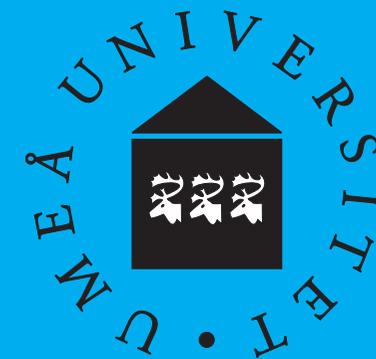


Acta Orthopaedica

Chronic neck pain

**An epidemiological, psychological and SPECT study
with emphasis on whiplash-associated disorders**

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Original Papers

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

- I. Guez M, Hildingsson C, Nilsson M, Toolanen G. The prevalence of neck pain: A population-based study from northern Sweden. *Acta Orthop Scand* 2002; 73 (4): 455-9.
- II. Guez M, Hildingsson C, Stegmayr B, Toolanen G. Chronic neck pain of traumatic and non-traumatic origin. A population based study. *Acta Orthop Scand* 2003; 74 (5): 576-9.
- III. Guez M, Nasic S, Hildingsson C, Toolanen G. Chronic low-back pain in individuals with chronic neck pain of traumatic and non-traumatic origin. A population-based study. Accepted for publication in *Acta Orthop*.
- IV. Guez M, Brännström R, Nyberg L, Hildingsson C, Toolanen G. Neuropsychological functioning and MMPI-2 profiles in chronic neck pain: A comparison of whiplash and non-traumatic groups. *J Clin Exp Neuropsychol* 2005; 27 (2): 138-157.
- V. Sundström T, Guez M, Hildingsson C, Toolanen G, Nyberg L, Riklund K. Cerebral blood-flow pattern in patients with chronic neck pain. A comparison of chronic whiplash syndrome with chronic neck pain of non-traumatic origin. Accepted for publication in *Eur Spine J*.

Abstract

Chronic neck pain, a common cause of disability, seems to be the result of several interacting mechanisms. In addition to degenerative and inflammatory changes and trauma, psychological and psychosocial factors are also involved. One common type of trauma associated with chronic neck pain is whiplash injury; this sometimes results in whiplash-associated disorder (WAD), a controversial condition with largely unknown pathogenetic mechanisms.

We studied the prevalence of chronic neck pain of traumatic and non-traumatic origin and compared the prevalence of, sociodemographic data, self-perceived health, workload and chronic low-back pain in these groups. In a ready-made questionnaire (MONICA study), we added questions about cervical spine and low-back complaints. 6,000 (72%) completed a self-administered questionnaire. 43% reported neck pain: 48% of women and 38% of men. Women of working age had more neck pain than retired women, a phenomenon not seen in men. 19% of the studied population suffered from chronic neck pain and it was more frequent in women. A history of neck trauma was common in those with chronic neck pain. Those with a history of neck trauma perceived their health worse and were more often on sick-leave. About 50% of those with traumatic and non-traumatic chronic neck pain also had chronic low-back pain.

We assessed the subjective and objective neuropsychological functioning in 42 patients with chronic neck pain, 21 with a whiplash trauma, and 21 without previous neck trauma. Despite cognitive complaints, the WAD patients had normal neuropsychological functioning, but the WAD group especially had deviant MMPI results—indicating impaired coping ability and somatization. WAD patients had no alterations in cerebral blood-flow pattern, as measured by rCBF-SPECT and SPM analysis, compared to healthy controls. This contrasts with the non-traumatic group with chronic neck pain, which showed marked blood-flow changes. The blood-flow changes in the non-traumatic group were similar to those described earlier in pain patients but—remarkably enough—were different from those in the WAD group. Chronic neck pain of whiplash and non-traumatic origin appears to be unique in some respects. A better understanding of the underlying pathological mechanisms is a prerequisite for prevention of the development of such chronic pain syndromes and for improvement of the treatment of patients with severe symptoms.

Key words: Prevalence of chronic neck pain, chronic low-back pain, whiplash, WAD, neuropsychology, Personality, MMPI-2, Brain imaging, Somatization, coping.

Summary in Swedish—Svensk sammanfattning

Förekomsten av ospecifik nacksmärta är hög i de industrialiserade länderna. Vi fann att 18 % av befolkningen i Norrland angav kronisk nacksmärta och 16 % kronisk ländryggsmärta. Kronisk nacksmärta var vanligast hos kvinnor i arbetsför ålder. Mer än var fjärde person med kroniska nackbesvär angav tidigare nack- eller skalltrauma; i en tredjedel av fallen angavs ett whiplashtrauma. Bland dem med ett nacktrauma och kronisk nacksmärta fanns det en ökad andel yngre män. Vidare uppfattade sig dem i trauma gruppen ha sämre hälsa och var oftare sjukskrivna. Cirka hälften med kronisk nacksmärta, med eller utan nacktrauma, hade också kronisk ländryggsmärta. Samexistensen av kronisk nack- och ländryggsmärta kan vara ett tecken på att individen lider av ett mer generellt kroniskt smärtsyndrom. Patienter med kronisk whiplash-associerad smärta (WAD) klagade ofta över koncentrations- och minnesstörningar, men neuropsykologisk undersökning var normal. Däremot avvek de med kronisk nacksmärta vad avser personlighetsprofilen och mest de med ett whiplas-

htrauma. Det tycks vara så att subjektiva besvär och upplevelse av dålig hälsa hos patienter med kronisk nacksmärta delvis beror på somatisering och inadekvat coping, speciellt hos dem med kroniska besvär efter whiplashskada.

Ett sätt att objektivisera smärtupplevelsen och dess mekanismer är att kartlägga blodflödet i hjärnan och relatera till olika smärtcentra där. Vi mätte detta blodflöde och fann att whiplashgruppen inte skiljde sig från friska kontroller, vilket däremot de med kronisk nacksmärta utan trauma gjorde. Således tycks smärtuttrycket i hjärnan tolkat utifrån det regionala blodflödets aktivitet i hjärnan, väsentligen skilja sig mellan personer med kronisk WAD och de med kronisk atraumatisk nacksmärta.

Patienter med WAD och kronisk nacksmärta tycks skilja sig i olika avseenden från de med kronisk nacksmärta utan traumatisk genes. En kartläggning av vad som orsakar deras sjuklighet är en förutsättning för att förebygga och ta fram bättre behandling för dessa hårt drabbade patienter.

Thesis at a glance

	Aim of the study	Material	Methods	Results	Conclusions
I	To investigate the prevalence of neck pain of non-traumatic and traumatic origin.	6,000 samples from the MONICA project.	Questionnaire (Table 1).	43% reported neck pain, 19% chronic neck pain; more common in woman. More than one quarter of the subjects with chronic symptoms had a history of neck or head trauma and one-third of these had sustained a whiplash injury.	Neck pain and chronic neck pain are common. All types of neck trauma appear to be associated with chronic neck pain.
II	To compare two groups with chronic neck pain, one with a history of neck injury and the other without, concerning sociodemographic data, self-perceived health and workload.	4,392 samples from the MONICA project.	Questionnaire (Table 1).	18% reported chronic neck pain; almost one-third of them had a history of neck injury. The trauma group had a higher proportion of younger men, being more often on sick-leave, and perceiving their health to be worse than those without a neck injury.	Trauma-related chronic neck pain seems to be a separate entity, which may explain the differences found between traumatic and non-traumatic chronic neck pain.
III	To assess the prevalence of chronic low-back pain in individuals with traumatic and non-traumatic chronic neck pain, with special emphasis on whiplash injury.	6,000 samples from the MONICA project.	Questionnaire (Table 1).	The prevalence of chronic low-back pain in individuals with chronic non-traumatic neck pain was 53%, and 46% in those with chronic neck pain and with a history of neck trauma. There was no difference in the prevalence of chronic low-back pain between whiplash and other types of neck trauma.	The prevalence of chronic low-back pain was three times higher in individuals with chronic neck pain—irrespective of whether there was a traumatic or non-traumatic origin for the symptoms—as compared to the general population. Mechanisms other than a history of trauma, such as chronic muskuloskeletal pain syndromes, may be important to consider in the evaluation of these cases.
IV	To study physical complaints, the subjective and objective neuropsychological functioning, and personality profiles in patients with chronic neck pain with and without previous whiplash trauma.	42 patients with chronic neck pain, 21 with a whiplash trauma and 21 without a previous trauma.	We measured pain intensity (VAS), the neuropsychological functioning, psychosomatic complaints (GBB) and personality traits with MMPI-2.	Chronic neck pain did not interfere with neuropsychological functioning. The MMPI-2 profiles differed from the controls on several scales, however—more so in the whiplash group, which had more divergent test results than the non-traumatic group—in the MMPI-2 test.	In those with chronic neck pain and WAD, the symptoms appear to be closely linked to separate personality traits. There was no correlation between the subjective complaints and poor performance on neuropsychological testing in patients with chronic neck pain. There appears, however, to be an association between symptoms and somatization and inadequate coping, especially in chronic whiplash patients.
V	To investigate regional cerebral blood flow (rCBF) in patients with chronic WAD, and in those with chronic neck pain without a history of neck injury—and to compare the rCBF findings with those from healthy subjects.	46 patients with chronic neck pain, 26 had an earlier whiplash trauma, 20 had no previous whiplash trauma.	Investigation with rCBF-SPECT. The rCBF data were analyzed with SPM to detect regions with a deviant blood flow at rest.	The non-traumatic patients displayed changes in rCBF compared to both the whiplash group and the healthy control group. These changes included reduction in rCBF in a right temporal region close to hippocampus, and increased rCBF in the left insula. The whiplash group displayed no significant differences in rCBF relative to the controls. These results indicate altered rCBF in patients with chronic neck pain of non-traumatic origin, but not in patients with chronic neck pain after whiplash trauma.	Different cerebral blood-flow patterns in patients with chronic neck pain with and without WAD indicate different pain mechanisms.

Introduction

General

Neck pain is common. In Scandinavian studies, more than half of the individuals report some kind of neck pain, and one-quarter report chronic neck pain. Chronic neck pain is a frequent source of disability, and has a considerable influence on the quality of life and demands on healthcare and social security systems, quite apart from the pain and suffering experienced. It is common in all age groups, especially in women (Table 1).

Chronic neck pain consists of a heterogeneous group of conditions in which several mechanisms may act in concert, and the cause of chronic neck pain is thus complex and multifactorial in most patients. The pain *per se* is generally unspecific, difficult to analyze and impossible to quantify (IASP). Neck pain can be considered to be an illness seen as a social phenomenon put in a social context constituting a biopsychosocial model (Waddell 2000). Clinical and radiographic examinations seldom show organic lesions to be responsible for the symptoms in neck pain (Boden et al. 1990, Matsumoto et al. 1998), instead for example psychosocial and cultural factors have been proposed to be contributory factors (Richter et al. 2004). Also, alterations in the central nervous system (neural sensitization) have been suggested as an explanation for the persistence of pain (Purves 2005). Since we do not know the mechanisms, there have been few successful treatments for chronic neck pain.

Does trauma have any effect on the development of chronic unspecific neck pain? Multi-trauma patients with high-energy injuries, for instance, seldom develop chronic neck pain—in contrast to patients with moderate-to-mild trauma with no skeletal injury or any obvious muscle/ligament injury to the cervical spine (Mali and Lovell 2004). It is a paradox that there does not seem to exist any dose-response relationship. After injuries in other anatomical areas there is usually a rough correlation between the extent of tissue damage and impairment and disability. One well-known type of injury in this respect is whiplash injury, which can lead to whiplash-associated disorder (WAD) (Spitzer

et al. 1995, Swedish whiplash commission 2005). This disorder is controversial, since some reports have indicated that the prevalence of chronic neck pain is the same in WAD patients as in the general population (Bovim et al. 1994), while others claim that whiplash trauma results in a high prevalence of chronic neck pain (Croft et al. 2001). Obviously, sampling and definitions are very important. Non-contact cervical spine injuries have been studied biomechanically and are regarded as particularly harmful mechanisms of insult to the cervical spine (Hartwig et al. 2004). On the other hand, others consider non-traumatic mechanisms to be more important in the development of chronic neck pain (Richter et al. 2004, Kivioja 2004). Apart from whiplash injuries, other types of trauma may also result in chronic neck pain. Furthermore, it is not known whether a traumatic origin for chronic neck pain—especially whiplash injury—has any influence on the character of pain itself.

Pain

Definition and aspects of the pathophysiology

The International Association for the Study of Pain (IASP) defines pain as: “An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such.” Note that by definition, pain is always subjective. Each individual learns the application of the term through experiences related to injury in early life. Pain is that experience we associate with actual or potential tissue damage. It is unquestionably a sensation in part or parts of the body, and it is always unpleasant—and therefore also an emotional experience. Unpleasant abnormal experiences (dysesthesias) may also be pain, but are not necessarily so because, subjectively, they may not have the usual sensory qualities of pain. This means that pain perception is conditioned, i.e. that in certain circumstances stimuli not normally perceived as moderately painful can be recorded as extremely painful (Purves 2005).

Table 1. Prevalence of neck pain in earlier studies

A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	
Brattberg 1989	1 009	71	y	S	y	+	1	18-84	49					6 months of obvious pain.	Neck and shoulder pain the most fre- quent; the prevalence of obvious pain was reported most frequently.	Mailed question- naire, classifica- tion of intensity and disability, comprehensive questionnaire on prevalence of pain in the gen- eral population.
Mäkelä 1991	8 000	90	y	F	y	+	2	30-64	52	12	10	14		Past month. [?]	After the age of 55- 64 the prevalence decreased. Chronic neck pain assoc with history of neck pain, mental and physi- cal stress at work, chronic low-back pain.	Clinical investi- gation, interview and question- naire.
Anders- son 1993	1 806	90	y	S	y	+	3	25-74	50			15	19	Persistent/ recurrent pain for > 3 months.	Neck shoulder pain was the most common site of chronic pain which was common even in the youngest age groups, decreasing in those older than 50- 59 years.	Mailed ques- tionnaire and drawing on bodydiagram- chronic pain in the general population.
Bovim 1994	10 000	77	y	N	y	+	4	18-67	49	14	10	17		6 months or more.	Chronic neck pain is significantly more frequent in women.	Mailed survey.
Coté 1998	2 184	55	y	Ca	y	+	3	20-69	48	10	8	12		6 month prevalence grade I-III.	The importance of grading. Included both lifetime and point prevalence of neck pain; more woman than men had experi- enced neck pain in the past 6 months.	Mailed survey, including clas- sification of neck pain grade: high/low inten- sity/disability.
Lau 1996	800		n	Ch	n	+	5	>29		16	15	17		1-year preva- lence.	Neck pain is a common prob- lem, particularly in individuals with high socioeconomic status.	Interview.
Webb 2003	5 752	86	y	UK	gp	+	6	>15	49	14	11	17		1-month period prevalence related to severity.	Most people with neck pain also reported pain at other sites. The prev. of spinal pain with disability was lower, and the prevalence of neck pain was higher in woman.	Mailed ques- tionnaire x 2; site-specific questionnaire.
Average	4 222	78							50	13	12	16				

For abbreviations, see next page

How chronic pain is initiated, maintained and prolonged are crucial questions in the field of pain research. Apparently, there is not always a direct

association between tissue damage, pain perception and behavior. While acute pain has a clear and understandable biological function, chronic pain

Legends to Table 1.

- A First author, year
 B Number of cases
 C Response (%)
 D Population based
 E Area
 Ca Canada
 Ch China
 F Finland
 N Norway
 S Sweden
 F Population register
 gp reg – general practice registers
 G Type: cs – cross sectional survey
 H Sampling
 1 random sample in a country
 2 cluster sample from population register
 3 random sample
 4 random sample from natural region of Norway
 5 household survey
 6 regional urban survey
 I Age span
 J Women (%)
 K Neck pain total (%)
 L Neck pain men (%)
 M Neck pain women (%)
 N Definition
 O Conclusions
 P Comments

without any recognizable tissue injury does not seem to serve any purpose for the individual.

Nociception and pain

Generally transmitted nociceptive information supports the brain with exteroceptive and interoceptive afferent representation of the body's physiological condition. The pathways for pain transmission are complex. The system consists of two different components. The sensory-discriminative component, transmitted through the spinothalamic tract, is relayed via the thalamus to reach the somatosensory cortex and associated areas. The spinobrachial pathways have connections to brain regions involved in the affective-emotional component. The affective and motivational reactions to noxious stimuli are then mediated to several different centers in the brain (Figure 1).

Modulation: peripheral and central effects

It is well known that the subjective response to a given pain stimulus varies because of neuronal modulation. The gate control theory (Wall and Melzack 1989) has formed a basis for the description of its mechanism. Thus, the ascending nociceptive information may be modulated by both

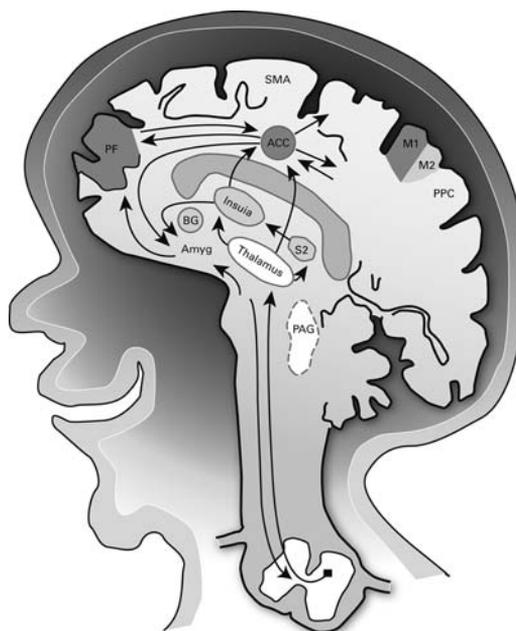


Figure 1. Schematic anatomical map of brain regions of interest in pain perception.

peripheral inputs and several central mechanisms (Figure 1). It seems that there will always be some degree of ongoing modulation of nociceptive information (Purves 2004). Neuronal plasticity means that the neurons involved in pain transmission are converted from a state of normosensitivity to one in which they are hypersensitive. Different descending pathways involving higher centers, such as the dorsolateral prefrontal cortex, may evoke both facilitatory and inhibitory influence on the nociceptive transmission, and thus on the pain perception (Pertovaara 2000, Lorenz et al. 2003).

This modulation is effectuated by neurochemical mediators. Important examples are the endogenous opioid and NMDA (N-methyl-D-aspartate) receptors (Purves 2005). Increased activity of the NMDA receptor can amplify the pain impulse coming from the periphery eg. wind-up phenomenon (Sandkühler 2000). The consequence can be central sensitization and hyperexcitability, which may increase the sensitivity to pain impulses in the whole spinal cord (Carpenter and Dickenson 1999). The result of such modulation can be hyperalgesia and allodynia (Purves 2005).

Chronic pain syndromes including chronic WAD and fibromyalgia show evidence of central nervous system hyperexcitability induced by central sen-

sitization (Banic et al. 2000; Sterling et al. 2003). Experimental studies have suggested a decrease in neuronal signals descending from the brain stem and normally inhibiting the upward transmission of pain in chronic pain patients (Kosek et al. 1995). The perception of pain depends on its context, and is therefore modified by the emotional situation at any given moment (eg. "fight and flight situation"), and also cultural, psychological, behavioral and social factors (Costigan and Woolf 2000, Turk and Floor 1999, Purves 2005). This may explain how psychological factors influence pain perception to the same extent as any other neuronal phenomenon, while also explaining psychosomatic pain problems in general (Purves 2005).

Cerebral blood flow and pain

In an attempt to visualize the expression of pain in the brain, different brain imaging techniques such as fMRI, PET scan and SPECT have been used. These techniques are based on the fact that active neurons have a higher metabolic activity than inactive ones, resulting in regional cerebral blood flow alterations.

Our knowledge of cerebral pain mechanisms is mainly based on experimental studies. Patients with different kinds of pain have different rCBF patterns, indicating various kinds of pain processing in acute and chronic pain (Peyron et al. 2000). The rCBF response in acute experimental noxious stimuli has been well evaluated and rCBF changes have been registered in the secondary somatosensory cortex (SII), anterior cingular cortex (ACC), and with slightly less consistency, in both the contralateral thalamus and the primary somatosensory cortex (SI)(Figure 2). Changes in these regions are thought to reflect the sensory, cognitive and affective dimensions of pain (Debyshire et al. 2002, Peyron et al. 2000). Studies comparing rCBF at rest in chronic pain patients have shown reductions or asymmetric changes in the thalamus and reduction in the frontal, temporal, parietal, and occipital regions (Wik et al. 2003, Nakabeppu et al. 2001, Kwiatek et al. 2000, Newberg et al. 2005). Parieto-occipital hypoperfusion in chronic WAD patients has been explained by possible activation of nociceptive afferent nerves from the cervical spine (Otte et al. 1997) (Figure 1).

T-scores

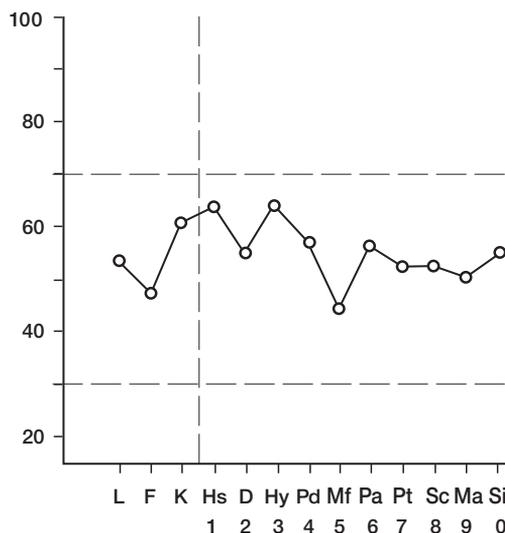


Figure 2. An example of how the result of the MMPI-2 test is often illustrated as a table with scales and their corresponding T-score.

Aspects of epidemiology

The prevalence of neck pain is high in several western countries (Table 1). Many studies have focused on the prevalence of neck pain in different time perspectives, such as point-prevalence (Webb et al. 2003) and period-prevalence (Lau et al. 1996). Others have related neck pain to grade of intensity of the pain, and disability (Brattberg et al. 1989, Webb et al. 2003). In addition, the definition of chronic neck pain has varied widely in different studies, as do sampling, questions, methodology and collection of information. Thus, different studies often measure different parameters and are not easy to compare. The prevalence of neck pain varies in different parts of the world, probably because of cultural, social and economic differences, and differences in healthcare systems (Lau et al. 1996).

The annual incidence in a recent Canadian study was 14.6%, and 0.6% of the same population developed disabling neck pain each year. Complete resolution of neck symptoms and of the patient's disability is rare (Cote et al. 2004).

Chronic low-back pain

There have been very few comparable prevalence studies on chronic low-back pain. Generally speak-

Table 2. Earlier studies on the prevalence of chronic low-back pain

A	B	C	D	E	F	G	H	I
Andersson 1993	1,806	1	S	49	23	Chronic low-back pain = persistent or regular recurrent pain with duration > 3 months.		Postal questionnaire; clinical examination of a subsample (agreement 75-86%).
Heliövaara 1991	5,673	2	F	48	12	A low-back syndrome was diagnosed if the person had a convincing symptom history of chronic low-back pain during the preceding month and a major pathologic finding on physical examination.		Questionnaire and interview; diagnosis by a physician.
de Silva 2004	3,182	3	B	56	4	um que estabelece a identificação da região lombar como o local da dor em uma figura de pessoa em posição ereta, supina e dorsal com as regiões lombar, torácica e cervical pintadas em cores diferentes ²⁴ , e outro que constata a presença desta dor por sete	The variables sex, age, marital status, schooling, smoking, body mass index, working in a lying position, heavy physical work, and repetitive movements were associated with CLBP.	Questionnaire, interview. Rural areas of Southern Brazil.
<p>A First author, year B Number of cases C Sampling 1 Random sample from population register. 25–74 years 2 Random population sample, 30–64 years; 90% response rate. 3 Population-based cross-sectional study, population aged 20 years and older. D Area B Brazil F Finland S Sweden E Women (%) F Chronic low-back pain (%) G Definition H Conclusions I Comments</p>								

ing, chronic-low-back pain is common—and more common in women—and results in a high rate of disability (Andersson 1999) (Table 2).

WAD

The incidence of reported whiplash injury is high in most western societies, and it is probably on the increase (Johnson and Zigler 2004). The annual incidence of whiplash trauma in northern Sweden was 4.2 per 1,000 inhabitants and about one-third reported some form of persisting symptoms at follow-up (Sterner et al. 2003). It has been esti-

mated that 14–42% of whiplash trauma progresses to a chronic WAD, and approximately 10% of the patients report constant severe pain (Barnsley et al. 1994).

Chronic musculoskeletal pain

The prevalence of self-reported chronic pain in the general population has been estimated to be no less than 47% (Elliott et al. 1999). The majority of subjects reporting chronic musculoskeletal pain, most commonly local (90%), tend to have it at more than one anatomical site, and those living

in socially underprivileged areas have more symptoms (Urwin et al. 1998; Andersson et al. 1993). The prevalence of chronic regional pain has been estimated to be 20–25%, and of chronic widespread pain about 10% (Gran 2003, Kohlmann 2003). Chronic widespread pain is more common in women (Andersson et al. 1993, Kohlmann 2003) and the co-morbidity with low-back pain is high (Huppe et al. 2004).

Neck pain

Definition of neck pain

The definition of neck pain usually includes pain and/or stiffness felt dorsally in the cervical region, somewhere between the occipital condyles and the C7 vertebral prominence. Neck pain, however, is often accompanied by occipital headache and pain in the shoulder, the upper thoracic region and the jaws. Clinically, it is well-known that even in subjects with no evidence of nerve root irritation or compression, neck pain may also be associated with pain referred to the anterior chest, arm, and dorsal spine regions (Rao 2004).

We used 6 months of continuous neck pain for the definition of chronic neck pain (IASP). It has also been defined as continuous neck pain lasting more than 12 weeks (SBU 2000). Chronic neck pain can also be defined as pain that persists even after the expected duration for healing has passed (Scofferman 2004).

Origin

Neck pain can emanate from many specific diseases, e.g. inflammation as in rheumatoid arthritis, infections, tumors, traumatic injuries to the cervical spine and cervical disk disease such as disk hernias—which may irritate the nerve root by mechanical and biochemical stimuli (Bogduk et al. 1988; Brisby et al. 2000). Nerve fibers and endings can be found in several anatomical locations in the periphery, even deep in the annulus fibrosus and nucleus pulposus (Freemont et al. 1997) all of which offer a possible mechanism for nociception.

Subaxial posterior neck pain is supposed to be the result of muscular or ligamentous factors related to posture, poor ergonomics, stress and chronic muscle fatigue (Fischgrund 2004). The

physiology of pain in the muscles involved is not well understood. However, patients with neck pain show greater activation of accessory neck muscles and may have a changed pattern of motor control compensating for reduced activation of painful muscles (Falla and Bilenkij 2004). Earlier studies have indicated that a change of motor control can be explained by a neurophysiological pain adaptation model and a “cognitive behavioral” fear avoidance model (Nederhand et al. 2000). There may be a reduction in the ability to relax cervical muscles after a physical load. However, there is no scientific support for the theory that increased muscle activity can be transformed into chronic pain.

Another source of pain is the facet joint, which is innervated by the posterior primary rami of the adjacent segmental and accessory nerves (Rao 2004). Provocative injections of contrast medium distending the joint capsule of the facet joints in pain-free volunteers produced a reproducible pattern of axial neck and shoulder pain (Dwyer et al. 1990). This pain could be blocked by anesthetic injections into the facet joint (Aprill C et al. 1990).

Even so, most neck pain can seldom be attributed to any specific origin and is often labeled as soft-tissue rheumatism or muscular/mechanical/postural neck pain, or other unspecific syndromes (Ferrari 2003). Unfortunately, radiographs and MRI rarely give sufficient information about the origin of pain in most patients, unless the patient has a specific pathology. Age-related degenerative MRI findings often have no clinical relevance, and these changes are frequent also in pain-free individuals (Boden et al. 1990; Matsumoto et al. 1998). Furthermore, it is difficult—if not impossible—to distinguish between ageing disks and pathologically degenerated discs causing symptoms. Radiographic changes of the cervical spine can only partially explain the neck and shoulder pain (Siivola et al. 2002).

Risk factors in chronic neck pain

The most important risk factor for prediction of neck and low-back pain is whether the individual has had a previous episode of pain in the neck or/and the back or concomitant pain elsewhere. Most

other potential risk factors have been questioned, and in practice, there has been no general agreement about them (SBU 2000; Croft et al. 2001).

History of neck injury

Cross-sectional and longitudinal studies have shown that a history of cervical spine injury is a risk factor in persistent neck pain (Croft et al. 2001). There is no consensus in the literature as to why individuals with a previous neck trauma report more pain and disability (Schröder et al. 1996; Bovim et al. 1994; Cote et al. 2000). Patients involved in high-energy road traffic accidents who sustained many other injuries have demonstrated a low incidence of neck symptoms from the soft tissues (Mali and Lovell 2004). If, however, cervical spine fractures heal with deformity/instability, this can lead to a state of chronic neck pain (Blauth et al. 1999, Fisher et al. 2002).

The influence of age and sex

Chronic neck pain has been found to be more common in woman, and to increase with age (Anderson et al. 1993; Webb et al. 2003). This sex pattern is seen in most types of body pain (Philips et al. 1977; Fordyce 1982). Age is a strong predictor of persistent neck pain (Hill 2004).

Psychosocial factors

Psychosocial factors play a major role in the development of acute pain into chronic pain, and are also relevant in the development of neck and low-back pain into chronic disorders (Leclerc et al. 1999; Schultz et al. 2004). The family seems to have a decisive influence on social learning, and on development of behavior regarding acute and chronic pain (Bradely et al. 1992; SBU 2000). There appears to be a relationship between low social class and low income level versus poor health (Folkhälsoinstitutet rapport 2005). Low educational level is associated with poor prognosis in chronic WAD (Sterner et al. 2003). In contrast, in another study of self-assessed musculoskeletal pain, marital status, geographic region, educational level and working status were found to be of no relevance for the individual being in a high-risk group regarding neck pain of musculoskeletal origin (Picavet and Schouten 2003).

Job factors

Work-related factors seem to increase musculoskeletal pain (Karasek and Theorell 1990; Bongers et al. 1993). In addition, it is associated with both acute and chronic neck pain—especially in women (Vingård and Nachemson 2000). Perceptions and beliefs about work and returning to work seem to be obstacles to recovery in patients with chronic musculo-skeletal pain and prolonged working disability (Marhold et al. 2002).

Compensation and insurance claims

Chronic neck pain has been associated with litigation, workers' compensation issues and financial gain (Rao 2004). Secondary gain plays a role in the development of chronic pain after neck trauma. Compensation status can contribute to poor physical functioning in patients with neck pain (Swartzman et al. 1996; Hee et al. 2002). Patients having unresolved financial disputes or litigation have been found to be half as likely to return to work as those whose claims are settled (Wright et al. 1999). Significant differences exist between chronic neck patients in and not in litigation. Litigators often have more subtle symptoms and fewer obvious symptoms, and also have different personality profiles (Duch et al. 1994). Rapid claim closure seems to give a better outcome after WAD, independent of the insurance system. However, in a cross-sectional study neck trauma patients reported more pain than patients without trauma, but not because of overriding litigation issues (Peterson et al. 2003). Elimination of an insurance system that compensates for symptoms such as pain and suffering was linked to reduced incidence and improved prognosis in whiplash patients (Cassidy et al. 2000).

Cultural factors

How specific symptoms are accepted as a disease is partly governed by cultural norms in society (Aronowitz 2001). Also, ability to work seems to be governed by the expectations and beliefs of the individual and society (Turk et al. 1987). From a historical perspective, several pain or disability syndromes have appeared and disappeared. For example, in 1828, Brown described the term spinal irritation and so the causal connection of the spine as a source of pain was founded—even though the pathology was never shown. In the nineteenth cen-

tury, the notion of “railway spine” was a popular concept. Train travellers were thought to sustain injury to the spine during low-speed accidents (minor injuries to the spine or cumulative trauma), with posttraumatic symptoms without apparent lesions. The diagnosis “railway spine” was associated with claims for compensation, but at the beginning of the twentieth century the diagnosis gradually disappeared as it came to be considered a functional neurosis (Siemrink-Hermans 1998, Waddell 1989).

The existence of specific somatic syndromes has even been suggested to be an artefact of medical specialization (Wessely 1999), and in such a context patients’ problems can be medicalized both by the patient and by the physician defined as somatic fixation (Biderman et al. 2003). Scientifically poorly-founded hypotheses largely rule our culture and thus also healthcare institutions, with sometimes negative effects for the individual and society (Nachemson 2000). The cultural differences may perhaps explain the varying prevalences of chronic pain disorders as medical entities in different countries (Honyman and Jacobs 1996; Richter et al. 2004). Functional somatic syndromes such as tension headache, chronic pelvic pain, fibromyalgia, chronic low-back pain, hypersensitivity to electricity and irritable bowel syndrome have much in common—and they seldom or never improve substantially from any specific medical treatment. The question has been raised as to whether part of the tremendous problem of somatic fixation and pain in society—resulting in sick leave and escalating costs—could partly be iatrogenic (Biderman et al. 2003).

Psychological factors

Psychopathology is one of the most important companions of chronic pain (Gatchel 1996) and thus it is more common in chronic pain patients than in the general population (Elliott et al. 2003). When treating chronic pain patients, it is therefore crucial to diagnose psychopathology like anxiety and depressive disorders. The same is valid for personality with tendency to somatize.

For example, depression is accompanied by pain in 15–100% of the cases (Elliott et al. 2003), and it is well-known that depression promotes pain and that pain promotes depression (Magni et al. 1994;

Fields 1991). Both intensity of pain and depression have been shown to be significant risk factors in the development of chronic pain (Turk 1997). In a recent study of chronic WAD patients, the most important psychiatric disorder both pre- and post-injury was depression (Kivioja et al. 2004). Patients with pain and depression are more often woman, and have an overall low response to treatment (Bair et al. 2003). Thus, depression must be treated; otherwise, the treatment of pain may fail (Elliott 2003).

The importance of predisposing personality characteristics/pre-morbid personality and a theory of how it influences pain-related behavior has been described in detail (Gatchel 1996). A specific MMPI profile, the so-called conversion V profile pattern when scales 1 and 3 are elevated relative to scale 2 (Butcher 1996) (Figure 2) seems common in patients with chronic pain, and is often associated with stress-related somatic complaints (Vendrig 2000). Tension and physical stress may also prolong the chronic pain state (Turk 1996) but this does not necessarily cause the pain directly—rather, it is the distress which exacerbates or complicates the pain, thereby hindering its natural resolution (Turk 1996). A conversion V pattern of response could also be regarded as a somatoform stress reaction, i.e. a functional disturbance. This kind of disorder may explain why individuals with disturbed premorbid personality respond differently to acute physical symptoms, and why these vulnerable individuals are less able to cope with post-accident stressors (Putnam and Millis 1994; Greiffenstein and Baker 2001; Gatchel 1996; Vendrig 2000). Concerning chronic whiplash syndrome, some authors consider that some patients may be predisposed to developing psychological problem after a whiplash injury (Radanov et al. 1999; Gargan et al. 1997).

Cognitive processes (coping and perception of illness), e.g. poor self-reported general health, whether the individual perceives a stimulus as harmful or not, and the character of pain are important in the individual perception of pain and are related to recovery in chronic pain patients (Weiser and Cederaschi 1992). Coping can be defined as the purposeful use of cognitive and behavioral techniques to manage demands that are perceived as stressful. The coping responses of an individual

are influenced to a great extent by psychological and physical factors (Romano et al. 2003). Cognitions and fear avoidance beliefs such as catastrophizing and passive coping are strongly related to pain and disability, and reduce the capacity to handle chronic pain (Linton 2000).

Whiplash-Associated Disorders (WAD)

Crowe coined the term “whiplash” in 1928 when he described symptoms related to a cervical spine injury caused by an acceleration/deceleration movement (Evans 1995). According to the Swedish whiplash commission a whiplash trauma is defined as the strain forced on the head and the cervical spine as a result of an acceleration-deceleration movement without any direct trauma against the head or neck. Most whiplash patients recover completely (Spitzer et al. 1995, Radanov et al. 1995) but 14–42 % of the cases develop chronic symptoms with varying degrees of disability, of whom 10% are severely disabled (Barnsley et al. 1994). During the past few decades, whiplash injuries have become more common—endemicity but not pandemics—since the prevalence varies considerably worldwide, indicating that factors other than biological ones may also play a role. Whiplash injuries are now one of the most common disabling disorders following traffic accidents in several western countries, as shown by insurance statistics (Spitzer 1995, Whiplash Commission 2005).

Definition and classification

The Quebec Task Force (QTF) on Whiplash-Associated Disorders (WAD) has adopted the following definition (Spitzer et al. 1998). “Whiplash is an acceleration-deceleration mechanism of energy transfer to the neck. It may result from rear- or side-impact motor vehicle collisions, but can also occur during diving or other accidents”. The impact can result in bone or soft-tissue injuries (whiplash injuries) which can in turn lead to a variety of clinical manifestations, e.g. WAD.

The QTF classifies WAD from 0 to 4, with increasing grade of severity. WAD includes grades 0–3, while grade 4 covers cervical fractures and dislocations. Pain, stiffness and impaired mobility

of the neck, radiating pain in the arms, headache and cognitive problems are common symptoms after a whiplash trauma (Sterner 2001). Recently, the Swedish Whiplash Commission suggested a WAD classification of grades 1–3. This excludes individuals without symptoms or signs (grade 0) and patients with fractures and dislocations (grade 4) (Whiplash Commission 2005).

Origin of injury and neck pain in WAD

The pathophysiological mechanisms of chronic WAD are unknown and puzzling. Chronic WAD patients may theoretically have injuries to several structures in the cervical spine (Guez et al. 2003). Standard radiographs, CT and MRI are seldom conclusive (Richter et al. 2004, Spitzer et al. 1995), but there is a discrepancy between clinical and experimental findings.

It is obvious that the degree of injury and dose-response pattern to an anatomical structure are dependent on the relative force of the kinetic energy transferred to the tissues at the accident (Ivancic et al. 2004, Sell P 2005).

Experimental studies have shown that the cranio-vertebral region as well as the mid- and lower cervical spine can be exposed to harmful translations (Penning 1992) and hyperflexion and extension by a whiplash trauma (Panjabi et al. 2004). Here follows some anatomical localizations where possible injuries to the cervical spine has been described (Figure 3):

- Cervical discs may be injured during a whiplash trauma (Davis 1991; Panjabi et al. 2004), and it has been argued to be more prevalent in individuals exposed to such an injury (Pettersson et al. 1997).
- The cervical facet joints have been proposed as source of chronic pain (Lord et al. 1996, Barnsley 1995). Post mortem studies have shown cervical facet joint compression and capsule injury after whiplash trauma, especially after high-energy trauma (Sigmund et al. 2001, Stemper et al. 2004, Hartwig et al. 2004, Pearson et al. 2004). Such lesions have not been verified in surviving patients, probably due to the fact that these injuries have been more severe than those commonly experienced during a car collision. Biomechanical studies of facet joint compression and excessive capsular ligament strain are not conclusive,

and it is unclear whether any injured part of the cervical facet joint can give chronic neck pain. (Kwan 2002).

- Laboratory studies indicate that injury of the anterior longitudinal ligament may lead to an instability (Panjabi et al. 2004), and the ligaments of the upper- and mid-cervical spine may also be injured with similar effects (Hartwig et al. 2004). However, MRI almost never shows any pathological changes after whiplash trauma (Ronnen et al. 1996).
- Transverse and alar ligament injuries have been held responsible for instability, thus generating chronic pain (Krakenes 2003). However, functional MRI has shown wide variation in segmental motion in the cranial cervical spine of healthy individuals also, making it difficult to verify instability (Pfirrmann et al. 2000, Volle and Montazem 2001, Wilmlink 2001). Furthermore, lesions in alar ligaments have not been seen after low-speed collisions (Hartwig et al. 2004) and their overall existence is therefore questioned (Kwan and Friel 2004).
- Chronic neck pain after whiplash injuries does not appear to result from muscle damage (Barnsley 1994; Whiplash Commission 2005). There is no strong evidence that whiplash trauma leads to injury to the nervous system, but there have been studies pointing out that a small proportion of individuals enduring high impact whiplash trauma may be affected in this way (Hildingsson et al. 1993; Guez et al. 2003).

Together with somatic symptoms, psychological reaction to a trauma depends on the type of trauma and also its duration—but also on the individuals' interpretation of the trauma. Personality and coping ability are important in this respect. In some cases, an acute whiplash injury may trigger an acute stress reaction, or later, a post-traumatic stress syndrome (Mayou and Bryant 2002; Gargan 2005).

WAD patients often complain of concentration problems and memory disturbances a long time after the trauma (Schnurr and MacDonald 1995, Provinciali et al. 1996). Temporarily impaired cognitive performance has been verified by neuropsychological testing in WAD patients (in terms of disturbances in functioning of divided attention and working memory (Kessel 2000; Bosma et al. 2002), but one comparative neuropsychological

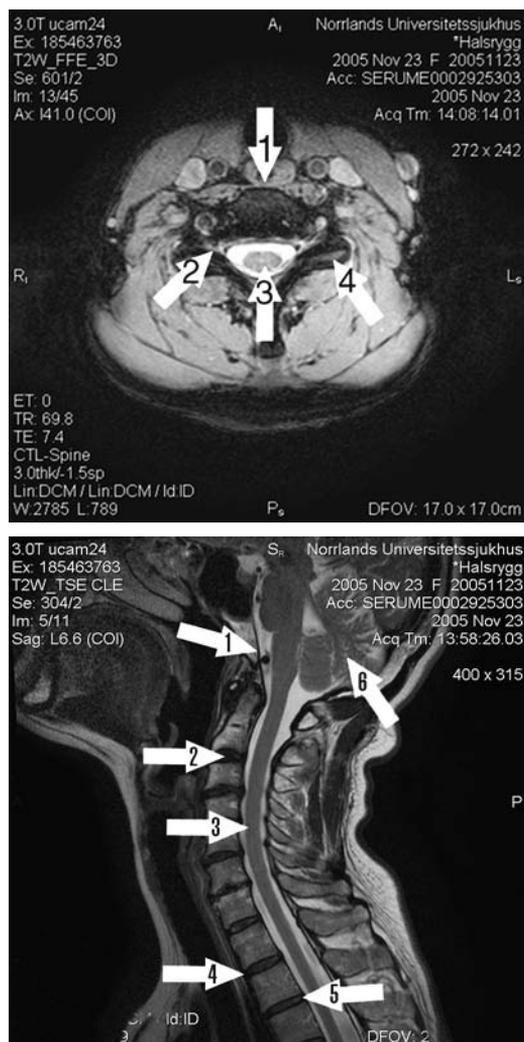


Figure 3. Anatomical localization of important structures in the cervical spine.

Upper panel: 1 = ligamentum longitudinale anterior, 2 = foramen/nerve root channel, 3 = medulla spinalis, 4 = facet joint.

Lower panel: 1 = superior longitudinal band of cruciform ligament; immediately below this is the alar ligament, 2 = cervical disc, 3 = medulla spinalis, 4 = ligamentum longitudinale anterior, 5 = ligamentum longitudinale posterior, 6 = cerebellum.

study could not differentiate between patients with chronic pain syndromes and WAD patients (Taylor 1996).

There is no convincing support for the hypothesis that long-standing cognitive disturbances and complaints after whiplash injury are due to organic

brain injury (Taylor et al. 1996, Otte et al. 1997, Radanov et al. 1999, Kessels et al. 2000, Bosma et al. 2002, Moismann et al. 2000). In other words, the cognitive complaints have not been clearly linked to any structural correlates of morphological or functional brain damage or even to measurable impaired cognitive performance. Instead, it has been claimed that the injury itself may trigger emotional and cognitive symptoms (Radanov 1999), which has been linked to personality (Vendrig 2000). Somatization, in combination with inadequate ability to cope, may play a role in the development, persistence, or aggravation of whiplash-related symptoms such as pain or cognitive dysfunction (Bosma et al. 2002).

Other symptoms

Chronic WAD patients may also suffer from a

plethora of other symptoms associated with the whiplash injury such as, e.g. temporo-mandibular joint problems (Magnusson 1999, Klobas et al. 2004), irritation of the brachial plexus (Ide et al. 2001), thoracic outlet syndrome, post-traumatic stress disorders (Berry 2000), and fibromyalgia (Magnusson 1999).

Lumbar spine injury

The lumbar spine soft-tissue seems to be less vulnerable than that of the cervical spine, but it might be injured by biphasic lumbar spinal motion induced by a whiplash trauma (Fast et al. 2002). There have been clinical studies which suggest that the seat belts may also give this type of lesion at the moment of trauma (Mullhall et al. 2003). However, such potential injuries have not been verified—either radiographically or clinically.

Aims of the study

- I: To assess the prevalence of non-traumatic and traumatic neck pain, and describe age, sex and demographic characteristics in a random sample from a geographically well-defined area in northern Sweden.
- II: To compare two groups with chronic neck pain, with and without a history of neck injury, using socio-demographic data, self-perceived health and workload.
- III: To assess the prevalence of chronic low-back pain in individuals with chronic neck pain of traumatic and non-traumatic origin.
- IV: To examine subjective and objective neuropsychological functioning and personality profiles in patients with chronic neck pain with and without previous whiplash trauma.
- V: To investigate and analyze cerebral blood-flow pattern with SPECT-scan in patients with chronic neck pain with and without a previous whiplash trauma.

Patients, methods and findings

Study I

The participants were sampled from the MONICA protocol. The northern Sweden MONICA study covers a population of 510,000 and a target population of 310,000 between 25 and 74 years old (Figure 4). We selected the population to be studied by stratified randomization regarding age and sex (Figure 5).

The sample included 8,356 subjects and 6,000 (72%) answered the questionnaire containing sociodemographic data and cardiovascular risk factors. The main objective of this project is to assess risk factors for cardiovascular diseases. The data was filled in by the participants during the visit for the health examination (MONICA 1990/2005). The

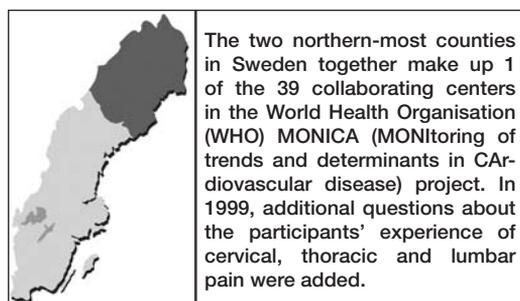


Figure 4. Map of Sweden showing the region of origin of the individuals under study (grey).

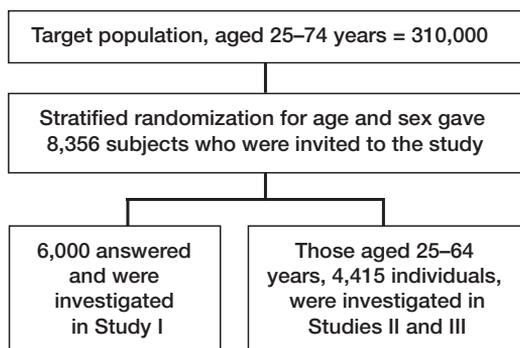


Figure 5. The MONICA project, a large cardiovascular health study, which was used to sample the patients in our studies.

supplementary questions to cervical and lumbar spine problems are shown in Table 3.

Chronic neck pain was defined as continuous neck complaints of more than 6 months duration. Patients seeking medical attention after a cervical spine injury with persisting post-traumatic complaints were defined as having injury-related chronic neck pain. The alternatives in the questionnaire were whiplash, other neck or head injury, or no injury. Each person could report more than one alternative.

43% of our population reported neck pain, 48% of all women and 38% of all men. Neck pain was less frequent in older women than in those of working age. This tendency was not seen in men. 43% of the women and 33% of the men reported neck

Table 3. Questions on cervical and lumbar spine complaints

- 1 *Have you visited a doctor because of a neck or head injury?*
 - Yes, due to whiplash injury
 - Yes, due to other neck injury
 - Yes, due to head injury
 - No
- 2 *If you have neck pain, for how long have you experienced the symptoms?*
 - In the last week
 - In the past six months
 - For more than six months
- 3 *If you have neck pain, how often do you have the symptoms?*
 - Continuously
 - A few times every month
 - A few times a year
- 4 *If you have low-back pain and/or ache, stiffness, for how long have you had symptoms?*
 - In the past week
 - For the past six months
 - For more than six months
- 5 *If you have low-back pain and/or ache, stiffness how often do you have symptoms?*
 - Continuously
 - A few times every month
 - A few times a year

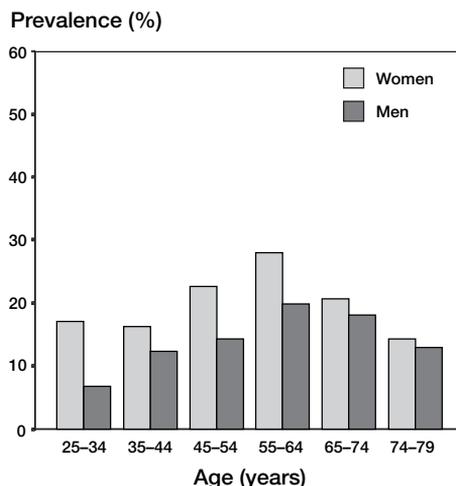


Figure 6. The prevalence of chronic neck pain.

pain with a duration of more than 6 months. About half of them had chronic symptoms, i.e. daily symptoms lasting more than 6 months. 18% of the population (19% of women and 16% of men) had chronic neck pain (Figure 6). Most (13%) were of non-traumatic origin, but about one-third (5%) of the total population with chronic neck pain had a history of trauma to the cervical spine. The total prevalence of whiplash injuries was 3.0%, other neck injuries 4.5%, and head and combined injuries 5.5%. Taking chronic neck pain patients with a history of cervical spine trauma separately, 89 of 181 whiplash cases (1.5% of the population) and 133 of 267 cases with other neck injuries (2.2% of the population) had chronic complaints. Women were overrepresented in the trauma group with chronic symptoms. This was particularly true in cases with a history of head injury, comprising 64% of women. They also accounted for 55% of the group with whiplash and other neck injuries. Prevalence of chronic neck pain was higher in small communities (of less than 15,000 inhabitants).

Study II

Paper II (n =4415) is also based on the MONICA study, with analysis of all participants between 25 and 64 years of age. All subjects with chronic neck pain were divided in two groups: those with or without a history of neck trauma. The following

Table 4. Multiple logistic regression modeling trauma

Covariate	p-value	OD	95% CI
Trauma/no trauma			
Men compared to women	0.02	1.5	1.1–2.0
Age	< 0.001	1.0	0.9–1.0
Sick leave	< 0.001	2.0	1.4–2.9
Self-perceived health, previous year			
Good/very good	0.02		
OK	0.03	1.5	1.0–2.1
Bad/very bad	0.01	1.8	1.1–2.8

variables were assessed: age, sex, married/cohabitant, education, body mass index (BMI), whether a regular smoker, community size (number of inhabitants), whether on sick-leave due to neck pain, heavy physical work, demanding physical leisure activities, and self-perceived health. An analysis of the psychosocial work situation was carried out with help of the Karasek questionnaire (Karasek and Theorell 1990). Of the 4,415 participants 14 participants did not answer the questions concerning trauma. 249 participants reported a neck or head trauma they were distributed as follows: whiplash n = 81, other neck trauma n = 105 and head or combination trauma n = 63. 565 individuals had chronic neck pain and no trauma. 167 were students, 291 were unemployed and 485 were retired and they did not fill in the Karasek questionnaire.

Evaluation of sociodemographic data, self-perceived health and working conditions showed that patients with a history of trauma and chronic neck pain were more often on sick-leave and perceiving their health to be worse than those with chronic neck pain without neck injury. Finally the group consisted relatively more of young men. We found no differences concerning BMI, marital status, educational level, smoking habits, psychosocial work situation, or different types of physical activity (Table 4). For more details, see paper II).

Study III

Paper III is based on the MONICA questionnaire and included 4,415 individuals, aged 25–64 years. Besides individuals with chronic neck pain, we also included those with chronic low-back pain, defined as continuous pain of more than 6 months duration. 828 individuals (25–64 years of age) reported chronic neck pain, and of those, 817 had completed data on items regarding neck trauma and low-back pain. 251 participants had a history of neck or head trauma of those 81 had sustained a whiplash injury and 105 had other neck trauma. Those with a head or combination of head and neck trauma were excluded. The supplementary questions are given in Table 3. Information from non-responders was collected from telephone interviews or additional questionnaires. Basic information on 50% of the non-participants was obtained.

The prevalence of chronic low-back pain was 15.7% (95% CI: 14.4–16.6) in the population under study 17.2% (15.7–18.8) of women and 13.6% (12.2–15.1) of men. The breakdown in terms of sex and age is presented in paper III.

The total number of patients with chronic neck pain was 752. 186 of these patients had a history of neck injury and 81 of them had sustained a whiplash injury. The prevalence of chronic low-back pain in different subgroups is presented in Table 5. Crude odds ratio for prevalence of chronic low-back pain in the whiplash group compared to the non-traumatic group was 0.90 (95% CI: 0.57–1.44). The prevalence of chronic low-back pain in individuals with chronic neck pain, irrespective of origin, varied only slightly between different age groups (see table, paper III). Factors such as sex, age, body mass index (BMI), marital status, and smoking habits were not statistically significant when tested as predictors of the prevalence of chronic low-back pain, so we did not have to control for these factors. The only factor that seemed to be a possible confounder was the level of education (see table, paper III). After adjusting for education in a multiple model there were no significant changes in risk for low-back pain. Looking at the population without chronic neck pain, the prevalence of chronic low-back pain was at the same level in those with and without a history of neck trauma. The prevalence was 6.7% in those without neck trauma and

Table 5. The prevalence (%) of chronic low-back pain in different subgroups

Subgroup	N	n	%	95%CI
The study population	4415	683	15.7	14.4–16.6
Individuals with chronic neck pain and no history of neck trauma	566	301	53.2	49.1–57.3
Individuals with chronic neck pain and a history of neck trauma	186	90	48.4	41.2–55.6
Whiplash trauma	81	41	50.6	40.0–61.5
Other neck trauma	105	49	46.7	37.4–56.2

9.6% in the whiplash group, with overlapping confidence intervals (see table, paper III).

The drop-out analysis showed that a smaller proportion of the non-responders were married or cohabitants. They were also more often regular smokers and had a somewhat lower BMI than the participants. In addition, fewer of them had been informed about high blood pressure. There were no substantial differences in level of education. More information about drop-out analysis and quality assessments in the MONICA project can be found in Eriksson et al. (2003).

Study IV

We studied 42 patients referred to Umeå University Hospital (Sweden) between 1997 and 2001, because of chronic neck pain. All patients had disabling chronic neck pain, full or half-time sick-leave, or had changed job because of their neck pain. They had required medical assessment and treatment because of disabling neck pain lasting more than 3 years. 21 subjects (7 men), with a mean age of 42 (range 25–66) years had a history of whiplash injury in a car accident. All had persistent symptoms, were investigated on average 6 years after the trauma, and had received the diagnosis chronic WAD. They were matched with a group of patients, 21 subjects (7 men), with a mean age of 45 (range 28–66) years with chronic neck pain without previous neck trauma (Figure 7 and 8).

The neuropsychological examination was performed by a neuropsychologist. The test battery was designed for detecting and diagnosing trau-

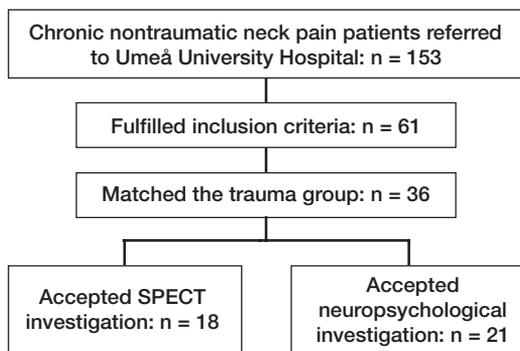


Figure 7. Sampling of controls for studies IV and V.

matic brain and brainstem injuries focusing on memory, executive functioning, concentration and selective attention abilities, including also objective indicators of dissimulation.

Personality profile was tested with the Minnesota Multiphasic Personality Inventory-2 (MMPI-2), a self-report questionnaire including 10 clinical scales: hypochondriasis, depression, hysteria, psychopathic deviation, masculinity/femininity, paranoia, psychasthenia, schizophrenia, mania and social introversion (Hathaway and McKinley 2000). All scores are reported as T values with a mean of $T = 50$ and with a standard deviation of 10. The Visual Analog Pain Scale (VAS 1–10) was used for pain assessment.

An abbreviated version of the Giessener Beschwerdebogen (GBB-24) (Braheler et al. 2000), a self-report inventory assessing physical symptoms and distress, was also used. Characteristics such as sex, marital status, level of education, profession, time on sick-leave during the previous 6 months, and the degree and duration of pain, were registered.

Subjective and objective neuropsychological functioning

Basic data concerning the patients in the whiplash group are presented in Table 6. They rated themselves as more forgetful and had impaired ability to concentrate compared to those in the non-traumatic group (see paper IV). 90% of the patients in the whiplash group reported forgetfulness. The whiplash group also had higher frequency of headache and radicular pain. In contrast, we could not find any significant differences between the whiplash and the non-trauma group using our battery

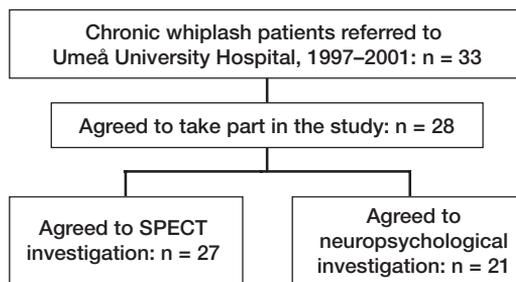


Figure 8. Sampling of chronic whiplash patients.

of neuropsychological tests, and there was no evidence of malingering according to the Rey test. Both groups had performance levels similar to the reference group (see paper IV).

Personality traits

Both groups had elevated scores in the MMPI-2 for the scales hypochondria, depression and hysteria (see paper IV). The whiplash group also had elevated scores on three other scales: paranoia, psychasthenia and schizophrenia (see paper IV). A comparison of the whiplash and non-traumatic groups revealed higher scores on several scales for the whiplash group (see paper IV). There were no significant differences between the two groups in two of the dissimulation scales, in frequency ($p = 0.123$) and F-K ($p = 0.080$). In the Lees-Haley Fake Bad scale, however, the whiplash group scored significantly higher than the control group ($p < 0.001$). The correlation between the F scale and the Lees-Haley Fake Bad scale was low and not statistically significant ($\rho = 0.21$, $p = 0.077$) as was the correlation with the F-K ($\rho = 0.19$, $p = 0.100$).

Both the whiplash and the non-traumatic group scored significantly higher on the L scale (see paper IV), which also contradicts dissimulation.

Evaluation of pain and physical complaints from GBB-24 is presented in paper IV. Significant differences were noted on the scales measuring overall distress and exhaustion. The comparison between the MMPI-2 and the GBB-24 scores for the whiplash group and for the non-traumatic group can be found in paper IV. The correlations were stronger and more consistent for the whiplash group. In the whiplash group, strong correlations were observed

Table 6. Basic data with pain ratings and duration of pain in the whiplash and the non-traumatic groups. The values are given as mean \pm SD. The sick-leave number is expressed as the %age of the group on sick leave. No statistical differences were found

	Whiplash group (n = 21)	Non-traumatic group (n = 21)
Sex: male/female	7/14	7/14
Age (range), year	41 (26–66)	44 (28–66)
Education (range) [SD], year	11 (9–17) [1.8]	10 (9–15) [1.5]
Pain duration [SD], year	6.5 [4.7]	7.6 [3.0]
VAS [SD] 1–10	5.3 [1.4]	5.5 [1.2]
Sick leave [SD] (%)	64 [45]	65 [42]

between scale 6-exhaustion, scale 6-overall distress, and scale 3-gastric complaints.

Study V

Paper V included 27 chronic WAD patients (9 men) with a mean age of 41 (range 26–65) years and an average duration of pain of 7 (3–20) years (Figures 7 and 8). The inclusion criteria were disabling chronic neck pain leading to full or half-time sick leave, or job change. They underwent a clinical investigation to exclude infection, rheumatoid arthritis, tumor or metastases. In addition, patients with a history of head injury, loss of consciousness, cervical spine fractures, serious psychiatric disorders, and other severe central nervous system disorders or drug abuse, were excluded. 18 subjects (5 men) age- and sex-matched patients with non-traumatic chronic neck pain, with a mean age of 44 (29–62) years and an average pain duration of 9 (3–15) years were included. They were selected from a hospital medical chart database. 61 patients fulfilled these criteria, 26 were age- and sex-matched, and 18 agreed to participate. They all had diagnosis based on symptoms most of them secondary to degenerative disorders (Figures 7 and 8). All 45 patients were referred to Umeå University Hospital, 1997–2001, and gave written informed consent to participate in the study.

15 healthy subjects (8 men) were included from a large prospective research project in the community of Umeå (Betula; Nilsson et al. 1997) as

healthy controls. The inclusion criteria were good subjective and objective health. The mean age of the control group was 55 (range 50–61) years. The Radiation Committee of Umeå University approved this group to be recruited among healthy individuals older than 50 years. Pain intensity was scored with a visual analog scale (VAS 1–10). Additional information was obtained through interviews. Mann-Whitney U test was used in the statistical evaluation.

The rCBF-SPECT studies were performed at the Department of Nuclear Medicine, Umeå University Hospital. A three-headed gamma camera was used with a technetium radiotracer.

Tracer uptake reflects brain function, which is related to the blood flow (Warwick 2004). To determine the anatomical localization of the SPM data, a conversion of MNI coordinates to the Talairach brain atlas was done using a nonlinear function described at the CBU Imaging website (<http://www.mrc-cbu.cam.ac.uk/Imaging/mnispace.html>). For further details of methods, see paper V.

Basic data concerning the chronic neck pain patients is given in Table 7. The WAD patients complained of more headache, forgetfulness and concentration problems than the non-traumatic pain group. All patients had complaints from the head, neck and back region. No significant differences in rCBF were detected between whiplash patients and healthy controls. At an uncorrected voxel level of $p = 0.001$, two small regions with relatively lower rCBF, one in the right temporal region and one in the left parieto-temporal region were seen.

Non-traumatic pain patients had relatively lower rCBF in the right hemisphere and cerebellum compared to healthy controls. The major cluster in the right hemisphere was located in the temporal and the limbic lobes, including a quarter of the caudate tail and approximately one-fifth of the hippocampus and a part of the parahippocampal gyrus. The minor cluster was located in the center of the cerebellum, with two-thirds in the left side involving mainly the anterior lobe. There was also a region with a lower rCBF in the right temporo-occipital cortex (uncorrected, $p = 0.001$). These patients also displayed relatively higher rCBF in the frontal lobe including the left insula region.

Non-traumatic pain patients had relatively lower rCBF in the right hemisphere, extending into the

right side of the brainstem, i.e. pons, compared to whiplash patients. The cluster was mainly located in the right temporal lobe, involving parts of hippocampus, the parahippocampal gyrus, and the limbic lobe. In addition, they had relatively higher rCBF in the parietal lobe, involving one-fifth of the precuneus. There was also a non-significant difference in the anterior part of the left insula (uncorrected, $p = 0.001$).

Cerebral regions with differences in rCBF between the non-traumatic, whiplash and healthy groups showing size, Talairach coordinate, anatomical location of significant ($p < 0.05$, corrected) clusters and non-significant peaks (uncorrected, $p \leq 0.001$, $k = 10$) (see paper V).

In summary, non-traumatic patients with chronic neck pain had blood flow alterations similar to those earlier described in patients with chronic neck pain. In contrast, the chronic WAD group had a pattern similar to healthy controls.

Statistics

Study I: We used logistic regression to test for differences in neck pain between different population groups. When appropriate the test and odds ratio estimates were adjusted for sex and age. Prevalence are presented together with 95% confidence intervals, calculated by normal approximations.

Study II: The chronic neck pain group with a history of neck trauma was compared to the chronic group having no trauma, using multiple logistic regression, modeling the probability of trauma. The variables were included as co-variables, and a stepwise forward likelihood ratio selection procedure was used to identify statistically significant co-variables. Odds ratios and corresponding 95% confidence intervals (CI) were calculated by univariate logistic regression.

Study III: Confidence intervals for prevalence rates and proportions were calculated by applying normal approximation to the binomial distribution. Univariate logistic regression was used to analyse the association between type of neck trauma as predictor and chronic low back pain as outcome where only individuals with chronic neck pain were included in the analysis. Some possible confounders as sex, age education, BMI and smok-

ing habits were tested one at a time as predictors for the chronic low back in a logistic regression model. Multiple logistic regression was used to further explore the association, adjusting for factors that turned out to be statistically significant in the univariate models. Odds ratios with corresponding 95% confidence intervals (CI) were calculated by logistic regression. The statistical package SPSS, version 11.5 was used for all calculations.

Study IV: Variables were summarized using standard descriptive statistics (mean, standard deviation and frequency). The Mann-Whitney nonparametric U-test was used to test if there was any differences between the whiplash and non-traumatic group concerning basic data and pain variables (Table 1). MMPI-2 data were compared with a normative sample (Hathaway et al. 2000). The Mann-Whitney test was used for analyses of the GBB-24 results and Spearman's rank correlation for the relationship between MMPI-2 and GBB scores. Concerning the personality tests all comparisons were planned. Several of the analyses were made between correlated variables. Thus, no correction for multiple comparisons, eg Tukey HSD test and Holmes correction was made. The level of neuropsychological test performance of each of the two groups was compared according to the test manual. Correction for multiple comparisons were made using Holmes Bonferroni method. Differences were statistically evaluated by testing whether Z/T-transformed observed test scores fell one or more standard deviation below the normative means. Chi-square test to test if the proportion of subjective complaints was equal in the two groups. The significance level was set to 5% (two-tailed). The statistical package SPSS, version 11.5 was used for all calculations.

Study V: Basic data from each group in the study were compared by Mann-Whitney U test. Differences in rCBF between the groups were estimated by Statistical parametric mapping 99 (SPM 99 Welcome Department of Cognitive Neurology). A SPM-cluster was considered significant at a p-value below 0.05 corrected for multiple non-independent comparisons. Peaks consisting of more than 10 voxels ($k=10$) with an uncorrected p-value of 0.001 is reported and related to previous findings. For further information see article V.

General discussion

Overall prevalence of chronic neck pain was 19%, and overall prevalence of chronic low-back pain was 16% in the present studies. Despite the fact that there were different study designs, similar prevalence figures have been reported in Scandinavia earlier (Table 1 and 2)—indicating that these chronic entities have not changed much during the past decade, even though the Swedish sick-listing certainly has. Moreover, the high unemployment rate and the sparse population in northern Sweden does not seem to have influenced the overall prevalence numbers. We defined chronicity as daily symptoms of more than 6 months duration, a definition that is commonly used (IASP 1994). We have, however, no information about the degree of pain, impairment or disability and we may therefore perhaps have overestimated the problems—since most of the individuals probably have pain of low and moderate intensity, and thus not disabling symptoms.

It is important to note that our findings in the prevalence studies were based exclusively on the patient's own report of neck pain and origin of neck pain. On the other hand, this is also the case in clinical practice and in most prevalence studies (Table 1). Nevertheless, when exploring the type of trauma the subjects had experienced, there may be a discrepancy between the patient's interpretation and our interpretation of the word "injury". Thus, it is possible that some patients relate unspecific neck pain to a previous minor trauma, work-related conditions, or other events, thereby increasing the trauma concept. However, this appears not to be the case in whiplash injuries which are well-known to the Swedish population. Unfortunately, our questionnaire did not include anatomic sites other than the neck and lumbar spine, and it is thus likely that a proportion of these individuals also had musculoskeletal pain in other parts of the body. In a recent review, the prevalence of chronic widespread musculoskeletal pain was estimated to be 11% (Clauw et al. 2003). It seems that neck and low-back pain often coexists (Cote et al. 2000) and may be the expression of similar problems or conditions, and

may be part of a more general chronic pain syndrome (Cassidy 2000, Croft 2001, 2003). The pain being referred to in the neck and/or lumbar spine may in some cases be the sum of all the patient's pain and suffering, although partly coming from other sites also. The patient's own description with pain-drawing would probably have reduced the risk of this kind of misinterpretation, but was not used in our study; moreover, the resolution and specificity of pain drawings do not seem to be high (Brismar et al. 1996). A standard questionnaire discriminating pain intensity as well as grade of disability would have been preferable, but we were only allowed to add a limited number of questions, not questionnaires, to the MONICA survey protocol.

Recent investigations have indicated that for some reason neck pain tends to be more persistent than pain from other organs (Cote 2004). "Whiplash" is feared by many, and being emotionally loaded, it is often associated with an expectation of persistent or disabling neck pain while other types of trauma do not have this reputation.

Most whiplash injuries heal spontaneously and only a small minority of the victims develop disabling symptoms, but these account for a large proportion of the overall impairment and disability figures from traffic accidents (Barnsley et al. 1994), measured by insurance costs. In fact, WAD is one of the most costly diagnoses for traffic insurance in Sweden. The annual cost for whiplash injuries in Sweden related to an incidence-based calculation was estimated to be over SEK 4 billion, the main part of the cost being due to the fall in production because of the individual's inability to work (Swedish Whiplash Commission 2005).

In this study the number of WAD cases might be overestimated since a proportion of those reporting chronic neck pain may be not correlated to the whiplash trauma. Further, it has been claimed that after a whiplash trauma, the existence of a symptom-free period is, if not typical, at least not uncommon—but this seems to stem from clinical anecdotes more than from scientific studies. This

fact may also increase the number of WAD cases in our series, since a proportion of those with late onset of symptoms would probably have developed neck problems without any trauma due to the high prevalence of spontaneous neck problems in the population.

As previously mentioned, in WAD there does not appear to be a dose-response relationship between the kinetic energy transferred at injury and the resulting impairment and disability. This is not often found in other injuries today, but it is not difficult to find historical parallels. I have previously discussed conditions such as railway spine, and we can add the Australian steel pen syndromes (Göthe et al. 1995) which are now extinct entities, and post-commotional syndrome, which is exceedingly rare. There are several common denominators in these disorders, eg the conditions are often disabling, the pathogenetic mechanisms are still unknown and they are notoriously difficult to treat (Wessely et al. 1999).

In addition, in our series, all types of self-reported neck injuries—especially those combined with head injuries—were more common in females. It is not likely that women are more prone to injury per se; rather the contrary: men are more involved in accident and trauma, probably because of greater exposure and behavioral factors (Gregersen and Berg 1994). Women tend to have smaller, weaker muscle masses and so the injuries get more severe consequences (Peterson et al. 2003). Another explanation for these figures may be that women in general seem to be more disposed to chronic pain disorders (Andersen 1993), which might then be triggered by a whiplash or other trauma. The discrepancies between injuries and their consequences indicate that secondary mechanisms may be involved.

There is no consensus why the cervical spine should be vulnerable to trauma than other parts of the body. It has been speculated that the cervical spine with its sophisticated musculoligamentous system has a special function in that it holds and determines the position of the relatively heavy head (Lajoie et al. 1993, White and Panjabi 2000). Further, its neuromuscular system is continuously coordinating with the balance and vision supporting the upright individual with important information. This can result in an innate vulnerability of

the cervical spine to trauma, eg whiplash trauma have been proposed to lead to disturbance of cervicocephalic kinaesthesia (Heikkilä et al. 1996). In our study the neck-trauma group with chronic neck pain perceived their health as worse and they were more often on sick leave than the non-trauma group, which is in accordance with other studies (Cote et al. 2000, Peterson et al. 2003). The degree of energy during the trauma and the resulting injury may of course influence the outcome, but it is difficult in many cases to explain disabling chronic symptoms after a moderate trauma. There may be an early stigmatization of the trauma, whiplash patients in Sweden are encouraged to seek medical attention immediately to have the injury confirmed, irrespective of the patients' symptoms (Sterner 2001). In psychologically fragile individuals, eg anxiety disorders and somatizing personality, the acute stress reaction may be unfavorable. At this stage the patients' symptoms may be due to or/and reinforced by her imaginations, which on her part can be influenced by descriptions in media, impressions from patients with similar symptoms, patient associations, iatrogenic factors and possibility for economic compensation. Though chronic neck pain was more prevalent in women, the post-traumatic chronic neck pain was relatively more common in men but still it was more common in women as found in other studies. Trauma types in men other than whiplash may explain this discrepancy, but we have no information as to why these injuries are disabling.

Chronic low-back pain is common in chronic WAD patients (Hildingsson et al. 1990). It has therefore been proposed that seat belts may injure the lumbar spine, a notion that perhaps has some support from one earlier study (Mulhall 2003). However, we found no difference in the frequency of chronic low-back pain in patients with non-traumatic chronic neck pain and WAD patients. Perhaps it is more likely that chronic low-back pain, especially when co-existing with chronic neck pain, is part of a chronic widespread musculoskeletal pain syndrome (Croft 1996, Papageorgiou et al. 1996, Bergman et al. 2001) or a functional somatic syndrome (Wessely et al. 1999). Not less than about half of our population reported some kind of lumbar pain during the last year. Thus, every second individual seeking medical attention

due to neck trauma had or had had a recent episode of lumbar pain which they may or may not have associated with the trauma. Patient recall is often uncertain, and thus the initial history of sickness is important when evaluating these cases. In addition, post-traumatic stress reactions and somatization may also trigger low-back symptoms (Pincus et al. 2002).

Independently of whether the chronic neck pain was of whiplash- or non-traumatic origin, the neuropsychological functioning did not differ from that of the healthy controls. A few neuropsychological investigations of chronic WAD patients have shown a transient pattern of cognitive dysfunction (Kessel et al. 2000, Bosma et al. 2002). Others are in line with our study (Taylor et al. 1996). We have no reason to believe that our neuropsychological test battery did not reveal obvious cognitive disturbances, but of course we did not use all available tests, as divided attention evaluation, which has been reported to be temporary pathological in some studies (Kessel 2000). In contrast to most other neuropsychological studies, we used a control group of patients with chronic non-traumatic neck pain to explore whether the history of trauma or neck pain itself has any influence on cognitive functions. It is important to note that none of our patients had test results indicating malingering. The Ray 15-item test has been questioned as an effective tool, but the result of the dissimulation scales of the MMPI-2 (Lees-Halet Fake Bad scale, F scale and the F-K index) (Butcher 2003) support this conclusion. Most patients were severely disabled and the consequences of WAD had often had disastrous effects on their personal and professional lives. The patients' histories were often characterized by their frustration at being mistrusted.

Since symptoms in chronic whiplash patients may be the expression of a functional somatic syndrome (Wessely et al. 1999, Gargan 2005), it is important to assess parameters associated with this. Pre-morbid personality may influence the reaction to acute physical symptoms, and some individuals find themselves less able to cope with post-accident stressors (Kay et al. 1992, Putnam et al. 1994, Greiffenstein 2001). Chronic pain patients with special characteristics, e.g. personality disorders, are significantly more common in this group than in the general population (Weisberg 2000).

The Minnesota Multiphasic Personality Inventory-2 (MMPI-2) appears to measure important characteristics associated with chronic pain, such as tendency for somatic symptoms and inadequate coping (Butcher and Williams 1992, Vendrig et al. 1998, Bosma et al. 2002). It has recently been proposed that personality and somatic complaints influence quality of life and psychological functioning to a considerable extent, but Versteegen et al. concluded that there are no differences in personality between those with and without complaints (Versteegen et al. 2003). Nevertheless, we found an association between personality and somatic complaints, especially in chronic WAD. This finding was further strengthened by the correlation between the psychosomatic variables (GBB-24) and the personality profile (MMPI-2 scales).

Previous neck trauma is an important factor in the development of chronic neck pain, and it is reasonable to believe that post-traumatic neck pain in some way differs from pain of other origin. Thus, we found it relevant to compare the cerebral processing of pain in non-traumatic chronic neck pain patients and chronic WAD patients. Pain is by definition inherently subjective, and we are aware of the sampling problems of the patients, which are difficult if not impossible to validate, since there are no or few objective physical signs or pathognomonic diagnostic tests for either one.

Another weakness in studies IV and V is that the sampling of the chronic whiplash patients was not consecutive and selection may have influenced the results. However, we have no reasons to believe that they did not represent a cohort of chronic WAD/neck pain patients. It is considered that chronic neck pain has a heterogeneous etiology and all of our patients had been examined with MRI. All chronic neck pain patients had also been examined clinically by several specialists, and there was no obvious explanation for their pain; therefore, they were given symptom-diagnosis. A few patients in both groups had radicular symptoms without neurological deficiencies. With these reservations in mind, we matched those with chronic neck pain of non-traumatic origin and chronic whiplash cases with respect to several important parameters in order to have only trauma history as the main difference. The chronic WAD patients were not WAD-graded, simply because the injury happened

before the classification was introduced, and furthermore it is important to note that recent research has questioned its prognostic value (Kivioja et al. 2004)

Patients with non-traumatic chronic neck pain showed an altered cerebral blood flow compared to healthy individuals. In contrast, the WAD group did not differ from the controls. The results of the blood flow measurements is of course dependent on which level of significance used in terms of voxels per volume. The rCBF pattern in patients with non-traumatic chronic neck pain with reductions in parts of the parahippocampal gyrus close to the hippocampus may reflect a suppression of brain systems subserving episodic memory and emotional response to a known aversive stimulus (Petrovic et al. 1999, Hsieh et al. 1999). The affected temporal regions participate normally in the cognitive processing of pain and memory, and the disturbances may either reflect a dysfunction in cognitive processing of pain, or be a coping strategy for handling a well-known painful situation in the non-traumatic pain group (Cloninger 1986, Liotti et al. 2000, Sugiura et al. 2000, Reiman et al. 1984). The decrease of rCBF in parts of cerebellum in the non-traumatic neck pain group is supported by studies showing motor-related areas, i.e. the striatum, cerebellum and supplementary motor areas, being associated with pain (Peyron et al. 2000, Derbyshire et al. 2002). The pronounced rCBF reductions in the medial temporal lobe support the notion of continuous pain processing at rest in these patients. We have no explanation as to why our chronic WAD patients do not express pain cerebrally. The cerebral blood flow is influenced by the emotional state of the patient, and although the chronic WAD patients were somewhat more depressed than the non-traumatic patients, it was not visualized on the SPECT scan. The blood-flow pattern in chronic WAD perhaps supports our proposals that psychological factors such as somatization and inadequate coping—may be important contributors to the pain behavior in chronic whiplash cases.

The lack of cerebral expression of pain in chronic WAD in our study, gives further support to the controversy of the interpretation of pain in these patients.

Conclusion

Chronic neck pain is common in the general population and a frequent cause of disability. Different types of trauma—not only whiplash—appear to be associated with unspecific chronic neck pain. Chronic neck pain secondary to trauma (including whiplash trauma) differs from spontaneous chronic neck pain in several respects, such as self-perceived health, working ability, personality profile and cerebral expression of pain. The chronic WAD patients especially seem to be more vulnerable and have impaired illness behavior.

The similarities are the closely related if not indistinguishable clinical manifestations, the high frequency of chronic low-back pain, the psychosomatic tendencies and the higher frequency in females. The reason for the gender or sex differences is unclear, as is the female propensity for chronic pain after trauma.

The pain of the WAD patients was not visualized by rCBF-SPECT unlike those with non-traumatic chronic neck pain. The cerebral expression of different kinds of pain requires further evaluation, and studies on the central pain mechanisms will probably increase our knowledge of the origin and persistence of chronic pain disorders. The importance of the social insurance system and also iatrogenic factors in chronic WAD would be interesting to evaluate. This is a prerequisite for better treatment of these unfortunate patients.

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