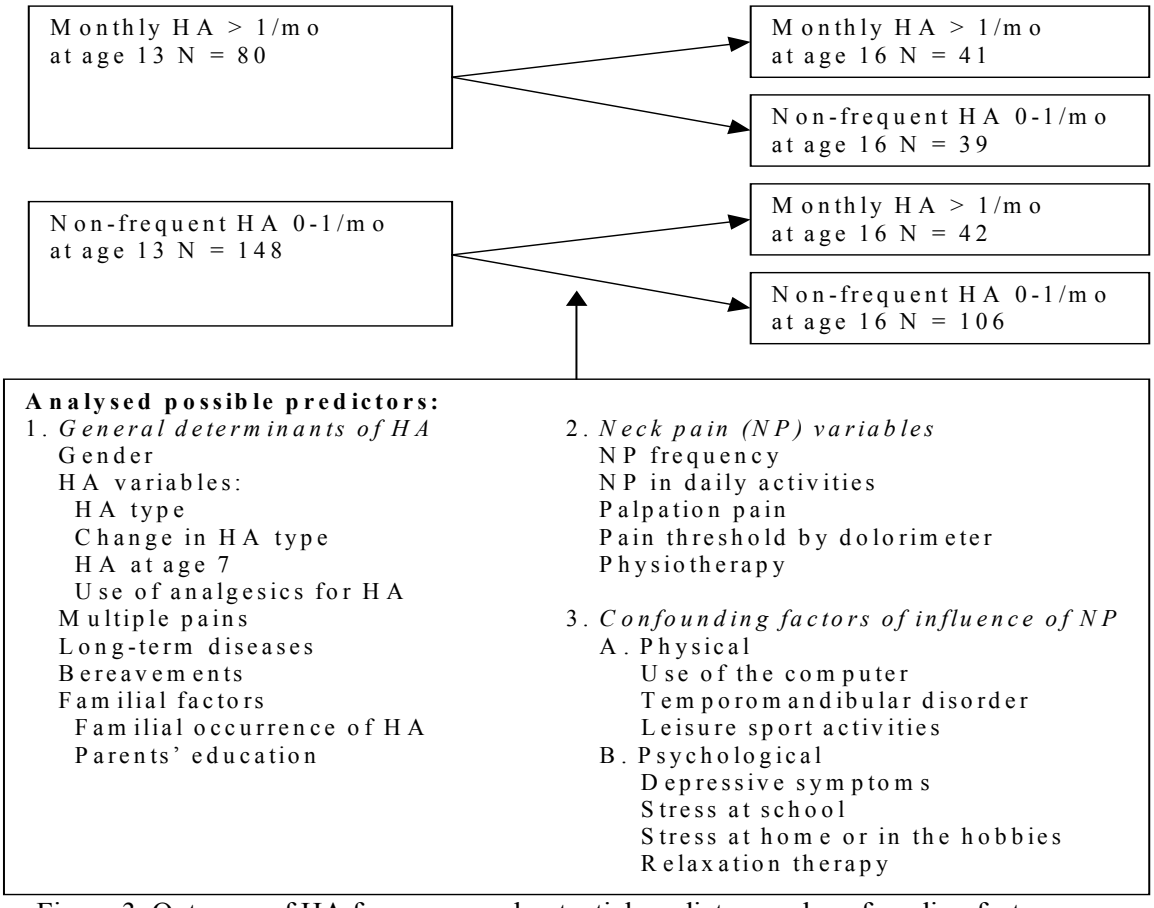

Figure 3. Outcome of HA frequency and potential predictors and confounding factors

In analysing the outcome of headache type from 13 to 16 years of age, adolescents with two or more types of HA at the age of 13 or 16 years (N=19) were classified according to their most frequent HA type. Tension-type HA (IHS 2) evolving to migraine (IHS 1) was compared with persistent tension-type HA and migraine evolving to tension-type HA was compared with persistent migraine. The classification of the HA type was based on a neurological examination including a structured interview and the criteria of the International Headache Society (ICHD 1, 1988). As the second, current edition of the International Classification of Headache Disorders (ICHD 2, 2004) had not yet been published at the time of data collection, ICHD 1 criteria were used. The outcome of HA type was an outcome variable in paper II, but was analysed as a predictive factor for the outcome of HA frequency in paper I.

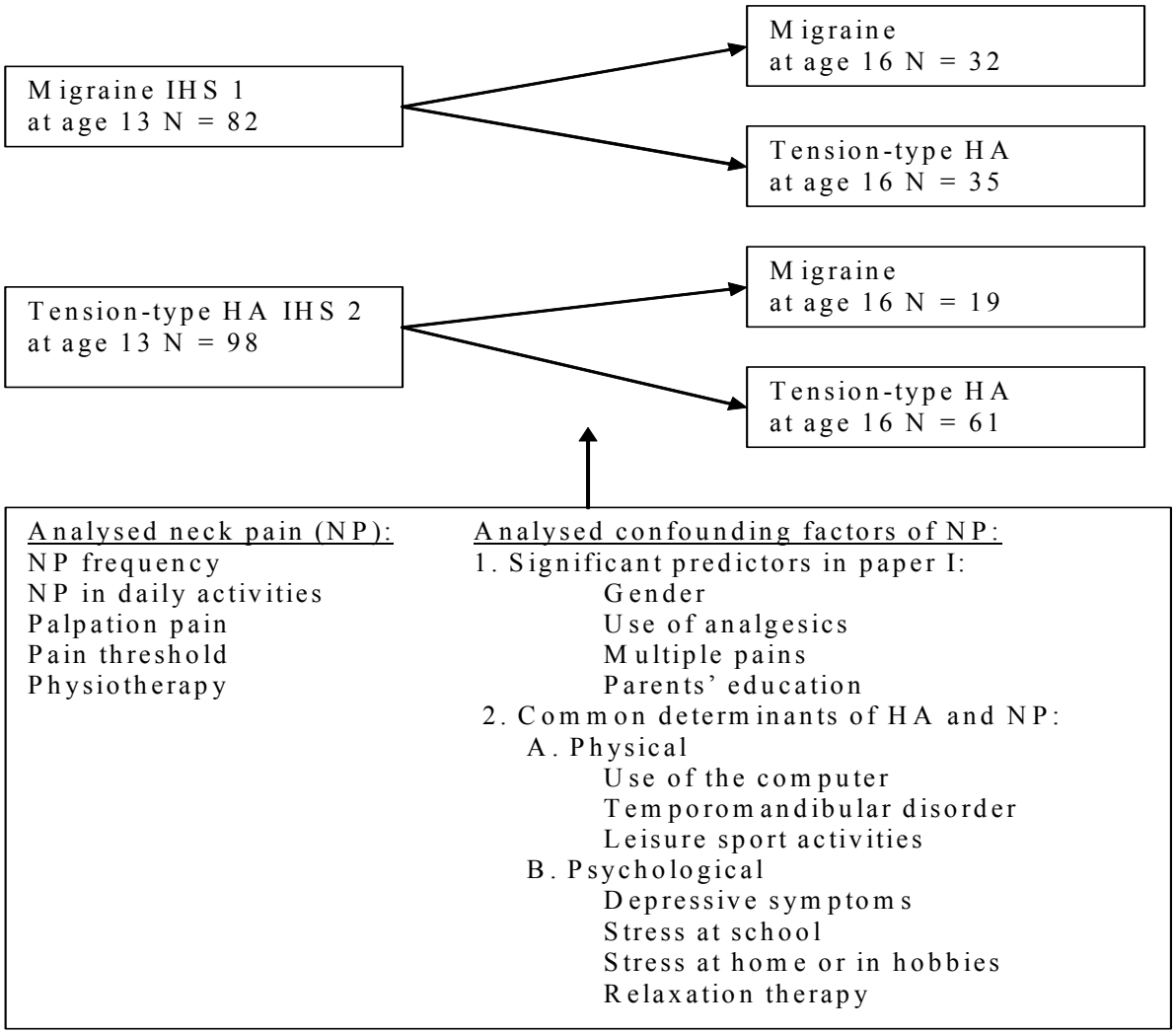

Figure 4. Outcome of headache type, analysed neck pain variables and possible confounding factors

4.2.1.2. Possible predictive and confounding factors (I, II)

Possible predictive and confounding factors of the outcome of HA from 13 to 16 years of age, can be seen in figures 3 and 4, and appendices 1-3 show the detailed questions of self-reported factors. In paper I, other factors than neck variables, so-called "general predictive factors" for the outcome of HA frequency were studied. These general predictive factors were factors, which have been associated with adolescent HA in cross-sectional studies. In paper II, self-reported NP and measured muscle tenderness of the neck were analysed as predictive factors for the outcome of HA, and factors associating with adolescent NP and HA in cross-sectional studies were analysed as confounding factors.

General predictive factors (I)

The use of analgesics was evaluated as the frequency of HA medication per month during the preceding 6 months. The analgesics used were non-steroidal anti-inflammatory drugs (ibuprofen 200–600 mg, $N = 107$; acetosalicylic acid 500 mg, $N = 16$; paracetamol 500 mg, $N = 15$; ketoprofen $N = 5$; naproxen $N = 3$; tolfenamic acid $N = 1$; non-defined anti-inflammatory drugs, $N = 14$). Ten different types of non-headache pain (back pain, neck pain, abdominal pain, limb pain, sore throat, earache, eye ache, toothache, chest pain and other pain) were classified by frequency using a four-step scale (1 = no pain, 2 = pain <1/month, 3 = 1–3/month, 4 = ≥4/month during the preceding 6 months). Accordingly, the sum frequency could vary between 10 and 40. Long-term illnesses consisted of allergy *(*allergic rhinitis $N = 54$, food allergy $N = 29$), bronchial asthma ($N = 23$), lactose intolerance ($N = 19$), developmental language disorder ($N = 4$), epilepsy ($N = 4$), deformities of the spine or feet ($N = 3$), psoriasis ($N = 2$), thyroid disease ($N = 2$), and arterial hypertension, heart disease, Turner syndrome, spastic hemiplegia, colitis ulcerosa, von Willebrand's disease, anorexia, hearing problems and cataract, one of each. No participants reported having coeliac disease, renal disease, diabetes mellitus, cancer or rheumatic disease. Bereavements between ages 12 and 16 years included parental divorce, parental change of jobs, parental unemployment, relocation of home, economic problems, domestic quarrels, long-term disease in the family and death of a close relative. The basic education of the parents was categorized according to whether both, one or neither of the parents had passed the secondary school matriculation examination meaning acceptable completion of 12 years of schooling and a national written examination. A question was asked about the occurrence of HA at the age of 7 years in a separate questionnaire study on HA at the age of 7 years, where 86% of the study population ($N = 196$) had also participated (Anttila et al 1999).

Predictive neck variables (II)

Self-reported neck symptoms and measured muscle tenderness were analysed as predictive NP factors for the outcome of HA frequency and HA type. Self-reported neck symptoms (detailed questions in App. 2) were the frequency of NP, occurrence of tenderness or stiffness of the neck region during daily activities, and the use of physiotherapy for NP or HA during six months before the first study visit. The use of physiotherapy prescribed before onset of the study was considered a predictive NP factor because it was thought to describe the intensity of NP at the beginning of the follow-up. Muscle tenderness was recorded at the age of 13 years by manual palpation and pressure dolorimeter. A trained physiotherapist carried out a structured manual palpation test on tenderness at seven neck sites (frontal and temporal muscles, the suboccipital muscle insertion, anterior aspect of C5-C7, origin of the supraspinatus muscle, midpoint of the upper border of the trapezius muscle, insertion of the levator scapulae muscle) bilaterally, graded on a four-step scale (0=no pain, 1=no visible reaction but reporting mild pain, 2=

reporting pain and distorting the face, 3= reporting considerable pain and withdrawing) (Langemark and Olesen 1987). Accordingly, the total tenderness score could vary between 0 and 42 (Anttila et al 2002b). A dolorimeter (Fischer 1986) was used for the measurement of the pressure pain threshold from five pericranial/neck sites bilaterally (the frontal and temporal muscle, suboccipital muscle insertion, midpoint of the upper boarder of the trapezius muscle, insertion of the levator scapulae muscle). Pressure pain was measured in kg/cm^2 units (Anttila et al 2002b). The mean dolorimeter score for the pressure pain threshold was calculated (range 0.0-10.0 kg/cm^2). The higher the score, the less muscle tenderness.

Confounding factors (II)

We wanted to exclude causation of the found association of NP on HA outcome by any other factor. Fig. 3-4 show analysed confounding factors. In addition of factors associating with adolescent NP and HA in cross-sectional studies, also significant predictive factors of the outcome of HA frequency found in the first study (Paper I: use of analgesics, basic educational level of parents, non-headache pain, change in headache type) were analyzed for exclusion as confounding factors. Of self-reported factors, detailed questions are in appendix 3.

In a stomatognathic examination carried out by a dentist, the severity of temporomandibular disorder (TMD) was graded using a TMD score. TMD score values increase from 0 to a maximum of 35 with severe symptoms. The TMD score included pain on palpation of the masticatory muscles or temporomandibular joints, pain on opening the mouth or on jaw movements, pain or stiffness on guiding the mandible, and joint sounds (Liljeström et al 2001). DSM IV criteria for depression were used to detect depressive symptoms (Anttila 2002a, American Psychiatric Association 1994). The sum score could vary between 0 and 10 the score increasing with depressive symptoms. Stress symptoms were separately adjusted for stress at school and for stress at home or in hobbies. Participation in relaxation training (N=19) at the age of 13 years included in the study protocol for those with monthly headache was included as a confounding factor, because the inclusion criterion for the training was the frequency of HA (>1/month) and the training could have influenced NP. This relaxation training included general information on headaches and five 30-minute, nurse-assisted relaxation sessions including muscle contraction relaxation and relaxation with visualization. Leisure sport activities were adjusted by the time the children spent in sports activities outside school hours so intensively that they were breathless or sweating. The children were also asked about the number of days per week used at the Internet or in playing computer games.

4.2.2. The assessment of headache and neck pain at the age of 16 years *(III, IV)*

Appendices 1 and 2 show the detailed questions of self-reported variables, and Fig. 5 shows the headache outcome variables and analysed neck pain variables at the age of 16 years.

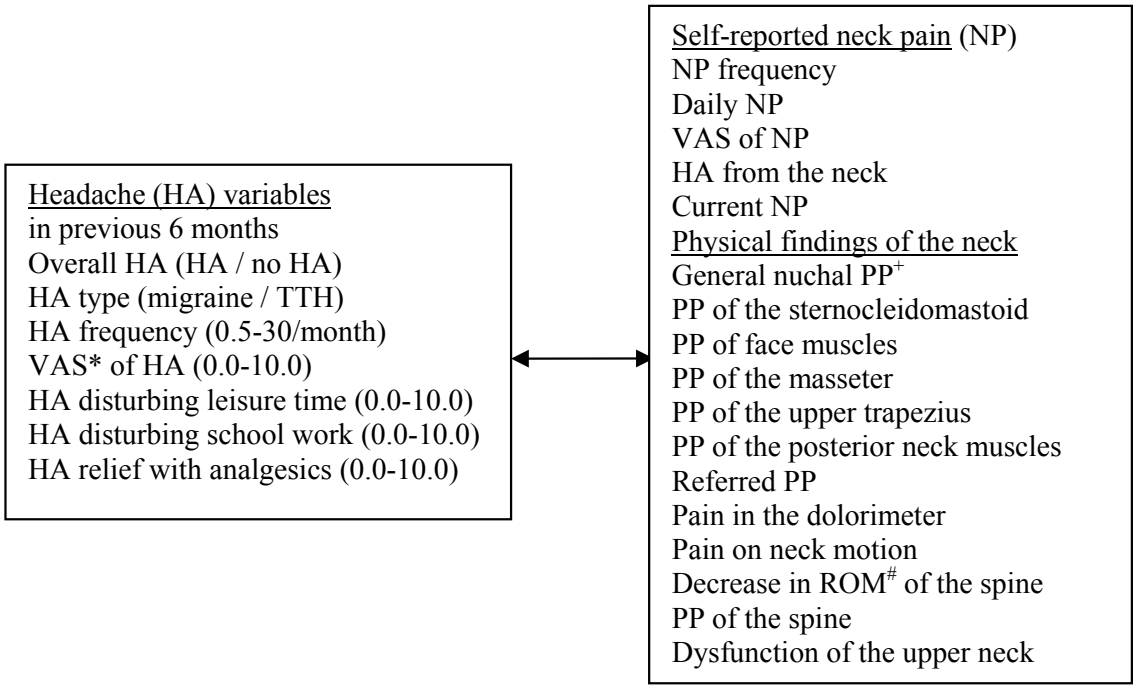

Figure 5. Headache variables and neck pain variables at the age of 16 years. * = visual analogue scale, $^{+}$ = palpation pain, $^{\#}$ = range of motion

4.2.2.1. Headache variables (III, IV)

HA at the age of 16 years was described by seven outcome HA variables (Fig. 5). HA type was defined as M (IHS 1) and TTH (IHS 2) (ICHD 1, 1988). The HA type of participants with two types of HA (N=16) was classified according to the most frequent type of HA. The intensity of HA, the disturbance of HA on leisure time and on school work, and HA relief with analgesics were evaluated by horizontal visual analogue scale (VAS) 0.0 cm meaning no HA, no influence of HA on leisure time or school work, or total relief of HA with analgesics, 10.0 cm meaning maximal intensity of HA, maximal disturbing influence of HA, or no relief of HA with analgesics.

4.2.2.2. Neck pain variables (III, IV)

NP at the age of 16 years was described by self-reported NP (App. 2 and Fig. 5), and by physical findings of the neck (Fig. 5). Of self-reported NP variables, NP frequency was defined as the number of NP episodes per month in the preceding six months, daily NP as the occurrence of tenderness or stiffness of the neck region during daily activities, VAS of NP as the intensity of NP rated by VAS (0.0 cm = no NP and 10.0 cm = the most NP imaginable). According to the criteria of HA associated with cervical spine (ICHD 1: IHS 11.2.1.), participants were asked whether their HA was usually triggered by the motion of the neck or a poor posture of the neck or head (HA from neck). Participants also reported, if they had NP at the beginning of the physical examination. The pain region was confirmed by the participants showing the pain region with hand.

The physical examination of the neck was done by a trained specialist in physical medicine and rehabilitation (K.L.) blinded for the subjects' pain history. The examination was performed in

the sitting position with the low back against the backrest, forearms on handrests. Only the palpation and the dolorimeter measurements of the posterior neck and upper trapezius muscles were done in the prone position to permit muscle relaxation. A structured manual palpation test was carried out bilaterally on tenderness and on referred pain of muscles receiving their sensory innervation from levels C1 to C3 (sternal division of the sternocleidomastoid, face muscles, the masseter, the upper trapezius, and posterior neck muscles). The masseter, sternal division of the sternocleidomastoid and upper trapezius muscles were examined using pincer palpation, grasping the belly of the muscle between the thumb and the index finger, and other muscles using flat palpation with the tip of the index finger at a force of 1 kg. The force was calibrated by exercising with a pressure dolorimeter between each participant. General nuchal PP was calculated by summing up the pain of all palpated muscles (range 0-28). PP was also separately analysed for sternal division of the sternocleidomastoid (range 0-4), face muscles (the frontal and temporal, range 0-6), the masseter (range 0-4), the upper trapezius (range 0-4), and the posterior neck muscles (the semispinalis capitis and cervicis, splenius capitis and cervicis muscles and the suboccipitalis area in the point of possible entrapment of the greater occipital nerve (=ceiling of the suboccipital triangle), range 0-10). In addition to local palpation pain, referred pain on muscle palpation to the head was recorded. This referred pain was regarded as possible myofascial pain of the head. To reach this diagnosis, the spot tenderness of trigger points (Travell and Simons 1999) of above mentioned muscles was palpated and subjects were advised to report referred pain on palpation. For palpation, a muscle map from the trigger point manual (Travell and Simons 1999) was used, and only muscles with a possible myofascial referred pattern to the head were palpated (muscles listed in Fig. 6).

A dolorimeter (Fisher 1986) was used for the measurement of the pressure pain threshold from those neck muscle points, where participants reported pain in manual palpation. The mean dolorimeter scores for pressure pain threshold were calculated. The lower the score, the more muscle tenderness, range 0.0-10.0. Pain on neck motion was defined as pain recorded on active and passive neck flexion, extension, rotations, lateral bendings and protraction of the head. The sum of the movements with reported pain was calculated (range: 0-16). Decrease in range of motion (ROM) of the cervical spine was evaluated by the examiner without measuring devices. The sum of the abnormal findings on neck flexion, extension, lateral bendings, and rotations was calculated (range 0-16). Reported PP of the cervical spine was evaluated by segmental palpation of the processus spinosus on slight flexion-extension motion in the sitting position. The upper neck was evaluated by passive rotation of the cervical spine in extreme cervical flexion in sitting position. Self-reported pain, self-reported crepitation and the limitation in the ROM was recorded, and the sum of these findings was calculated (range 0-6).

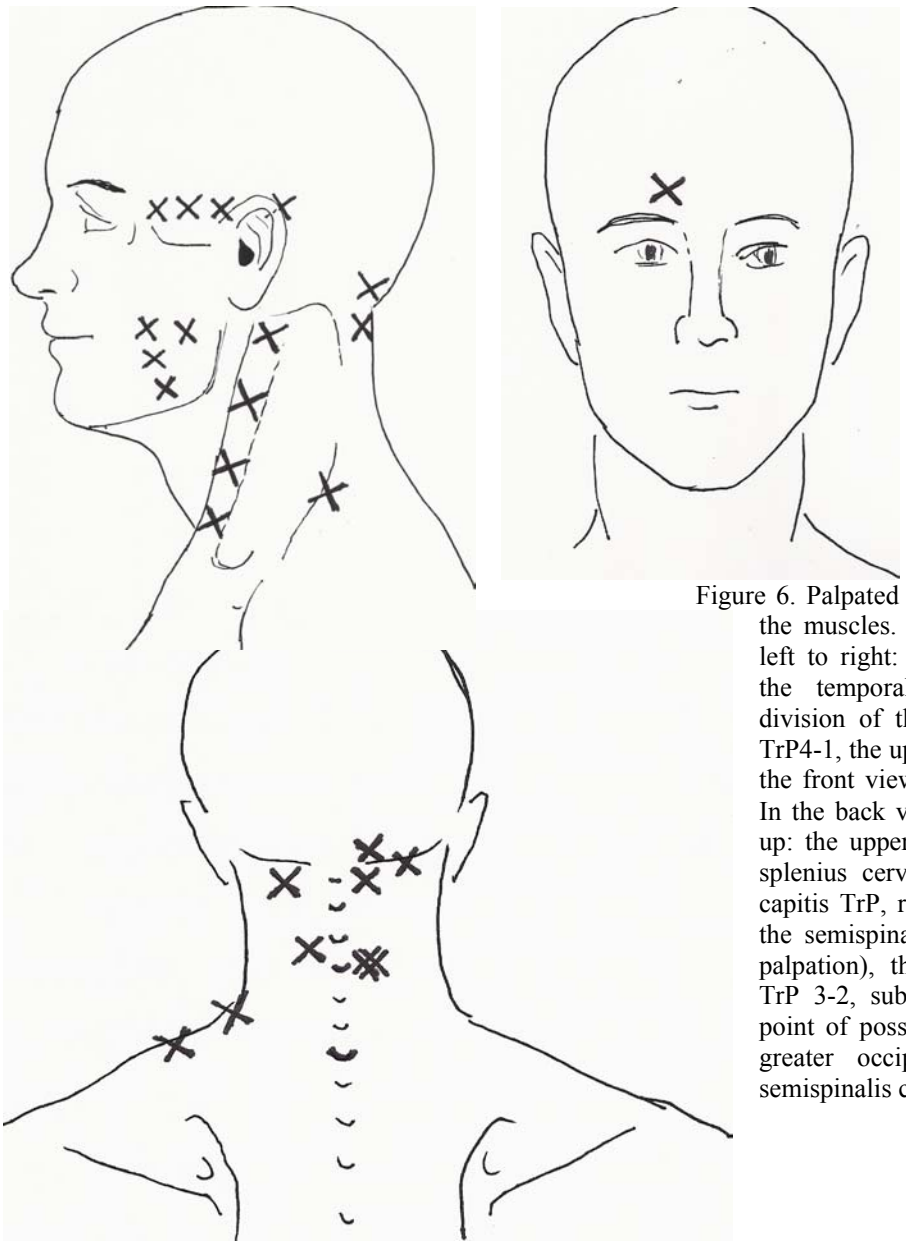

Figure 6. Palpated trigger points (TrP) of the muscles. In the side view from left to right: the masseter TrP 1-4, the temporalis TrP 1-4, sternal division of the sternocleidomastoid TrP4-1, the upper trapezius TrP 1. In the front view: TrP of the frontalis. In the back view left from down to up: the upper trapezius TrP2-1, the splenius cervicis TrP, the splenius capitis TrP, right from down to up: the semispinalis cervicis TrP (deep palpation), the semispinalis capitis TrP 3-2, suboccipitalis area at the point of possible entrapment of the greater occipital nerve, and the semispinalis capitis muscle TrP 1.

4.2.2.3. Intraexaminer reliability

Before onset of the examinations of 16-year-old participants, a sample of 47 schoolchildren aged 15-16 years (two secondary school classes) in Turku city filled in a questionnaire and 37 of the children underwent a physical examination twice at one week's interval. Reproducibility between the first and the second examination was analysed using the proportion of agreement (PA) and intraclass correlation coefficient (ICC). Reliability was good for reported NP frequency (PA = 66%), reported VAS of NP (ICC = 0.85), referred PP (PA = 86%), pain on neck motion (ICC = 0.67), PP of the spine (PA = 68%), and the sum of PP (ICC = 0.82). Mean pain threshold in the dolorimeter measurement (ICC = -0.01) was not repeatable after one week's interval.

4.2.3. MRI of the cervical spine at the age of 17 years *(III)*

Adolescents with HA at least 3 times a month and adolescents with no HA at the age of 16 years were invited to undergo MRI of the cervical spine 1 year later. Only HA sufferers with weekly NP or with infrequent NP (<1/month) were invited, and only those HA-free participants with NP frequency <1/month were invited (Fig. 2). HA and NP frequency were defined as the monthly number of HA episodes at the age of 16 years (Fig. 5, App. 1-2).

The mean HA frequency in HA sufferers was 5.7 times a month (SD 4.7), with 4.7/month (SD 2.5) for HA sufferers without NP and 7.5/month (SD 6.8) for HA sufferers with NP. Of participants with HA, 19 had migraine type HA (IHS 1), 27 had tension type HA (IHS 2) and one had HA not classifiable (IHS 13). Five participants had two kinds of HA at the age of 16 years. Their HA type was classified according to the most frequent type of HA.

The 1.5-T imaging system (Symphony; Siemens, Erlangen, Germany) was used for imaging with sagittal T1-weighted and T2-weighted images covering planes from the posterior fossa to the upper thoracic level. In addition, $T2^*$-weighted and T1-weighted axial images were obtained from the cervical spine. All scans were interpreted independently by three neuroradiologists (M.E., R.P. and P.S.) blinded to the participants' pain histories.

The degree of disc degeneration (DD) was graded as no, mild (a decrease in disc signal intensity), moderate (the disc darker than the vertebral corpus) or severe DD (decreased signal intensity and narrowed disc space). Localization of DD was analyzed in four ways: first, the occurrence of DD in the whole imaging area from C2 to Th 4; second, the occurrence of DD in the upper neck (levels C2/3 and C3/4); third, the occurrence of DD in the lower neck (from C4/5 to C6/7); fourth, the spread of DD was evaluated (no DD, DD at one level, two levels, or three or more levels). Disc bulgings of the cervical spine were graded as no bulging, protrusion and disc herniation. Any compression of the root and spinal cord was also recorded. Annular tears and foraminal stenosis were recorded, if present.

Extent of agreement

To prevent the influence of variation in the analysis between neuroradiologists commonly seen in mild degenerative changes, three independent examiners were used. The result was assessed as normal if at least two of the three neuroradiologists regarded it as normal. In the assessment of DD, the proportion of agreement was 81%. The first and the second neuroradiologists were of the same opinion on approximately 91% of findings, the first and the third on 77%, and the second and third on 77% of findings. Agreement was better in the lower cervical spine than in the upper cervical spine. In the assessment of disc bulging, the first and the second neuroradiologist agreed on 96%, the first and third on 90%, and the second and third on 92% of findings.

4.3. Statistical methods

The descriptive values were expressed as means and standard deviations (SD), medians and interquartile ranges, or frequencies and percentages. Univariate associations between two categorical variables were evaluated using the χ^2 test and Fisher's exact test when appropriate, between continuous and categorical variables using the Mann-Whitney U-test, and between two continuous variables using the Spearman correlation coefficient. In paper I differences in

changes were calculated using the Wilcoxon signed rank test, and changes in HA type were analysed using the test for marginal homogeneity.

To find independent predictive variables, the significant variables of the univariate analysis were entered in multivariate models. Logistic regression (Hosmer and Lemeshaw 2000) was used for categorized outcome variables and linear models for continuous outcome variables. Results of logistic regression were quantified using odds ratios (OR) with 95% confidence intervals (CI). The results of linear models were expressed using regression coefficients with standard errors.

Sample size calculation was used to find adequate study group size at the age of 13 years. For the follow-up studies at the age of 16 and 17 years, sample size calculations were not used, because all the participants fulfilling the inclusion criteria, were recruited.

In paper I gender-adjusted odds ratios were calculated for significant predictive factors of univariate analysis using logistic regression. For logistic models, continuous explanatory variables were divided into three classes consisting of the lowest quartile, the combined second and third quartile and the highest quartile, because of the non-linear relation of these continuous variables and logit-function.

In paper II interactions between predictive NP variables and gender or HA type were analysed with the logistic regression outcome of HA frequency as a dependent variable. Logistic regression was also used in analysing interactions between NP during daily activities and confounding factors on the outcome of non-frequent HA.

In paper III, because of gender differences between the study groups, data were analysed using gender-adjusted logistic regression.

In paper IV, first multivariate analysis was done with all significant NP variables of the univariate analysis, the second analysis with only measured NP variables of the physical examination, and the third analysis with these measured NP variables, current NP and outcome HA variables. Because of positively skewed distributions, HA frequency and VAS of HA were log(x)-transformed and other continuous HA variables log(x+1)-transformed for multivariate analysis.

In paper III, the reliability of the MRI analysis was tested by calculating the proportion of agreement between examiners. In paper IV, the intraexaminer reliability of physical examination of the neck and the repeatability of self-reported NP symptoms were tested by analysing the difference between two examinations by calculating the proportion of agreement for categorical variables and the intraclass correlation coefficient for continuous variables.

P-values <0.05 were considered statistically significant. Statistical computations were done using the SAS System for Windows, release 8.02 (SAS Institute, Cary, NC, USA).

The study design and the informed consent procedures were approved by the Joint Ethics Review Committee of the Turku University Medical Faculty and the Turku University Central Hospital. Informed consent was signed by both the parents and participants in all phases of the study.

5. RESULTS

5.1. Outcome of headache from 13 to 16 years of age

Outcome of headache frequency (I, II)

The overall changes of HA frequency from 13 to 16 years can be seen in table 1/I, and the outcome of monthly (>1/month) and non-frequent HA (≤1/month) in table 2/I. The mean HA frequency increased in girls from 2.6 to 3.1 times a month ($P = 0.28$). In boys, HA frequency decreased from 2.1 to 1.2 times a month ($P = 0.0002$) during the follow-up. The mean HA frequency at the beginning of follow-up was 4.5 times a month (SD 4.2) for monthly HA and 0.39 times a month (SD 0.38) for non-frequent HA. The overall percentage of adolescents suffering from monthly HA was virtually the same at age 13 years (35%) as at age 16 years (36%). However, internal changes in the study group appeared. In half (49%) of the 13-year-olds with monthly HA, HA improved to non-frequent HA, and in equally many (51%) monthly HA persisted. Of adolescents with non-frequent HA, in more than one-quarter (28%) HA frequency increased to monthly HA, while in 72% HA remained unchanged. The outcome of both monthly and non-frequent HA was poor in girls when compared to boys (tables 3/I and 4/I).

General factors associated with outcome of headache frequency (I)

Frequent use of analgesics, female gender and non-headache pain were associated with persistence of monthly HA (Table 3/I). The familial occurrence of HA was associated with persistence of monthly HA in boys ($P = 0.04$) but not in girls ($P = 1.00$). In adolescents with TTH, HA frequency persisted monthly more often in girls than in boys ($P = 0.03$). When incident monthly HA was compared with unchanged non-frequent HA, incident monthly HA was associated with female gender, persistent migraine and the matriculation examination of one parent compared with parents with no matriculation examination. Further, there was a trend of incident monthly HA to be associated with the use of analgesics (Table 4/I). Gender-adjusted odds ratios were calculated for factors that were significantly associated with persistent or incident monthly HA. Frequent use of analgesics was the most powerful determinant of persistent monthly HA (Table 5/I). The frequency of use of analgesics was low when compared to the IHS criteria of analgesic overuse HA (analgesics >15 days/month) (ICHD 2 2004). The mean frequency of analgesics use was 1.79 times a month for monthly HA, and only eight of 228 (4%) participants used analgesics weekly. Two factors showed an independent association with incidence of monthly HA in the gender-adjusted analysis (Table 6/I), namely persistent migraine and the matriculation examination of one parent.

Neck pain and the outcome of HA frequency (II)

At the beginning of follow-up, monthly HA was associated with a high frequency of NP ($p = 0.04$) and NP during daily activities ($p = 0.003$). When analysing the influence of possible predictive NP factors on the outcome of HA frequency for both genders together, NP factors were not associated with the outcome of monthly HA or with the outcome of non-frequent HA (Tables 2/II and 3/II). A high frequency of NP during daily activities was associated with incidence of monthly HA in boys ($p = 0.03$) (Table 4/II), and use of physiotherapy was associated with persistent monthly HA in boys ($p = 0.004$) (Table 5/II). Of the confounding factors frequent use of computer was associated with persistent monthly HA in boys ($p = 0.04$).

When interactions of confounding factors and NP during daily activities on the outcome of non-frequent HA were analysed, no significant interactions were found.

Outcome of headache type (I, II)

During follow-up, the HA type changed in 65% of participants (Table 1/II). In migrainous (IHS 1) children, HA remained as M, evolved to TTH, or disappeared in 43%, 50%, 7% of the girls, and in 37%, 37%, 26% of the boys, respectively. The difference in changes was not significant between the genders ($p = 0.06$). In children with TTH (IHS 2), HA remained as TTH, evolved to M, or discontinued at the follow-up in 54%, 33%, and 13% of the girls, and in 71%, 8%, and 22% of the boys, respectively. The difference in changes was significant between the genders ($p = 0.008$). Of the 9 adolescents with two or more types of HA at the age of 13 years, one became HA-free, three had only M, and five had only TTH at the age of 16 years.

Neck pain and the outcome of HA type (II)

Self-reported NP or physical findings of the neck were not associated with the persistence of TTH or persistence of M in three years follow-up. Gender was associated with the outcome of TTH: TTH evolved to M more often in girls than in boys ($p = 0.004$). Of confounding factors, temporomandibular disorder was associated with persistent TTH in boys ($p = 0.03$) and the use of analgesics was associated with persistent M when the genders were analysed together ($p = 0.02$) and separately in girls ($p = 0.02$).

5.2. Neck pain in headache at 16 years of age *(IV)*

Table 3a/IV shows the number of subjects with HA and NP, and the mean values of analysed variables at the age of 16 years. Of 247 HA sufferers 75% and of 57 HA-free subjects 35% reported NP from the previous six months. Of HA sufferers 64% and of HA-free subjects 30% had muscle palpation pain (PP). Of HA sufferers 7% had PP referred to the head.

The associations of neck pain with headache variables

Tables 3a/IV and 3b/IV show the univariate associations of NP variables with HA variables. Of self-reported NP, the visual analogue scale (VAS) of NP and NP frequency were positively associated with all HA outcome variables except the HA type. Daily NP was associated with frequent and intensive HA, but not with variables describing disability. Current NP was associated with frequent HA and HA unresponsive to analgesics.

Of measured NP, especially PP and referred PP were positively associated with HA variables. General nuchal PP was associated with frequent HA disturbing leisure time and HA unresponsive to analgesics. Of the separate muscle groups, PP of the sternocleidomastoid muscles was the only type of PP associated with intensive HA. PP of the sternocleidomastoid, masseter, and posterior neck muscles was associated with HA disturbing leisure time or school work. PP of the sternocleidomastoid, masseter and upper trapezius muscles was associated with HA unresponsive to analgesics. Referred PP was associated with frequent HA and HA disturbing leisure time.

Only a few differences were found between the genders in the association of significant predictive NP variables with the HA variables. Daily NP ($p = 0.04$) and PP of the masseter muscles ($p = 0.004$) were associated with overall HA only in boys. When migraine was compared with tension-type HA, spinal pain was associated with tension-type HA only in girls ($p=0.02$). Frequent NP ($p = 0.04$), NP in daily activities ($p = 0.01$), current NP ($p = 0.04$), and PP of the sternocleidomastoid ($p = 0.02$) and upper trapezius muscles ($p = 0.02$) were associated

with frequent HA only in girls. NP variables were associated with HA disturbing leisure time or school work only in girls, but on the other hand, PP of the sternocleidomastoid ($p = 0.04$) or masseter muscles ($p = 0.01$) was associated with HA unresponsive to analgesics only in boys.

Neck pain variables associated with headache variables in multivariate analysis

Of significant self-reported NP variables, independent associations were found between daily NP and frequent HA, and between intensive NP and frequent, intensive and disturbing HA (table 4/IV). Of physical findings of the neck, spinal pain was independently associated with overall HA, PP of the posterior neck muscles with HA disturbing school work, PP of the sternocleidomastoid muscles with intensive HA, and referred PP with frequent HA. Current NP had no influence on the results.

The correlations of neck pain variables with each other

To study whether clinicians treating adolescents with HA could find co-occurrent NP with only a few questions or with one single measurement, correlations of different NP variables with each other were analysed (Table 7). Significant correlations between NP variables (marked with bold in table 7) were found, but on the other hand, many of the NP variables were not associated with other NP variables, and seemed to measure different aspects of neck disorder. NP frequency, NP interfering daily activities and VAS of NP were strongly correlated with each other and were also correlated with physical findings of the neck. On the other hand, HA beginning from the posture or movement of the neck was only correlated with VAS and frequency of NP. Measured muscle PP was correlated with reported NP variables, but referred PP only with intensive or current NP. Dolorimeter measurements, ROM of the spine and dysfunction of the upper neck were not correlated with self-reported NP variables.

5.3. Disc degeneration of the cervical spine at 17 years of age

Degenerative findings of the cervical spine

Of all participants, 67% had DD at least at one level from C2 to Th4. Table 1/III shows the location of the degenerative changes in detail. DD was mainly mild and most commonly found at level C5/6 (46% of participants). Moderate DD was found in four participants and severe DD in one. Annular tears were found in three participants, all at level C5/C6. Mild foraminal stenosis was found in two participants at levels C3/4 to C5/6. Thirty disc bulgings were found in 20 participants, 57% of them at the C5/6 level. Four girls had disc herniations, but no compression of the nerve root or spinal cord was found. Annular tears were associated with concomitant disc bulgings and DD at the same level. Foraminal stenosis and 80% of disc bulgings were associated with DD at the same level. Because of the small number of discs with severe degeneration, mild, moderate and severe DD were combined in a DD group, and protrusions and herniations were combined in a disc bulging group for statistical analysis.

Differences in degenerative findings between study groups

When HA sufferers were compared with HA-free controls, no significant differences were found in the occurrence or distribution of DD, disc bulging, foraminal stenosis or annular tears (Table 2/III). When HA sufferers with weekly NP were compared with HA sufferers with infrequent NP (<1/month), degenerative changes were not associated with concomitant weekly NP (Table 3/III). Using gender-adjusted logistic regression did not influence the results. No significant differences were found in degenerative changes between participants with migraine (IHS 1) and those with tension-type HA (IHS 2).

Table 7. Correlation of predictive neck pain (NP) variables presented with Spearman Correlation Coefficient-values

	Self-reported NP					**Measured NP**						
Self-reported NP	**NP frequency**	**Daily NP**	**VAS of NP**	**HA from neck**	**Current NP**	**PP**	**Referred PP**	**Dolori-meter**	**Motion pain**	**ROM**	**PP of the spine**	**Upper neck**
NP frequency	**1.00**											
Daily NP	**0.63**	**1.00**										
VAS of NP	**0.72**	**0.57**	**1.00**									
HA from neck	**0.31**	0.21	**0.26**	**1.00**								
Current NP	**0.45**	**0.31**	**0.37**	0.09	**1.00**							
Measured NP												
PP	**0.49**	**0.34**	**0.39**	0.15	**0.36**	**1.00**						
Referred PP	0.24	0.21	**0.26**	0.04	**0.29**	**0.32**	**1.00**					
Dolorimeter	-0.14	-0.19	-0.17	0.10	-0.07	**-0.32**	-0.14	**1.00**				
Pain in motion	**0.31**	**0.31**	0.24	0.09	**0.34**	**0.48**	0.15	-0.24	**1.00**			
ROM	0.14	0.10	0.18	0.10	0.06	0.09	0.09	-0.12	0.19	**1.00**		
PP of the spine	**0.26**	0.20	0.19	0.004	**0.29**	**0.49**	0.08	**-0.40**	**0.32**	0.03	**1.00**	
Upper neck	0.13	0.12	0.10	0.14	0.17	0.19	0.13	-0.11	**0.34**	**0.52**	0.12	**1.00**

HA from neck = Pain reported as starting from the motion or posture of the neck, Current NP = NP at the beginning of the physical examination, PP = sum of palpation pain of sternocleidomastoid, face (frontalis and temporalis), masseter, upper trapezius muscles and posterior neck (the semispinalis capitis and cervicis, splenius capitis and cervicis muscles and the suboccipitalis area at the point of possible entrapment of the greater occipital nerve), Referred PP = referred pain from neck to the head on muscle palpation, Dolorimeter = pain in dolorimeter, Pain in motion = pain in the motion of the cervival spine, ROM=decrease in the range of motion of the spine, Upper neck = dysfunction of the upper cervical spine.

6. DISCUSSION

6.1. Study design

Study population

The present results are based on a prospective follow-up of a randomly selected cohort of a whole age group (6th grade primary school children) at the age of 12 years. The high participation rate throughout the study indicates that the study cohort represents the adolescent HA population without any serious selection bias. It is, however, possible that drop outs had more health problems than the responders, which would in turn underestimate the severity of HA, as seen in a study of chronic pains in Dutch adolescents (Merlijn et al 2003).

Although children and adolescents with less severe HA constitute the largest group of HA sufferers, they are often overlooked because they are less likely to attend specialty clinics. However, HA clinic populations include highly selected cases as only a minority of HA sufferers ever consult a doctor for their HA symptoms (Wang et al 2006, Scher et al 2002, Bandell-Hoekstra et al 2001). When adolescents (N = 37,187) visiting a general practitioner were studied, only a few HA sufferers were referred to HA specialist care (Van der Wouden et al 2000). It is important to separate the risk factors of NP and HA from risk factors for seeking medical advice. With this aim in mind, the population-based approach is the only possible one.

Methods

Many previous studies have evaluated the factors associated with adolescent HA, mainly cross-sectionally. Two of the four original publications of this thesis focused on determinants of changes in HA instead of factors associating with the prevalence of HA, which is important for finding ways to prevent an unfavourable course of HA.

The classification of HA was based on a structured interview and neurological examination. If adolescents have different kinds of HA, they probably recall the most frequent one when interviewed, and the nature of other types remains obscure without a HA diary (Metsähonkala et al 1997). Even if some recall bias might have occurred, it was assumed that the face-to-face interviews were accurate enough in diagnosing HA and clarifying the frequency of HA (Stovner et al 2006, Laurell et al 2003, Metsähonkala 1999, Rasmussen et al 1991). Questions about the occurrence of HA and NP in the previous 6 months were evaluated. European epidemiological HA studies have not shown any great differences between 1-year and 3-month prevalence rates. A neutral question about HA with additional questions, in the manner of the present study, has been regarded as optimal (Stovner et al 2006).

To identify useful tools for clinicians examining adolescent HA sufferers, only conventional, simple methods for the measurement of NP were analysed. The visual analoque scale (VAS) has been used to measure pain intensity in epidemiologic studies (Stovner et al 2006, Roth-Isigkeit et al 2004). We chose to use the conventional palpation method instead of a pressure-controlled palpometer, although manual palpation has been criticized for being subject to bias (Bendtsen et al 1995). In subjects aged 13 years, one trained physiotherapist carried out palpation and dolorimeter measurements using validated measurements (Langemark and Olesen 1987, Fischer 1986). In subjects aged 16 years, the physical examination of the neck was done by one trained specialist in physical medicine and rehabilitation. For palpation, a muscle map from the trigger point manual (Travell and Simons 1999) was used, and palpation force was calibrated by means of testing with a pressure dolorimeter between each participant. Reliability

testing in another adolescent population with mainly HA-free subjects carried out before the onset of the study found that reported NP frequency, VAS of NP, muscle PP (palpation pain), referred PP, pain in motion, and PP of the spine were reliable when recorded at one week's intervals. In adults, the reliability of the physical examination is better in symptomatic subjects (Fjellner et al 1999), and we assume that the reliability of the physical examination of the neck in adolescent HA sufferers with more permanent neck symptoms is also good.

Some studies define any soft tissue pain as myofascial pain, but in the present study myofascial pain was diagnosed only if the palpation of trigger points in the neck or face muscles referred pain to the head (Merskey and Bogduk 2004, Travell and Simons 1999, Davidoff 1998). Cervicogenic HA was not diagnosed, because this diagnosis requires abolition of HA after successful treatment of the causative disorder, and the criteria do not thus allow this diagnosis in a population-based study (Bogduk 2004, ICHD 2 2004). Instead, the report of HA usually beginning from the posture or movement of the neck, which is one symptom included in the criteria of cervicogenic HA from 1988 (ICHD 1), was analysed.

It has been shown that intra- and interobserver differences in defining cervical degeneration in MRI can be remarkable (Kolstad et al 2005). To reduce the influence of such errors, MRI scans of 17-year-olds were interpreted by three experienced, independent neuroradiologists. Although some differences were seen in their analyses, the rates of agreement were fairly good. The MRI study had sufficient power to detect relevant differences in the prevalence of disc degeneration, but because of the low number of HA-free participants, the study was not sensitive to detect small differences. Further, the number of foraminal stenoses and annular tears was so low that these findings rendered statistical analysis insensitive.

6.2. Neck pain in adolescent headache

6.2.1. Importance of co-occurring neck pain in adolescent headache

In this study of 16-year-old adolescents, NP was associated with disturbing, intensive HA. Although gender differences occurred, muscle pain was associated with HA variables in both genders, but with disturbing HA only in girls and with HA unresponsive to analgesics only in boys. The found associations emphasize the importance of concomitant muscle pain in adolescent HA regardless of gender. The present study supports earlier studies showing that multiple co-occurring pains in adolescents are more intensive and induce more disability than one single type of pain (Fearon and Hotopf 2001, Mikkelsson et al 1997). Psychological symptoms characteristic of HA may also result from co-occurring NP, making HA more intensive or severe (Powers et al 2006, Härmä et al 2002). In this study, NP concurrence with HA was associated with disturbed school work. Of all adolescent pains, HA and NP have been reported to have the severest effect on concentration (Smedbråten et al 1998). School-related factors have been thought to be associated with adolescent HA because of the stress or deteriorated school performance caused by HA (Dooley et al 2005, Gordon et al 2004), but the treatment of co-occurrent NP may be one way of making school work easier.

We tried to find a simple way of measuring NP in adolescent HA sufferers with only a few questions or with one single measurement. When the correlations of NP variables with each other were analysed, they were surprisingly low, suggesting that different NP variables measure different aspects of a neck disorder. Thus NP concurrent with adolescent HA can not be

excluded by one or two questions. It is also possible that there are differences in the treatment of HA depending on the characteristics of co-occurring NP (Sjaastad et al 2006).

The concurrence of NP and HA in this study population was clear. However, no association of NP was seen with HA type. Although pericranial tenderness and NP have traditionally been associated with TTH (ICHD 2 2004, Jensen et al 1998), muscular factors could play a role in both M and TTH in adolescence.

Although NP frequency and daily NP were positively associated with the characteristics and consequences of HA, the intensity of NP by VAS was the strongest independent factor explaining different HA variables. The intensity of NP could be a more important indicator of the sensitization process of pain than the frequency of NP alone. Probably also NP interfering daily activities at the age of 13 years was predicting the worsening of HA because it was more intensive and disabling than non-interfering NP.

Of the physical findings of the neck at the age of 16 years, muscle pain especially was positively associated with HA variables. Pericranial muscle tenderness increased with increasing frequency of HA, as seen in adults (Jensen 1999, Lipchik et al 1996). Of the studied muscles, the influence of the sternocleidomastoid muscles on HA could result from the weakness of these neck flexors when compared to the spine extensors, increasing the imbalance of the neck (Falla and Farina 2006). A sedentary way of life, on the other hand, could induce excessive loading of all studied neck muscles and irritate the muscle-nerve system of the neck with unfavourable positions, changes in posture and the difficulty of muscle relaxation.

Myofascial referred PP was found in HA sufferers, indicating that myofascial pain may also contribute to HA in adolescence like in adults (Fernández-de-las-Peñas et al 2006, Hou et al 2002, Travell and Simons 1999, Davidoff 1998). Adolescent HA with concomitant NP was unresponsive to analgesics when compared to HA without NP, confirming the results of previous adult studies, where medications alone have provided only modest benefit for HA associated with neck disorder (Biondi 2005). NP associating with HA probably requires other treatment than analgesics (Holroyd 2002).

Muscular neck pain seems to be clearly associated with disturbing HA in a non-chronic adolescent population. Although no studies exist of the treatments of concurrent NP in adolescent HA sufferers, it seems that concomitant NP should be considered in adolescent HA sufferers, and a thorough cervical and muscle evaluation is recommended when planning the treatment of HA.

6.2.2. The role of neck problems in modifying headache

The association of NP and HA in adolescence is probably complex and potentially bi-directional. The presence of other pains concurrent with HA has been shown to determine a worse prognosis for HA (Scher et al 2006). In this follow-up study from 13 to 16 years of age, the focus of interest was in the predictive role of concomitant NP in adolescent HA. NP interfering daily activities was associated with the outcome of HA in boys, and when interactions of NP and factors that we know to have a predictive role in the outcome of HA were analysed, other factors did not explain the independent role of NP.

It has been proposed that adult HA may stem from the neck, but firm evidence for NP and peripheral muscle pathology as a cause of chronic HA is lacking (Ashina et al 2002, Graff-Radford and Newman 2002, Sjaastad and Fredriksen 2000). In the present study, the predictive role of muscle tenderness in 13 year-olds for the outcome of HA could not be confirmed, and

although muscle pain at 13 years of age is associated with HA, the muscle pain of 13-year-olds may be only a temporary phenomenon with no capacity to change the outcome of HA.

In this study population of non-chronic HA sufferers at the age of 16 years, the tenderness of all neck muscle groups separately was associated with HA, in agreement with a previous study of female students aged 17-26 years (Lipchik et al 1996). It has been thought that intensive frequent HA can lead to muscle tenderness. If pericranial muscle tenderness were only a consequence of central neuroplastic changes in HA, it would probably not be associated with non-frequent low-intensity HA. The present study, however, showed an association of muscle pain with intensive frequent NP but not with intensive HA, and muscle pain could therefore not be only a consequence of HA. Muscular NP at the age of 16 years was intensive, and probably because of its intensity, muscle pain was one of the factors leading to disturbing HA refractory to analgesics. Individual, physical and psychosocial risk factors of muscular NP were not studied, but an associative role of the sedentary way of life was suspected. Although the association of muscular NP with disturbing HA was only studied cross-sectionally at the age of 16 years, previous studies have shown that NP and muscle tenderness in 15-18-year-old adolescents predicts NP in adulthood (Siivola et al 2004, Hertzberg 1985). It can be presumed that the muscle pain seen in this study group at the age of 16 years is important for predicting pain in adults, as shown by previous studies.

NP variables associating with frequent or intensive HA can be a cause or a consequence of HA or NP and HA can be part of widespread pain with common determinating factors. In addition to muscular NP, HA reported as triggered by an awkward posture or movement of the neck was associated with intensive NP, but not with intensive or frequent HA. HA triggered by neck posture or movement was surprisingly common, in agreement with an earlier adult study (Grimmer et al 1999), and disturbed leisure time activities and school work more often than HA that was not triggered by the neck. This symptom could thus be one important sign of NP leading to HA in adolescence.

Muscular neck pain could be one cause of HA in adolescence. On the other hand, muscle pain may be only an indicator of the true risk factors of adolescent HA, such as psychological and physical risk factors. HA could be called a neck-related symptom in many adolescents, even if the etiology of HA is multifactorial

Degeneration of the cervical spine

The degeneration of the cervical spine in the present study and in a recent study of young adults was more common than previous adult studies have suggested (Ishikawa et al 2003, Siivola et al 2002, Petren-Mallmin and Linder 1999, Matsumoto et al 1998, Lehto et al 1994, Boden et al 1990). It is possible that degenerative changes in the adolescent cervical spine have increased. One reason for the possible increase of degeneration could be the sedentary way of life inducing more stress to the spine. The biomechanical models of the cervical spine support this hypothesis of the influence of the sitting position on the increase in degeneration by increasing joint loads on the spine (Choi and Vanderby 2000, Kumaresan et al 2001, 1999, Jäger et al 1997). In the present study, degenerative changes were most common at level C5/6, in agreement with previous findings in adults (Krasny et al 2005, Matsumoto et al 1998, Jäger et al 1997, Lehto et al 1994, Dai 1998).

Although the joints of the upper cervical spine of adult patients have been shown to be a common origin of occipital headaches, neither the dysfunction of the upper neck nor the disc degeneration of the spine was associated in the present study with adolescent HA (Aprill et al 2002). It seems that in this age group the association of self-reported NP with HA cannot be

explained by degenerative changes or by permanent structural changes of the spine. It could, however, be presumed that the flexible spine in this age group is prone to become loaded, but the loads induce only reversible dysfunction of the spine (Kumaresan et al 2000). These reversible functional changes could be more important than the degeneration of the spine for pain symptoms in this age group. In adolescents, the neck muscles, however, seem to play a more important role in HA than spinal changes.

According to the present study, NP and muscle pain contribute to the risk of HA in adolescence. NP is not the only factor associated with HA, but the role of NP is significant, because contrary to many potential determinants, NP and muscle pain are probably modifiable and provide a concrete target for the prevention of disturbing HA.

6.3. Outcome of headache in adolescence

Comparable to the results of present study, recent population-based studies have reported that both the frequency and type of HA substantially change during adolescence (Laurell et al 2006, Larsson and Sund 2005, Wang et al 2005, Camarda et al 2002, Virtanen et al 2002, Fearon and Hotopf 2001). In the present study, in half of adolescents with monthly HA, HA improved, and in more than one-quarter of adolescents with non-frequent HA, HA frequency increased to monthly HA. HA type changed in 65% of participants. Migraine remained as migraine in 40% of migraineurs, and TTH remained as TTH in 59% of TTH sufferers.

This study focused on the determinants of changes in HA frequency and HA type instead of associating factors of the prevalence of HA, which is important for finding ways to prevent an unfavourable course of HA. These determinants may indicate or contribute to the worsening of HA. The focus of interest was in the predictive role of concomitant NP in adolescent HA. Although intensive disturbing NP was found to determine the change of HA from 13 to 16 years of age, muscle pain at the age of 13 years was not proved to be of importance. Female gender, use of analgesics, persistent migraine and higher basic educational level of one parent were independently associated with the outcome of HA frequency during the adolescent years.

In agreement with the results of previous studies in this age group, in this study monthly HA was more likely to appear and persist in females than in males (Laurell et al 2006, Larsson and Sund 2005). This may depend on differences in the genetic background of HA between girls and boys, earlier age of onset of migraine in boys and illness behaviour encouragement of girls from parents (Russell et al 2006, Fichtel and Larsson 2002, Pothmann et al 1994).

Monthly HA persisted more often if adolescents were using analgesics for their HA, and the influence of using analgesics was not explainable by the primary frequency of HA or by excessive use of analgesics. Although the use of analgesics has been associated with HA frequency in adolescence, medication overuse has emerged in clinical studies as an uncommon cause of chronic daily HA (Dyb et al 2006, Bigal et al 2004, Galli et al 2004). Instead of being explicable by overuse of analgesics for HA, the results could indicate either changing sensitivity to pain or a changing attitude to pain during the process of HA becoming chronic (Bendtsen 2000). The use of analgesics in those with a poor outcome of HA would thus be a sign of increased physiological or psychological sensitivity to pain rather than a cause of persistent frequenct HA. On the basis of the results of this study, it is not claimed that it is harmful to treat HA; on the contrary, it is considered important to treat HA episodes properly to arrest the pain sensitization process.

The results of this thesis do not support those of previous studies suggesting that migraine has a poorer outcome than the other types of HA (Kienbacher et al 2006, Brna et al 2005, Camarda et al 2002, Guidetti and Galli 1998). On the other hand, the study result of HA type being unassociated with the outcome of non-frequent or monthly HA is in line with the recent population-based follow-up study of Laurell and her colleagues (Laurell et al 2006).

The association of widespread pain with persistent monthly HA indicates that the spreading of pain is a marker of HA chronicization. In agreement with the known association of family history of HA with adolescent HA and migraine (Laurell et al 2005, Virtanen et al 2002, Waldie and Poulton 2002, Bandell-Hoekstra et al 2001, Aromaa et al 1998), a trend was seen for persistence of monthly HA if there were other HA sufferers in the family. In agreement with most previous follow-up studies, concomitant diseases or HA in early life did not predict worsening or persistence of HA at puberty (Virtanen et al 2002, Aromaa et al 2000, Guidetti et al 2000).

In this study it was possible to analyse associations between changes in HA frequency and bereavements occurring concurrently, which had not been analysed in previous studies. No causal relationship was evident between a reported personal loss and change in HA frequency. This indicates that although stress factors may have a temporary provoking role in headaches, they do not have the capacity to change the overall outcome of HA in adolescence. However, measuring the influence of stress factors is complex. Responses to different stress factors are highly subjective, and timing of severe anguish after bereavement is difficult. For example, parents' quarrels may have burdened a child years before their divorce. Psychiatric disorders, anxiety and depressive disorders associated with HA may predict the outcome of HA in an individual (Larsson and Sund 2005, Galli et al 2004, Waldie and Poulton 2002, Rhee 2000, Guidetti et al 1998), although this study population showed only a trend for depressive symptoms to be associated with the outcome of monthly HA.

6.4. Recommendations for future studies

Because of marked changes in NP and HA seen in adolescent years, it is important to define age ranges of data collection in future studies. There is a lack of longitudinal studies following adolescents into adulthood. Therefore, it is difficult to establish a pattern of HA occurrence and the influence of NP on HA during this transition phase (Grimmer et al 2006). Comorbidity of adolescent HA and NP creates a need to study determinants and risk factors in a different way than studying pure HA or pure NP. In future studies of adolescents, risk factors of muscular neck pain in HA sufferers should be considered.

The increasing prevalence of adolescent NP and HA, and the disturbance of HA with concomitant NP shown in this study, calls for effective interventions to be offered to adolescents. To find appropriate interventions, prospective studies of treatment of NP concomitant with HA are important, including the evaluation of specific physiotherapy, exercise, behavioral treatments, lifestyle changes and recommendations for school work. It seems to be important to evaluate muscle pain in adolescent years, and as to the intensity of NP and HA, the visual analoque scale seems appropriate in this age group. The influence of degenerative changes of the adolescent cervical spine on adult pain should also be evaluated.

7. CONCLUSIONS

The present study warrants the following conclusions:

1. Substantial changes occur in the frequency and type of headache in adolescence. Adolescents with frequent use of analgesics constitute a risk group for a poor outcome of HA. Girls fitting this description particularly should be considered a target group when planning and implementing preventive measures.
2. The risk of worsening HA in adolescence is more probable if the HA is associated with NP interfering with daily activities. NP is, however, not associated with the change of HA type.
3. Self-reported NP and physical findings of the neck are associated with adolescent HA. Especially, muscle pain and intensive, frequent NP are associated with disturbing HA unresponsive to analgesics. Even if there are no studies of treatment of NP co-occurring with adolescent HA, this study indicates that concomitant NP should be considered in adolescent HA sufferers.
4. Mild degenerative changes of the lower cervical spine seem to be common in adolescents, but the early degeneration does not seem to be associated with headache.

The causes of HA in adolescence seem to be complex. The common association of NP with disturbing HA unresponsive to analgesics emphasize, however, the importance of a thorough cervical and muscle evaluation in HA sufferers when planning the treatment of HA in this age group.

ACKNOWLEDGEMENTS

This study was carried out in the Departments of Public Health and Physical Medicine and Rehabilitation, and statistical expertise and analyses were provided by the Department of Biostatistics in the University of Turku from 2000 to 2007. The study was supported by grants from the Turku University Foundation, the City of Turku, and the University Hospital of Turku, which I gratefully acknowledge.

I owe my gratitude to a great number of people. I express my warm gratitude to all the adolescents, who participated in this headache study, to the personnel, who performed the initial examinations in 1998-1999, and to those who worked with me and supported me during the years 2000-2007.

The encouraging attitude of my first supervisor Docent Jouko J Salminen was important for my entrance into the world of research. He also supported me with all his knowledge and skills. My supervisor Professor Matti Sillanpää deserves my deepest gratitude for intelligent and accurate remarks on my work. His vast experience in scientific research and his willingness to teach me have been of importance for the progress of my study. My supervisor Docent Marja Mikkelsson guided me on several occations being an encouraging mentor. My supervisor Docent Liisa Metsähonkala deserves a special thank for encouraging me in all phases of the study, also when the cessation of the study was in the consideration. She put her heart into my work and I had an expert listener and commentator throughout the years.

Tero Wahlberg, MSc, guided me in the world of statistical analysis, and he was able to make complicated matters understandable. My collegue Pirjo Anttila, MD, PhD made an extensive contribution by her pediatric and neurological examinations of the study participants and by arranging the funds for the study. My friend and co-author, Docent Minna Aromaa, deserves thanks for arranging me a working room in the University and supporting me in all phases of the study. I acknowledge the work of the study nurses and secretaries, which was crucial for the success of the study. I also want to thank Olli Kaleva BSc for his skilful computation of the statistical analyses, and mrs Sari Kuitunen for data recording. I am grateful to Docent Päivi Rautava, who enabled the MRI study, to Docent Minna Erkintalo, who helped in planning, and carrying out the MRI study and Riitta Parkkola, MD, PhD and Pirkko Sonninen, MD, who analysed the MRI scans with Minna Erkintalo.

I want to thank all the co-authors and co-researchers of the Turku Pediatric Headache Team for a pleasant co-operation. The reviewers of the study Professor Eira Viikari-Juntura and Professor Heikki Rantala offered valuable and stimulating comments and I appreciate their knowledge in the fields of epidemiology, physical medicine and child neurology. I appreciate Simo Merne, MA, for checking the English language of all my manuscripts.

I am grateful to my co-workers in the departments of Public Health and Family Medicine for an inspiring and delightful working environment. Especially I want to mention Ruut Virtanen and Carita Suominen, who have lived in this project with me, Inger Vaihinen, who kindly assisted me in many ways throughout the study and Selena Nitecki, who assisted me with the final preparation of the text. The professors in Public Health Markku Koskenvuo, Risto Tuominen and Sakari Suominen have all been kind to courage me in this project. Chief Physician of Rehabilitation Center Petrea Ismo Takala, MD, PhD made the study possible by favourable attitude towards my study from the very beginning. I also want to thank Jari Hlavaty, Eeva Halonen and other friends of mine in the rehabilitation centre Petrea of sincere interest for my study.

My family and friends made it all worthwhile, balanced my life, and brought colour into my life. I thank my beloved husband Markku for his sense of humor and all the support at home, and my wonderful sons Jussi and Tommi for their patience in these years. I also thank my parents for encouragement, listening, buying the computer and for all support. I appreciate my sisters, my brother and my friends Arja Siro, Marjut Romppainen, Päivi Sutinen, Riitta Jarvansalo, and Maija Karinkanta, who have supported me in these years. And I thank all of my friends for praying, because without many miracles this would not be possible.

Turku, July 2007

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APPENDICES

The questions for self-reported symptoms used in original publications and in this thesis are published here.

Appendix 1. Headache variables (in English, translated by the author)

Clinical interview at the ages of 13 and 16 years
Papers I-IV:
Have you had headache in previous 6 months? No / Yes
How many times a month have you had headache in previous 6 months?_____

Papers I-IV: Headache type was diagnosed by criteria of IHS (ICHD 1, 1988).

Questionnaire at the age of 16 years
Paper IV: Estimate how intensive your headache was in previous six months during headache. Mark on the line with X, how intensive your headache usually was (the left end of the line represents a painless situation, the right end the worst possible pain).
How intensive was your pain?
No pain I_____I worst possible pain

Estimate in what degree headache made following functions difficult in previous six months. Estimate the limitation of the function during headache. Mark X on the line to the place of the amount of limitation usually induced by your headache (the left end of the line represents a painless situation or normal capability, the right end represents the worst pain possible or total incapability)

How much does the pain disturb your leisure time?
Not at all I_____I I cannot do anything
Does your pain disturb work / schoolwork?
Not at all I_____I prevents totally
In what degree do analgesics relieve your pain?
eliminate pain I_____I do not relieve at all

Headache questionnaire at the age of 7 years to the parents of pupils of the first grade of elementary school 9.1992
Paper I: Does your child currently have headache (during the preceding six months)?

1. No
2. Less than once a year
3. About once a year
4. 2-11 times a year
5. About once a month
6. 2-3 times a month
7. About once a week
8. 2-6 times a week
9. Daily

Appendix 1. Päänsärkymuuttujat (in Finnish)

Kliininen haastattelu 13- ja 16-vuotiaana
Artikkelit I-IV:
Onko sinulla ollut päänsärkyä viimeisten 6 kuukauden aikana? Ei / Kyllä
Kuinka monta kertaa sinulla on ollut päänsärkyä viimeisten 6 kk aikana keskimäärin kk:ssa?___

Artikkelit I-IV: Päänsärkytyyppi luokiteltiin IHS kriteereiden mukaan (ICHD 1, 1988).

Kyselylomake 16-vuotiaana
Artikkeli IV:
Arvioi, kuinka voimakas päänsärkysi oli viimeisen puolen vuoden aikana päänsäryn aikana. Merkitse viivalle X:llä, kuinka kovaa päänsärkysi yleensä oli (viivan vasen pää merkitsee kivutonta tilannetta, oikea pää pahinta mahdollista kipua)
Kuinka paha kipusi oli?
Ei lainkaan kipua I_____I pahin mahdollinen kipu

Arvioi, kuinka paljon päänsärkysi on vaikeuttanut viimeisen puolen vuoden aikana seuraavia toimintoja. Arvioi toiminnan rajoitus päänsäryn aikana. Merkitse X siihen viivan kohtaan, minkä verran päänsärkysi yleensä vaikeuttaa (viivan vasen pää merkitsee kivutonta tilannetta tai normaalia toimintakykyä, oikea pää pahinta mahdollista kipua tai täydellistä toiminta-kyvyttömyyttä)

Kuinka paljon kipu haittaa vapaa-ajan viettoasi?
Ei lainkaan I_____I en voi tehdä mitään
Haittaako kipu työntekoa/koulunkäyntiä?
Ei rajoita lainkaan I_____I estää täysin
Kuinka hyvin kipulääkkeet vaikuttavat kipuusi?
Poistavat kivun I_____I eivät lievitä yhtään

Päänsärkykysely 7-vuotiaiden vanhemmille ensimmäisellä koululuokalla 9.1992
Artikkeli I: PÄÄNSÄRKYÄ (viim. 6 kk aikana)

1. ei
2. alle kerran vuodessa
3. noin kerran vuodessa
4. 2-11 kertaa vuodessa
5. noin kerran kuussa
6. 2-3 kertaa kuussa
7. noin kerran viikossa
8. 2-6 kertaa viikossa
9. päivittäin

Appendix 2. Self-reported neck pain variables (in English, translated by the author)

Questionnaire at the ages of 12 and 16 years
Paper II-IV:
Have you had following symptoms in preceding six months and how often:
Neck pain
1. Not at all
2. Less than once a month
3. 1-3 times a month
4. once a week or more often

Questionnaire at the age of 16 years
Paper IV:
Estimate how intensive pain you had in previous six months in neck region. Mark on the line with X, how intensive your neck pain was (the left end of the line represents a totally painless situation, the right end the worst possible pain).
How intensive was your pain usually?
No pain I_____I worst possible pain

Clinical interview at the age of 13 and 16 years
Papers II, IV:
Do you have situations in daily life where you feel neck pain or stiffness of the neck region?
1. Hardly ever
2. Sometimes
3. Often

Clinical interview at the age of 16 years
Paper IV:
Were following symptoms associated with your headache in previous six months?
HA is triggered by the neck motion or poor posture of the neck or head. 1. No 2. Yes

Questionnaire at the age of 13 years
Paper II:
Have you had thermal therapy, massage or physiotherapy because of neck pain or headache in previous 6 months? 1. No 2. Yes

Appendix 2. Tutkittavan raportoimat niskakipumuuttujat (in Finnish)

Kyselylomake 12- ja 16-vuotiaana
Artikkelit II-IV: Onko viimeisen puolen vuoden aikana ollut seuraavia oireita ja kuinka usein:
Niskahartiaseudun kipua
1. Ei lainkaan
2. Alle kerran kuukaudessa
3. 1-3 kertaa kuukaudessa
4. Kerran viikossa tai useammin

Kyselylomake 16-vuotiaana
Artikkeli IV:
Arvioi, kuinka kovaa kipua Sinulla on ollut viimeisen puolen vuoden aikana niskahartia-seudussa. Merkitse viivalle X:llä, kuinka kova kipusi oli (viivan vasen pää merkitsee täysin kivutonta tilannetta, oikea pää pahinta mahdollista kipua).
Kuinka paha kipusi yleensä oli?
Ei lainkaan kipua I_____I pahin mahdollinen kipu

Kliininen haastattelu 13- ja 16-vuotiaana
Artikkelit II, IV:
Syntyykö jokapäiväisessä elämässä tilanteita, joissa niskahartiaseutusi kipeytyy tai tuntuu jäykältä?
1. Ei juuri koskaan
2. Toisinaan
3. Usein

Kliininen haastattelu 16-vuotiaana
Artikkeli IV:
Onko päänsärkyysi liittynyt viimeisten 6 kk aikana seuraavia asioita
Särky alkaa niskan liikkeestä tai huonosta niskan tai pään asennosta. 1. Ei 2. Kyllä

Kyselylomake 13-vuotiaana
Artikkeli II:
Onko Sinulle niskahartiaseudun kivun tai päänsäryn vuoksi annettu lämpöhoitoa, hierontaa tai lääkintävoimistelua viimeisten 6 kuukauden aikana? 1. Ei 2. Kyllä

Appendix 3. Other analysed self-reported variables (in English, translated by the author)

Clinical interview at the age of 13 years

Papers I-II:

In how many headache attacks do you get analgesics, usually what analgesics____

1. Not at all
2. less than in every third headache attack
3. in every third headache attack
4. in half of headache attacks
5. in every headache attack

Paper II:

Outside school hours: How many hours a week do you usually spend in sports activities so intensively that you are breathless or sweating?

1. Not at all
2. about half an hour
3. about one hour
4. 2-3 hours
5. about 4-6 hours
6. 7 hours or more

Paper I:

Do your family members have recurrent headache? 1. No 2. Yes, who____ (mother, father, sister and brother were taken into the analysis)

Paper II:

In how many days a week do you play with the computer or surf the Internet?_____d

Questionnaire at the age of 12 years

Papers I-II:

How often did you have following symptoms in preceding six months:

	Not at all	<1/month	1-3/month	once a week or more often
Abdominal pain	1	2	3	4
Limb pain	1	2	3	4
Sore throat	1	2	3	4
Earache	1	2	3	4
Eye ache	1	2	3	4
Toothache	1	2	3	4
Back pain	1	2	3	4
Chest pain	1	2	3	4
Neck pain	1	2	3	4
Other pain	1	2	3	4

Papers I-II:

Basic education of parents	Mother	Father
Elementary school or less	1	1
Part of the middle school	2	2
Part of the senior high school	3	3
Secondary-school matriculation examination	4	4

Paper II:

Have you had following symptoms almost every day at least for 2 weeks in previous 6 months:

	No	Yes
Depressed mood most of the day, irritability	1	2
Sad smile, tearfulness most of the day	1	2
Loss of interest or pleasure in almost all daily activities	1	2
Significant involuntary loss or gain of weight, or reduced or increased appetite	1	2

Insomnia or hypersomnia	1 2
Psychomotor agitation or retardation	1 2
Fatigue or loss of energy	1 2
Feelings of worthlessness or excessive guilt, self-accusations	1 2
Diminished ability to concentrate, indecisiveness, or reduced thinking ability	1 2
Recurrent thoughts of death or suicide, or desire for death	1 2

Paper II:

Do you have conflict situations	often	quite often	sometimes	hardly ever
At home	1	2	3	4
During participation in hobbies	1	2	3	4

Paper II:

Have you had at school (Circle more options if necessary)

	often	quite often	sometimes	hardly ever
Fear of school	1	2	3	4
Exposure to bullying	1	2	3	4
Fear of teachers	1	2	3	4
Loneliness	1	2	3	4
Behavioral problems	1	2	3	4
Learning difficulties	1	2	3	4
Fear of failure	1	2	3	4
Problems with other pupils	1	2	3	4
Fear of coping	1	2	3	4
Feeling of insufficiency	1	2	3	4
Stress in school	1	2	3	4

Questionnaire at the age of 12 years and clinical interview at the age of 16 years

Paper I:

Has the child a long-term illness as / What long-term illnesses or recurrent diseases do you have? rheumatic disease, diabetes mellitus, bronchial asthma, allergy, lactose intolerance, coeliac disease, thyroid disease, renal disease, heart disease, arterial hypertension, developmental language disorder, minimal brain disorder, cancer, other disorder, what_____

Clinical interview at the age of 13 and 16 years

Paper I:

Have changes occurred in the family situation after the last study?

Change:	No	Yes	
parenteral divorce	1	2	
unemployment	1	2	
change of jobs	1	2	
relocation of home	1	2	
long-term disease in the family	1	2	
economic problems	1	2	
domestic quarrels	1	2	(only at 16 years)
end of courtship	1	2	(only at 16 years)
your moving from home	1	2	(only at 16 years)
death of a close relative	1	2	(only at 16 years)

Appendix 3. Tutkittavan raportoimat muut muuttujat (in Finnish)

Kliininen haastattelu 13-vuotiaana

Artikkelit I-II:

Kuinka moneen päänsärkyyn saat särkylääkettä, yleensä mitä lääkettä_____

1. en ollenkaan
2. alle joka kolmanteen
3. joka kolmanteen
4. joka toiseen
5. jokaiseen

Artikkeli II:

Koulutuntien ulkopuolella: Kuinka monta tuntia viikossa tavallisesti harrastat liikuntaa vapaa-aikanasi niin, että hengästyt ja hikoilet?

1. En yhtään
2. noin ½ tuntia
3. noin tunnin
4. 2-3 tuntia
5. noin 4-6 tuntia
6. 7 tuntia tai enemmän

Artikkeli I:

Onko perheessä toistuvaa päänsärkyä? 1. Ei 2. Kyllä, kenellä_____ (äiti, isä, sisko, veli otettiin analyysiin)

Artikkeli II:

Kuinka monena päivänä viikossa harrastat tietokonepelien pelaamista tai internetissä surffailua?_____pv

Kyselylomake 12-vuotiaana

Artikkelit I-II:

Kuinka usein viimeisen puolen vuoden aikana on ollut seuraavia oireita?

	Ei lainkaan	<1/kk	1-3/kk	kerran viikossa tai useammin
Vatsakipuja	1	2	3	4
Raajasärkyjä	1	2	3	4
Kurkkukipua	1	2	3	4
Korvasärkyä	1	2	3	4
Silmäsärkyä	1	2	3	4
Hammassärkyä	1	2	3	4
Selkäkipuja	1	2	3	4
Rintakipuja	1	2	3	4
Niskahartiakipua	1	2	3	4
Muuta, mitä?__	1	2	3	4

Artikkelit I-II:

Vanhempien peruskoulutus	Äiti	Isä
Kansakoulu tai vähemmän	1	1
Kansakoulu ja osa keskikoulua	2	2
Keskikoulu ja osa lukiota	3	3
Ylioppilastutkinto	4	4

Artikkeli II:

Onko ollut lähes päivittäin vähintään kahden viikon ajan viimeisten 6 kk aikana seuraavia oireita:

	Ei	Kyllä
Masentunut mieliala suurimman osan päivästä, alakuloisuus, ärtyneisyys	1	2
Surumielinen hymy, itkuisuus suurimman osan päivästä	1	2
Mielenkiinnon tai mielihyvän väheneminen lähes kaikissa päivittäisissä toiminnoissa	1	2

Merkittävä tahaton painon nousu tai lasku, tai lisääntynyt tai vähentynyt ruokahalu	1	2
Unettomuus tai liiallinen nukkuminen	1	2
Kiihtyneisyys, levottomuus, rauhattomuus, hitaus	1	2
Väsymys, voimattomuus	1	2
Arvottomuuden tunne, aiheeton syyllisyyden tunne, itsesyytökset	1	2
Keskittymiskyvyttömyys, päättämättömyys, ajattelukyvyn heikkous	1	2
Toistuva kuoleman tai itsemurhan ajattelu, tai halu kuolla	1	2

Artikkeli II:

Esiintyykö ristiriitatilanteita	Usein	Melko usein	Joskus	Ei juurikaan
Kotona	1	2	3	4
Harrastuksissa	1	2	3	4

Artikkeli II:

Onko ollut koulussa (Rengasta tarvittaessa useampi vaihtoehto)

	Usein	Melko usein	Joskus	Ei juuri koskaan
Koulupelkoa	1	2	3	4
Kiusatuksi joutumista	1	2	3	4
Opettajan tai opettajien pelkoa	1	2	3	4
Yksinäisyyttä	1	2	3	4
Käytösongelmia	1	2	3	4
Oppimisvaikeuksia	1	2	3	4
Epäonnistumisen pelkoa	1	2	3	4
Oppilaiden kanssa ongelmia	1	2	3	4
Selviytymisen pelkoa	1	2	3	4
Riittämättömyyden tunnetta	1	2	3	4
Koulustressiä	1	2	3	4

Kyselylomake 12-vuotiaana ja kliininen haastattelu 16-vuotiaana

Artikkeli I:

Onko lapsella pitkäaikaissairaus kuten / Mitä pitkäaikaissairauksia tai toistuvia sairauksia sinulla on? reuma, diabetes, astma, allerginen nuha, ruoka-aineallergia, laktoosi-intoleranssi, keliakia, kilpirauhassairaus, munuaissairaus, sydänvika, verenpainetauti, puhehäiriö, MBD, syöpä, muu, mikä_____

Kliininen haastattelu 13- ja 16-vuotiaana

Artikkeli I:

Onko perhetilanteessa tapahtunut muutoksia viime kyselyn jälkeen

Muutos:	Ei	Kyllä	
vanhempien avo-tai avioero	1	2	
työttömyys	1	2	
työpaikan vaihto	1	2	
asunnon vaihto	1	2	
pitkäaikaissairaus perheessä	1	2	
taloudelliset huolet	1	2	
perheriitoja	1	2	(vain 16-vuotiaana)
seurustelun katkeaminen	1	2	(vain 16-vuotiaana)
muuttosi pois kotoa	1	2	(vain 16-vuotiaana)
läheisen kuolema	1	2	(vain 16-vuotiaana)