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THE VALIDITY OF POSTCONCUSSION SYNDROME IN ADULTS

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Contents

Abbreviations

BSRF – brain stem reticular formation

CBF– cerebral blood flow

CPA – patient with concussion

CT – cerebral computed tomography

DAI – diffuse axonal injury

DSM – Diagnostic and Statistical Manual of Mental Disorders

ECT – electroconvulsive treatment

EEG –electroencephalography

fMRI – functional magnetic resonance imaging

GCS – Glasgow Coma Scale

IHS – International Headache Society

KUH –Kaunas University Hospital

LOC – loss of conciousness

MRI – magnetic resonance imaging

MTBI – mild traumatic brain injury

PCH – possible cervicogenic headache

PCS – Postconcussion syndrome

PET – positron emission tomography

rCBF – regional cerebral blood flow

RCH – Red Cross Hospital

RPQ – Rivermead Postconcussion Symptoms Questionnaire

SD – standard deviation

SPECT – single - photon emission computed tomography

VAS – visual analogue scale

vs - versus

WM – working memory

I. Introduction

After concussion a significant proportion of subjects reports persisting symptoms that include headache, cognitive dysfunction, dizziness, fatigue, and irritability. This cluster of rather non-specific symptoms has been termed as the postconcussion syndrome (PCS), a condition that has been debated since the 19th century. As an example, in 1882, Erichsen suggested that patients with posttraumatic physical symptoms who had no observable findings nevertheless might have microscopic alterations in nervous system structure. In response, Page (1885) argued that the patients suffered from purely psychic disorders.

Also in the second part of the 20th century the condition continued to be controversial concerning its definition, causes, incidence and contributing factors (Carrillo et al., 1951; Denker and Perry, 1954; Chavannaz,1961; Bonnal,1963; Zwirner,1967; Parker,1977; Binder, 1986; Jacobsen et al., 1987; Lishman, 1988; Goldstein, 1991; Bohnen and Jolles, 1992; Kay *et al.*, 1992; Newcombe *et al*., 1994: Karzmark *et al*., 1995; Jacobsen, 1995; Binder *et al*., 1997; Binder, 1997; Gerard, 2000; Gunstad and Suhr, 2001; Aaron and Buchwald, 2001; Miller, 2001; Gunstad and Suhr, 2002; Greiffenstein et al., 2002).

Despite that the clinical usefulness (i.e., validity) and status as a nosologic entity is still much debated (Smith-Seemiller et al., 2003; King, 2003; Rees, 2003; Ryan and Warden, 2003; Wood, 2004; Mackenzie and McMillan, 2005; Nečajauskaitė *et al.*, 2005), the PCS remains a substantial health and economic burden in many Western countries.

One important reason for the debate and diverging results by different investigators is that research concerning the natural history of the rather unspecific symptoms of PCS faces an unusual high number of methodological challenges (Dikmen and Levin, 1993). Numerous confounding factors or considerations need to be taken into account. First, there is the important issue of obtaining an adequate control group (Dikmen *et al*., 2001). A control group must not only be carefully matched by age and sex but should also be similar for other sociodemographic factors and, preferably, have the same prevalence and degree of psychosocial problems. This is because both occurrence and severity of several of the symptoms of PCS are related to these factors. For example, low socio-economic status (Hagen *et al*., 2002), and also depression and anxiety disorders (Zwart *et al*., 2003) are associated with a higher prevalence and frequency of headache. The same holds true for most of the other symptoms attributed to PCS. Since symptoms of PCS such as altered cognitive and/or psychosocial functioning (e.g., attention, memory, and depression) can be caused by

orthopedic injury, chronic pain, and other factors, the use of a general trauma group (i.e., a non-head injured group) has been advocated as a control group for studies on the development of postconcussive symptoms (Alexander, 1996; Satz et al., 1999). However, in a literature review of 1999 (Satz *et al.*) only 11 studies with this design could be found (Schwartz et al., 1987; Bijur *et al.*, 1990; Dacey *et al.*, 1991; Newcombe *et al.*, 1994; Dikmen *et al.*, 1995a; Dikmen *et al.*, 1995b; Asarnov *et al.*, 1995; Masson *et al.*, 1996; Taylor *et al.*, 1996; Barry *et al.*, 1997; Mittenberg *et al.*, 1997) eight of which showed the same level of performance when comparing the head injury group with the non-head injured group. Four studies were in children. Three studies indicated more problems in the head injured group. In only two studies (one of them in children) the subjective postconcussion symptoms were evaluated in general (Masson *et al.*, 1996; Mittenberg *et al.*, 1997). In both these studies there were more symptoms in the head-injured group. In the other 9 studies, cognitive and/or psychosocial functioning were investigated. Except for one study (Dacey *et al.*, 1991), no differences were found between the groups.

Since 1999 (when Satz et al. published their review and recommendation), no further studies on the validity of PCS were performed in which the authors included a non-head injured control group, except for the present and a recent Lithuanian study in children (Nečajauskaitė *et al.*, 2005).

Possibilities of selection or participation bias for the study cohort and recruitment bias in prospective studies (McCullagh and Feinstein, 2003) are other confounding factors. In a study on the outcome of 626 consecutive patients with mild traumatic brain injury (MTBI) (i.e., concussion) those who agreed to participate were compared with those who refused (McCullagh and Feinstein, 2003). The results showed that all early indices of concussion severity were significantly worse for the participants group. Consistent with these findings, healthcare utilisation rates were no different before injury, but were significantly increased after injury for the participants, even beyond the period of study enrolment. In investigations with an inadequately matched control group in which there are more subjects who agree to participate, a low participation rate in the study cohort may significantly increase the prevalence of symptoms in this group in comparison to a control group. This, in turn, may lead to erroneous assumptions that support the concept of PCS.

In prospective PCS studies it is well-known that there are high drop out rates (Dikmen and Levin, 1993). This has the potential to confound results and thereby compromise the study conclusions. In a number of studies, the proportion of subjects lost for follow up has approached 50% or greater (Middleboe, 1992; Levin *et al.*, 1987; Alves *et al.*, 1993; Bohnen

et al., 1993; Wade *et al.*, 1997; Ponsford *et al*., 2000). For example, Middleboe *et al.* (1992) examined the long term effects of concussion on general health. However, more than 40% of the subjects dropped out of serial assessments over a one year follow up period. Compared with study completers, this group had less prominent symptoms at baseline, suggesting the presence of a selection bias among those completing the study.

The fact that symptoms constituting PCS are not only non-specific but also very common in the general population is another problem that has to be adressed in PCS studies. Increased awareness, recall bias and the possibilities of secondary gain may result in amplification and misattribution of pre-injury symptoms and spontaneously appearing post-injury symptoms (Mittenberg *et al*., 1992). In this context, the question arises about the reliablity of using questionnaires such as the The Rivermead Post Concussion Symptoms Questionnaire (King, 1996; Ingebrigsten *et al*., 1998) that for grading of the severity of symptoms are based on comparison between pre-accident and post-accident symptoms.

Symptoms exaggeration and malingering in a medico legal context is an additional major problem for studying consequences of concussion in Western countries. These phenomena occur both in the general clinical examination setting and in neuropsychological assessment (Binder and Willis, 1990; Iverson and Binder, 2000). Malingering is the intentional production of false or greatly exaggerated symptoms for the purpose of attaining some identifiable external reward (American Psychiatric Association, 1994). Areas of potential exaggeration include pain, dizziness, depression, memory problems, poor concentration, and personality change. Among the reasons for a person to decide to malinger is to receive more money in a personal injury lawsuit. In this setting, poor effort in test situations is also common. Consequently, by including patients who are in a medico legal setting (or may be so in the future) in studies on PCS, a substantial confounding factor will be introduced.

In the vast majority of earlier studies there have been problems concerning identification of symptoms that are a consequence and those that merely have a temporal relationship to the head trauma.

Evidence against a causative role of concussion for persisting complaints are reports of no or even inverse relationship between the symptoms of PCS and the severity of the injury (Long and Webb, 1983; Alves and Jane, 1990). Another conflicting evidence is that the condition is uncommon after sporting events (Ferguson *et al*., 1999).

Several authors have proposed a biopsychosocial model to explain the chronic PCS (Jacobsen, 1995; Karzmark *et al*., 1995; Binder, 1997; McMillan, 1997; Ferrari, 1999; Aubrey

et al., 1989; Mittenberg *et al*., 1992). In this model, psychosocial factors operate within a given culture to produce a behavior following the acute injury that in turn generates the pattern of symptoms seen in the chronic syndrome. One important aspect that supports this biopsychosocial model is the phenomenon of symptom expectation.This phenomenon arises from the commonly held expectation in North America, for example, that an acute head injury may cause chronic symptoms and disability (Aubrey *et al.*, 1989; Mittenberg *et al*., 1992).

In a study by Ferrari, Obelieniene *et al.* (1999), a symptom checklist was administred to two subject groups selected from local companies in Kaunas, Lithuania, and Edmonton, Canada, respectively. Subjects were asked to imagine having suffered a concussion in a motor vehicle accident, and to check off symptoms they expected might arise from the injury. For symptoms they anticipated, they were asked to select the period of time they expected those symptoms to persist. The results showed that both in the Lithuanian and Canadian groups, the pattern of symptoms anticipated closely resembled the acute symptoms commonly reported by accident victims with concussion, but while many Edmontonians also anticipated symptoms to last months to years, very few Lithuanian subjects selected any symptoms as persisting in a chronic manner.

In Lithuania, several other studies on concussion have been performed and published in the last decades (Klumbys L, 1959 and 1969; Jaržemskas E, 1969; Kinderienė S, 1969; Parnarauskienė R, 1970 and 1989; Starkuvienė S, 2003 and Nečajauskaitė O *et al.*, 2005). However, in addition to the above study of Ferrari, Obelieniene *et al*. in 1999, only one investigation (Nečajauskaitė O *et al.*, 2005) was a properly controlled study on the concept of the PCS.

On the background of the paucity of studies that had an adequate methodological design and were free of the confounding factors which are present in Western societes, the aim and objectives of the present study were formulated.

II. The aim and the objectives of the study

The aim of the study

By historical and prospective cohort studies to investigate the validity of postconcussion syndrome as a useful clinical entity in adults.

The objectives of the study

1. To determine the prevalence and severity of headache, dizziness and cognitive dysfunction as well as headache diagnoses after concussion and in controls with minor non-head injuries 2-3 years after the trauma and to make a comparison of these symptoms in both groups.

2. To evaluate the severity of all other symptoms attributed to the postconcussion syndrome 2-3 years after concussion and to compare it with the severity of the same symptoms experienced by controls with minor non-head injuries.

3. By historical and prospective cohort studies to determine the prevalence and duration of acute posttraumatic headache.

4. To determine the prevalence and severity of symptoms of the postconcussion syndrome after concussion and in controls with minor non-head injuries 3 months and 1 year after the trauma and to make a comparison of these symptoms in both groups.

5. To compare the severity of symptoms 1 year after the trauma between concussion patients and controls in relation to marital status and education.

6. To evaluate the influence of duration of unconsciousness and anterograde amnesia on the severity of headache and cognitive dysfunction.

III. The scientific novelty, practical significance of the study and the authors personal participation in the study

1. The scientific novelty of the study

Almost all previous research on the PCS has been conducted in Western countries where high awareness and expectation in the general population for postconcussive symptoms as well as possibilities of secondary gain act as counfounding factors. In particular, there is for many accident victims a good possibility for economic winning due to financial compensations for claimed disability due to PCS (McKinlay, 1983; Iverson and Binder, 2000). Consequently, in Western countries, symptoms reporting may be unreliable because of deliberate underreporting of pre-accident symptoms and exaggeration of present symptoms. There is also a possibility of malingering.

In Lithuania, awareness and expectation of chronic symptoms after minor head injury is less than in western countries (Ferrari, Obelieniene *et al*., 2001). Possibilities for monetary compensation are minimal since the newly established insurance companies do not recognize PCS as a compensatable sequela after concussion. An opportunity therefore exists to study PCS without several confounding factors that are present in western societies. By performing both a controlled historical cohort study and a controlled prospective cohort study in a country with few confounding factors it has for the first time been possible to thoroughly investigate the validity of the postconcussion syndrome. To the best of our knowledge, the present scientific investigation is the first with this design.

In the vast majority of earlier studies, registration of symptoms of PCS has been limited to the determination of prevalence of different complaints in the study group in comparison to prevalence of pre-accident symptoms and/or symptoms in a control group. This applies also to the only earlier study in adults in which a (small) non-head injured control group (Masson *et al.*, 1996) was included and subjective postconcussion symptoms were evaluated in general.

In view of the above methodological limitations, an additional novelty of the present studies is that by use of extensive and validated questionnaires from previous whiplash studies (Schrader et al., 1996; Obelieniene et al., 1998, Obelieniene et al., 1999) and use of visual analogue scales (VAS), a more detailed quantification of symptoms of the PCS could be performed.

With a methodology and design superior to previous investigations the present study was unable to confirm the concept of the postconcussion syndrome as a useful diagnostic entity. The postconcussion syndrome has therefore little validity.

2. The practical significance of the study

In most industrialized countries a significant proportion of patients who have sustained a concussion fear that this mild brain trauma may result in persisting and possibly disabling symptoms such as headache, memory and concentration problems, dizziness and fatigue, i.e. the postconcussion syndrome. The results of the present thesis show that this fear is unwarranted and that the prognosis in the vast majority of cases with concussion is excellent. Information by doctors to the individual patient and the general public that postconcussive symptoms usually last a short time and maximally a few months without leaving a permanent brain damage may result in a more optimistic attitude by the patients. This may reduce the risk that pre-existing symptoms and spontaneously appearing post-accident symptoms through fear and negative expectation are falsely attributed to the injury. Hence, the number of patients may be reduced who on wrong premises experience a chronic disability with resulting negative consequences for their social life and working capacity.

In western countries, exclusion of the postconcussion syndrome from the list of compensatable conditions in health and car insurance policies may reduce the magnitude of the insurance premiums and thus benefit all policy-holders. Exclusion of the postconcussion syndrome from what can justify a disability pension may lessen the cost of the social security system.

3. The author's personal participation in the study

In view of the extraordinary complexity of the issue and the fact that the PCS is one of the most debated conditions in medicine, it was necessary to perform the present investigations as an collaboration study together with researchers from the Department of Neurology at the University Hospital in Trondheim, Norway, and with colleagues from hospitals in Kaunas (Diana Obelieniene and Danguole Surkiene from the Department of Neurology at the Kaunas University of Medicine; Raimondas Kunickas from the Out-patient Department of Traumatology at the Kaunas Red Cross Hospital).

In Trondheim, professor Harald Schrader, professor Lars Jacob Stovner and the leader of the department, professor Trond Sand, have had many years experience in research on consequences of minor neck and head traumas. Professor Trond Sand has also considerable experience in statistical analysis, whereas professor Lars Jacob Stovner is the leading international expert on headache epidemiology.

The original idea for the investigations was conceived by professor Harald Schrader. The author of the present theses then investigated the possibilities of performing the studies in hospitals in Kaunas, developed with professor Harald Schrader and professor Stovner's advice the appropriate methodology and adapted this methodology to the situation in the Kaunas University of Medicine and in the Red Cross Hospital. Throughout the study the author was the leading investigator, i.e., she organized and coordinated the identification of patients and controls in the involved hospitals, identified herself all participants in the Red Cross Hospital and did all practical work with mailing and collecting of the questionnaires. After receiving all answered questionnaires from patients and controls that were identified in the hospitals, the data were by her transferred to the Excel database from which she extracted the results. With suggestions and advice by professor Schrader the results were then transferred into appropriate presentations. In the statistical work, chi-squared tests and Student t-tests were performed by the author and controlled by professor Schrader. Professor Trond Sand performed the power analysis and the multiple regression models.

IV. Review of the literature

A prerequisite for the concept and validity of the PCS as an organic sequelae after concussion is that this trauma is capable of producing permanent functional and/or morphological traces in the brain. For the present thesis it was therefore considered essential to make a thourough literature review on the concussion before the consideration of the literature on epidemiology and concept of the postconcussion syndrome.

1. Definition, clinical symptoms, epidemiology, pathophysiology, and pathological anatomy of concussion

Cerebral concussion is the mildest and by far the most common type of traumatic brain injury. According to McCrory and Berkovic (2001), one of the greatest Arabic physicians, Rhazes (AD 850-923?) was the first to use the term concussion in a similar way as we use it today. The recognition that concussion represents a transitory abnormal physiologic state rather than a severe brain injury is the critical turning point in the history of the understanding of this condition (Mettler, 1947; Rhazes, 1548). In the second millenium, Lanfrancus (d. 1306) was the first physician to view concussion as a separate entity (de Chauliac, 1499; Mc Henry, 1969). He recognized that symptoms after a concussion could rapidly disappear and were the result of a transient paralysis of cerebral function caused by the brain being shaken. This concept of brain shaking or commotion had a great influence on the later understanding of the pathophysiology of concussion (Mettler,1947; Courville, 1944). Guy de Chauliac (1300-1368) empasized the usually good prognosis of concussion in contrast to the "perilous" outcome of skull fracture and penetrating brain wounds (de Chauliac, 1499).

Concussion is usually the result of a blow to the head causing it to accelerate (or decelerate) and is characterized by a sudden shortlasting impairment of consciousness. There is no universally accepted definition of concussion in the literature. The most widely used definition by other European traumatologists, neurosurgeons and neurologists includes loss of consciousness (LOC) (usually below 15-30 minutes) (McMillan, 1997) whereas some, especially American authors, also accept a definition of concussion as a trauma induced alteration in mental status that may or may not involve LOC (Quality Standards Subcommittee of ANN, 1997). While this may be acceptable from a theoretical point of view, the difficulties of separating head trauma induced symptoms of emotional shock from

confusion and memory dysfunction secondary to brain damage makes this definition difficult to use both in a medicolegal context and in research. For this reason, only head injured individuals with LOC were investigated in the studies underlying the present thesis.

Many authors use the term mild head injury instead of concussion defining it between others by Glasgow Coma Scale (GCS) scores 13-15 (Teasedale and Jennett, 1972). In addition, there should be no subsequent deterioration. The definition of mild closed head injury meets, however, more difficulties than that of concussion. The problem with the term mild head injury is mainly the uncertainty of whether the patient suffered brain injury from the trauma. In the vast majority of a mild head injury that almost everyone experiences several times throughout life there are no signs of traumatic brain injury such as altered consciousness, amnesia, or confusion. Objective evidence of injury, if any, is often limited to extracranial structures such as superficial bruises and swellings. The term of mild head injury appears therefore less useful and specific than the term concussion. The failure to differentiate between mild head injury and MTBI (i.e. concussion) may also mislead both physicians and laymen to assume that everyone who has a mild head injury also has a mild brain damage. If this was true, everybody would then acquire a traumatic brain damage during life, an assumption which seems quite unlikely.

A problem specifically connected to the isolated use of the Glasgow Coma Scale scores 13-15 for the definition of mild traumatic head injury is that the scoring in most cases is made at admission to the hospital. Depending on the time between the head trauma and the admission, patients with a transitory LOC of longer than 15-30 minutes, i.e. with more severe traumas, may be included in the category of mild head injury. It has also been shown that patients with a GCS score of 13 or 14 frequently show parenchymal lesions on cerebral magnetic resonance imaging (MRI) indicating that the patient has suffered more than a “mild injury” (Uchino, Okimura *et al*., 2001).

Because of these uncertainties the use of the term mild head injury and the use of GCS score were not considered suitable for the purpose of the present studies.

MTBI, an alternative term to concussion, is more acceptable, but does not express the uniqueness of symptoms connected to the term concussion, i.e. the immediate and shortlasting LOC.

Judging by clinical observations as well as experimental animal studies the symptoms of concussion include besides transient unconsciousness (usually from few seconds to few minutes) respiratory arrest, abolition of various reflex functions including corneal, pupillary and withdrawal responses, relatively prompt flaccidity of the musculature with the patient

collapsing into a heap, short-lasting convulsive spasms, irregularities of heart rate including both bradycardia and tachycardia, alterations in cerebral blood flow (CBF) and fluctuations in blood pressure. Upon regaining consciousness, headache, nausea, vomiting, dizziness, malaise, restlessness, irritability and confusion may all be commonly experienced. The most significant effect of concussion besides loss of awareness is traumatic amnesia (Russell and Nathan, 1946; Symonds, 1962; Benson and Geschwind, 1967; Russell, 1971), usually lasting from few minutes to few hours and maximally 24 hours. There appears to be an intimate link between amnesia and concussion so much so that if a patient claims no memory loss, it is unlikely that concussion has occurred (Denny-Brown and Russell, 1941; Verjaal and Van 'T Hooft, 1975). Traumatic amnesia usually has two components. Pre-traumatic or retrograde amnesia refers to a loss of memory for events prior to the concussion. Post-traumatic or anterograde amnesia applies to loss of memory for events after consciousness has been regained. It is often assumed that the severity of a concussive blow correlates with the duration of post-traumatic amnesia (Russell, 1971). The duration of anterograde amnesia is usually longer than that of the retrograde amnesia. Both have a tendency to shrink in the time following concussion, in particular the retrograde amnesia (Benson and Geschwind, 1967) which sometimes may disappear entirely.

According to the data of Lithuanian Ministry of Health, Lithuanian Health Information Centre (2005), 40 380 adults and adolescents with head traumas (14.23 cases per 1000 individuals in the general population) were registered in 2004 in Lithuania. In 4 961 cases of these traumas (1.75/1000) skull fractures were detected. However, there are no data on the incidence of concussion in the general population in Lithuania. In the USA, concussion or mild closed head injury accounts for approximately 90% of the 100 000 new cases of medically diagnosed head injuries each year (Annegers, 1983; Kraus, Fife *et al*., 1986). To this one must count all the cases which do not come to the attention of health care providers. Assuming that the distribution of concussion and more heavier brain traumas is similar in Lithuania and USA one can estimate a minimum annual incidence of 13 cases with concussion per 1000 inhabitants in Lithuania.

In a study on prevalence of mild head injury in American high school adolescents (14 to 18 years) it was found that it was almost 10 times higher than the hospital-reported prevalence of mild head injury among children, which was 2% to 3% (Segalowitz and Brown, 1991). In a subsequent study on high school and university students, 30% to 37% of subjects reported having experienced a head injury incident, with 12% to 15% of the total group of subjects reporting such an incident with loss of consciousness (Segalowitz and Lawson,

1995). Similarly, in a study of Triplett *et al*. (1996) on a nonclinical population of college students 21% had previously had one or more head injuries resulting in unconsciousness.

In a recent questionnaire based survey on Norwegian physicians (mean age 37 years) attending a postgraduate course on headache, 24% females and 34% men reported on one or more concussions earlier in their life with 83% of them having had a LOC for some seconds to 5 minutes, 6% having had a LOC from 5 to 30 minutes, 6% having only had amnesia and dizziness and 6% having had amnesia, dizziness and confusion (Schrader, 2003). In a subsequent questionnaire based survey on Norwegian physicians (mean age 37 years) attending a postgraduate course on neurotraumatology, 36% females and 40% men reported on one or more concussions earlier in their life with 83% of them having had a LOC for some seconds to 5 minutes, 6% having had amnesia alone, 6% having had amnesia and dizziness and 6% having had amnesia, dizziness and confusion (Schrader, 2003). There are no studies in the literature on the life time prevalence of concussion, but the cited studies would indicate that it may approach 40% - 50%.

What pathophysiologically causes the transitory LOC in concussion is still uncertain. Studies on experimental animals during the past half century have resulted in five theories. These are the vascular, reticular, centripetal, pontine cholinergic and convulsive hypotheses. It is outside the scope of the present thesis to present arguments for and against all these theories. From a recent "state of the art" review on the neurophysiology of concussion (Shaw, 2002) only the two most prominent theories are presented, the reticular and the convulsive.

The reticular theory has been the pre-eminent explanation for the pathophysiology of concussion for almost half a century. The main postulate of the reticular theory is that a concussive blow, by mechanisms which have never been satisfactorily explained, temporarily paralyses, disturbs or depresses the activity of the polysynaptic pathways within the brains stem reticular formation (BSRF).

There are, however, several limitations of this theory (Shaw, 2002): 1. BSRF normally exercises a kind of inhibitory control over the pacemaker functions of the medial thalamus. However, if the BSRF is incapacitated, then the medial thalamic nuclei are free to resume their role of coordinating and synchronizing slower high amplitude cortical rhythms. It follows, therefore, that if a concussive injury temporarily incapacitates the BSRF, then the EEG recorded from the cortex would predictably be of a relatively low frequency high voltage type. In experimental concussion in almost all instances, acute spontaneous cortical activity could, however, reasonably tidily be classified into one of two quite contrasting patterns. The first involved attenuation in voltage often with an almost total suppression of the

EEG. The second involved a brief period of excitation often consisting of both high frequency and higher amplitude activity. The genesis of these two conflicting patterns remains a matter of dispute, but neither is compatible with the predictions of the reticular theory. On not a single occasion was a sleep-like EEG reminiscent of a relaxation of BSRF control obtained in these studies. It is difficult to reconcile the near universal failure to observe the predicted EEG pattern with the theory that concussion involves depression of reticular activity. 2. Depression of BSRF activity can account for muscle flaccidity and reflex paralysis which follow cerebral concussion. It can, however, not explain the initial convulsive movements which are a feature of so many animal models of concussion as well as anecdotal reports in clinical concussion.

3. Traumatic memory loss with retrograde and anterograde amnesia is among the most important signs of concussion. This symptom can hardly be explained by transient dysfunction of BSRF which may only explain the memory loss during the state of unconsciousness (the socalled congrade amnesia) (Symonds, 1962). 4. It is difficult to understand exactly how a concussive insult could temporarily depress reticular function. A variety of neurochemical, neuropathological and neurophysiological mechanisms have been proposed but there is, as yet, no consensus as to which, if any, might be feasible. If the reticular theory was a genuinely robust one, it would seem incontrovertible that there should have been a better appreciation of its mechanism of action by now. 5. Finally, there is the more general question of whether LOC would necessarily ensue even if a concussive insult did manage to arrest or disrupt activity within the BSRF. For example, there has long been a good deal of evidence that sleep-waking patterns may survive, or at least be re-established, following even quite extensive destruction of BSRF tissue (Milner, 1971).

In the review (Shaw, 2002) it is concluded that only the convulsive theory seems compatible with the neurophysiological data and can provide a totally viable explanation for concussion. When potential methodological flaws and limitations such as anesthetic protocols, infliction of multiple blows and delay in onset of recordings are taken into account, two general principles can be adduced from animal experiments. First, the immediate post-concussive EEG is excitatory or epileptiform in nature. Second, the cortical evoked potential waveform is totally lost during this period. Evoked potentials and EEGs recorded acutely following concussive trauma are the same or similar to those obtained following the induction of a state of generalized seizure activity. The main argument of the convulsive theory is that since the symptoms of concussion bear a strong resemblance to those of a generalized epileptic seizure, then it is a reasonable assumption that similar pathobiological processes underlie them both. When applying the convulsive theory to what happens during concussion

Shaw hypothesizes that the energy imparted to the brain by the sudden mechanical loading of the head may generate turbulent rotatory and other movements of the cerebral hemispheres and so increase the chances of a tissue-deforming collision or impact between the cortex and the boney walls of the skull. In this conception, LOC is not due to transient dysfunction of the brainstem reticular activating system. Rather, it is due to functional deafferentation of the cortex as a consequence of diffuse mechanically-induced depolarization and synchronized discharge of cortical neurons. A convulsive theory can also explain traumatic amnesia and autonomic disturbances more adequately than the other theories of concussion. In addition, the symptoms of minor concussion (a.k.a. being stunned, dinged, or dazed) are often strikingly similar to minor epilepsy such as petit mal.

It remains still an unsettled question whether and to what extent common concussion causes brain damage visible on microscopical examination. The most characteristic feature of diffuse pathology in traumatic brain injury is diffuse axonal injury (DAI) a form of brain injury that is characterized by morphological changes to axons throughout the brain and brainstem. The microscopic features are axon retraction balls and microglial clusters located primarily in the corpus callosum, adjacent deep white matter, and upper brainstem (Ng *et al*., 1994; Crooks, 1991; Clark,1974). Most authorities agree that DAI requires a sudden severe acceleration – deceleration (Gennarelli *et al*., 1982; Ommaya, 1995; Gennarelli *et al*., 1995) which stretches delicate axons. Over the next 4-24 hours stretched axons undergo transection with death of the distal axonal segment and sealing off of the proximal axonal stump (Fitzpatrick *et al*., 1998; Maxwell *et al*.,1997). The distal axon is phagocytosed by microglial cells leading to microglial clusters (Clark, 1974; Geddes 1997; Torvik and Søreide, 1975). Once axonal transport starts up again, the products being transported from the cell body accumulate against the sealed axonal stump, causing it to ba1loon up into an axonal retraction ball (Povlishock *et al*., 1992). If the initial forces were not too great, the only injury to the axon is a temporary stagnation of axonal transport. The amount of force necessary to cause axonal stagnation is still unknown, as is the threshold force for axonal transection. Whether axonal stagnation causes clinical symptoms is also unknown.

DAI can probably not be seen on MRI directly. Indirect evidence consists of small, ovoid, low-attenuation lesions with their long axis parallel to the direction of the affected axon (Gentry *et al*., 1988). At the gray-white junction, these lesions are thought to represent leakage of the blood-brain barrier (Hayes *et al*., 1992). Other circumstantial evidence is the presence of petaechial haemorrhages, particularly at the gray-white junction and corpus callosum (Levi *et al*., 1990; Osborn, 1994).

There are three grades of DAI. In grade I DAI, there is widespread axonal damage in the white matter of the hemispheres. In grade II DAI, there are also focal abnormalities in the corpus callosum, often associated with small hemorrhages called *tissue tear* hemorrhages. In grade III DAI, the most severe form, there are also axonal abnormalities in the rostral brain stem and usually tissue tear hemorrhages (Gennarelli *et al*. 1998). Although DAI of all grades is considered a hallmark for severe head injuries, in a study on fatal non-missile head injuries (survival ranging from 2 hours to 14 years) only 28% of 434 cases showed DAI (Adams *et al*., 1989). In another study on autopsied cases who died of non-missile head injury or its sequelae axonal retraction balls, the most specific pathological findings in DAI, were only found within myelin pallor suggesting the presence of brain swelling after the injury (Onaya, 2002). These findings indicate that it may be difficult to accept the notion of DAI, that is, the presence of axonal retraction balls without brain swelling. Brain swelling does, on the other hand, usually not follow a concussion.

Diffuse axonal changes with organelle loaden-swelling in the axons causing ultimately loss of continuity with the distal axonal segment has been demonstrated experimentally in cats exposed to minor brain injury. This injury was generated by a hydraulic pressure gradient that traveled through a reservoir and a hollow metal shaft to strike the brain (Povlishock *et al*, 1983). It remains questionable whether this trauma mechanism can be compared to concussion in humans. In a frequently cited experimental study in which head injury was induced in primates (which best replicates brain injury in humans), all the 15 concussed monkeys with coma of less than 15 minutes had good recovery and none had DAI (Gennarelli *et al*., 1982). Even in animals with LOC of 16-119 min, only 3 of 6 animals had grade I DAI. Nevertheless, in a review article on MTBI Alexander (1997) cites Genarelli *et al*.'s study as being in support of the postulate that the neuropathology of MTBI is DAI, an obviously incorrect statement as concerns MTBI with LOC of less than 15 minutes. In another review article 2 years earlier Alexander (1995) also attributes DAI to MTBI. In response to a critical letter (Peterson,1995) he gives an evasive and unconvincing answer without providing any arguments in support for DAI occurring in MTBI with short-lasting LOC.

Probably the most quoted clinical study of DAI in concussion in a human being is Oppenheimer's 1968 report of microglial clusters in various parts of the brain and axon retraction balls in the midbrain of a single mildly head-injured patient who died of pneumonia 13 days after having been knocked down by a motor scooter, causing parietal bruise but no skull fracture (Oppenheimer, 1968). In four other mildly head injured patients who also died for reasons unrelated to their head injury, Oppenheimer reported microglial clusters but made

no mention of axon retraction balls. Microglial clusters alone may be seen with old head trauma or as part of an immune response to insults like anoxia (Adams *et al*., 1989) (Oppenheimer's patient died of pneumonia), contusion, fat embolism, infarction, encephalitis, or haemorrhage (capillary haemorrhages were also very frequent in Oppenheimer's material) (Gennarelli *et al*., 1998; Blumberg's, 1998).

Oppenheimer's study has never been replicated. Blumbergs did report disturbances of axonal transport by staining of amyloid precursor protein, but not axon retraction balls or microglial clusters, in five mildly head injured patients dying 2-99 days post injury (Blumbergs, 1994). Whether these axonal changes were permanent or clinically significant is unknown. Oppenheimer's and Blumbergs' studies suggest that axonal injury can occur in a number of axons after concussion, but they have not demonstrated the presence of the hallmark of DAI, i.e. diffuse axonal retraction balls. Unless further carefully controlled autopsy studies on such patients shortly after the injury show these specific lesions, it seems unjustified to assume that concussion or MTBI with LOC of less than 15 minutes causes DAI. Merritt's Textbook of Neurology (1989) (Rowland, Sciarra eds.) even suggests that this condition is not likely to be present unless there is LOC for somewhere around 6 hours.

2. Neurodiagnostic studies

2.1. Cerebral computed tomographic scanning and magnetic resonance imaging

In the majority of cases, concussion does not result in intracranial structural lesions that can be visualized by cerebral computed tomography (CT) (Bergvall, Kjellin *et al*, 1978) (Kant R, Smith-Seemiller *et al*., 1997). Exceptions are the few cases of extradural or subdural hematomas and parenchymal hemorrhagic lesions. In a consecutive series of 702 cases with GCS scores of 15 who presented with history of amnesia or LOC after closed-head injury, 9.4% had CT scan evidence of intracranial damage (Jeret *et al*., 1993). A similar CT scan abnormality figure of 7.6% among patients with 10 min or less of unconsciousness was found earlier (Sekino *et al*., 1981). When skull fracture was among the findings, CT scanning demonstrated abnorma1ities in 18.4% of 689 patients (Stein *et al*., 1993).

Evidence obtained over the past 15 years has shown that magnetic resonance imaging (MRI) is more sensitive than is CT scanning to the lesions caused by traumatic brain injury. In a series of 50 cases of mild to moderate closed-head injury, as categorized by GCS scores

of 9-15, 80% had lesions detected by MRI, as compared to 20% with lesions detected by CT (Levin *et al*., 1992). One and three months follow up MRI findings showed substantial resolution of lesions. In contrast, in a study on EEG, CT and MRI in patients with minor or moderate traumatic brain injury, only 3 (11%) of 27 patients with concussion had lesions in MRI (Krüger *et al*., 1991).

There are few studies that selectively have investigated MRI findings in concussion and no study could be found in which the most common form of concussion has been investigated separately in a greater trauma population, i.e. in those who had head traumas with LOC lasting from few seconds to up to 5 minutes. In a series of 58 patients whose head injuries with concussion did not require hospitalization after emergency room evaluation, MRI scans demonstrated abnormalities in only 6 patients including 3 with subdural hematomas and 3 with contusions (Doezema, King, Tandber, Espinosa, Orrison, 1991). In a series of 12 patients with very mild traumatic brain injury and transient LOC of less than 20 minutes (i.e., all grades of concussion) (Voller, Benke *et al*.,1999) only three patients showed traumatic lesions within 24 hours after trauma (slight epidural hematoma, haemorrhagic contusions and white matter lesions that by the authors where suspected to indicate "diffuse axonal injury"). After 6 weeks, one of these patients had a normal MRI, one patient showed a reduction of lesions and the MRI of one patient was equal to the first examination. For the latter patient a traumatic origin was thus uncertain. In a study with normal CT findings after mild head injury, MRI with T2-weighted spin-echo sequence showed lesions assumed to be of traumatic origin in 45% of 20 patients (Mittl, Grossman *et al*., 1994). In a study on the relationship of MRI, single-photon emission CT (SPECT) and neurocognitive performance after mild traumatic brain injury, 57% of 21 patients had abnormal MRI findings (Hofman, Stapert *et al*., 2001). Of those with LOC up to 5 minutes 50% (7/14) had lesions in T2-weighted fast spin-echo and/or T2 weighted fluid-attenuated inversion recovery (FLAIR). Only 4 in this group (29%) had lesions on both MRI investigations. A serious drawback of this study was it did not include a control group that enabled blinded neuroradiologists in a reliable way to detect specific traumatic pathologies that were different to unspecific lesions. One recent study with use of diffusion tensor MRI (which shows diffusion characteristics of traumatized brain tissue) showed that the 5 patients with mild traumatic brain injury had significant reduction of diffusion anisotrophy in several regions compared with the homologous ones in the contralateral hemisphere (Arfanakis, Haughton *et al*., 2002). Such differences were not observed in control group. The reduction was often less evident 1 month after injury. A

drawback of this study was that the controls on average were 6.7 years younger than the traumatized individuals.

A general methodological problem for studies with structural neurodiagnostic techniques that have been performed in the last 25 year is that many studies did not have a control group and in those who had, the control group was not adequate. Psychopathology may predispose to injuries (Jin *et al*.,1991; Poole *et al*., 1997) and there are more pathological MRI findings in people with psychopathology than in healthy individuals (Lewine, Hudgins *et al*., 1995; Raine, Lencz *et al*., 2000; Laakso, Vaurio *et al*., 2001). An adequate control group would thus be age-and sex matched individuals with minor non-head injuries. Presumably, such group would have a more similar socio-economic status as well as a similar degree of accident-proneness and psychopathology than a control group of healthy individuals. Connected to the lack of an adequate control group is the problem that many studies do not provide convincing evidence that the lesions shown really were of acute traumatic origin. Traumatic white matter lesions may be confused with the nonspecific hyperintense punctate changes seen in the white matter of normals that are associated with normal aging, hypertension (Rao, Mittenberg, Bernadin, Haughton, & Leo, 1989; Schmidt *et al*., 1991), and affective disorders. (Coffeyetal., 1993; Dupont*et al*., 1990; Dupont *et al*., 1995). Measurement of these high signal intensity foci also suffers from inadequate interrater reliability (Mittl *et al*., 1994).

Taken the results of studies with CT and MRI on concussion and the mentioned methodological shortcomings into account it can be concluded that the majority of individuals who have sustained a concussion do not have lesions shown by conventional structural neurodiagnostic techniques. In those who have true traumatic abnormalities, these will in most cases resolve or diminish within 3 months.

2.2. Other neurodiagnostic techniques (electroencephalography , auditory evoked responses, positron emission tomography, photon emission computed tomography and regional cerebral blood flow testing)

Routine electroencephalography (EEG) with visual inspection of the EEG tracings has little role in the evaluation of concussion patients. Already in 1944 a study in an Oregon shipyard (Dow *et al*, 1944) demonstrated that even if EEGs are obtained within 2 hours of the injury, the prevalence of frequency slowing was not greater than of controls (10% definitely abnormal as compared to 8% in the controls). Since than several other studies have confirmed

that the EEG tracing usually fails to identify significant abnormality after concussion (Krüger et. al., 1991; Fenton, 1996; Voller *et al*., 1999). Quantitative EEG (EEG brain mapping, computerized EEG) frequently shows abnormalities in the first few days after concussion (MacFlynn, Montgomery, Fenton, & Rutherford, 1984; Tebano *et al*., 1988; Fenton, 1996). A panel of the American Academy of Neurology concluded that, "the sensitivity and specificity fail to substantiate a role for these tests" (American Academy of Neurology, 1989, p. l100). Another panel (American Psychiatric Association Task Force on Quantitative Electrophysiological Assessment, 1991) agreed that the diagnostic utility of the technique was not established. Auditory evoked responses may demonstrate abnormalities acutely (Montgomery, Fenton, McClelland, MacFlynn, and Rutherford, l991), but they show little predictive relationship with symptomatology or neuropsychological findings (Schoenhuber & Gentilini, 1986).

Single-photon emission computed tomography (SPECT) lacks evidence of validity for clinical evaluation of concussion patients (American Academy of Neurology, 1996; Society of Nuclear Medicine Brain Imaging Council, 1996).

It has been reported that selected cases of poor outcome after concussion were associated with positron emission tomography (PET) hypometabolic abnormalities (Ruff *et al*., 1994), but this study had considerable methodological limitations. There was no adequate control group, i.e. non-head injured, age-and sex matched controls. Only 24 controls of unspecified age were tested, no control data were provided, and the concussion patients averaged 46 years.

Interpretation of regional cerebral blood flow (rCBF) testing is complicated by the imperfect specificity of the technique (Deutsch, 1992). Blood flow reduction in frontal lobes is common in many disease states and also is associated with reduced mental activity and with personality disorders (Goyer *et al*., 1994).

3. Concept and epidemiology of the postconcussion syndrome

There is no widely accepted definition of postconcussion syndrome. Usually, the term postconcussion syndrome is connected to a cluster of different symptoms such as headache, dizziness, cognitive dysfunction, irritability and fatigue that persist after a concussion and that are assumed to be causally related to the head trauma. However, a medical syndrome is not only defined as a set of symptoms that have a tendency to cluster, but the clustering of symptoms should also have a uniform cause. The symptoms listed as part of the concussion

syndrome can with the same or similar clustering be seen in different other conditions such as pain and depression. In a large sample of non-head-injured persons with chronic pain (Iverson and McCracken, 1997) 42% had l or more symptoms of cognitive dysfunction (disturbed memory or concentration and difficulty maintaining attention) and 81% of those subjects had 3 or more symptoms that are included in the research criteria for postconcussional disorder in the *Diagnostic and Statistical Manual of Mental Disorders* (DSM), 4th edition. In a Danish study (Hollnagl *et al*., 1980) patients with chronic daily headache not caused by concussion had a very high prevalence of persistent postconcussive syndrome symptoms. Suhr and Gunstad (2002) investigated whether any subset of self-reported postconcussion (PCS) symptoms or specific PCS symptom is sensitive and/or specific to head injury in individuals with head injury and depression, head injury without depression, depression without head injury, and controls. Results showed that depression, not head-injury status, largely accounted for elevation in PCS symptom reports, including cognitive symptoms. Thus, report of PCS symptoms is not specific to head injury.

Common clinical experience show that acute symptoms after concussion such as headache, nausea/vomiting, dizziness, tinnitus, somnolence and cognitive impairment such as concentration and attention problems usually resolve in the majority of patients within some days or few weeks. Prolonged disability from work and persistent symptomatology occur probably in only a minority of concussion patients. However, there is considerable variability between investigations in the frequency of reported complaints across studies and few studies provide sufficient detail to explain this great variability (Binder, 1997). Several authors have assumed that up to 15% of subjects with concussion are at risk for the postconcussion syndrome (Rutherford et al., 1978; Dicmen et al., 1986; Alexander, 1995; Bernstein, 1999), but it has also been claimed that 58% of patients with concussion had PCS at one month after initial presentation (Bazarian and Atakaki, 2001). Given that the life-time prevalence of concussion approaches 40 to 50% (see below), one would from these prevalences expect that several hundred thousand persons of the present Lithuanian population have had or will develop a more or less chronic PCS during their life time. In view of that such patients seldom are seen in neurological out-patient clinics, this assumption seems rather unlikely. Another reason why these figures probably are far too high is that they been selectively derived from inpatient populations and not from an unselected inception cohort. People with preexisting psychological problems including depression and anxiety, headaches and other pain may be more prone to contact health service providers after a concussion than individuals without

pre-existing complaints. Hence, in selected patient populations a significant fraction may already before the head trauma have had a set of symptoms similar to that ascribed to PCS.

Seven studies reported data on symptoms 6 months or more after concussion in relatively unselected samples (Alves, Macciocchi; & Barth, 1993; Bohnen, Twijinstra, & Jolles, 1993; Carlsson *et al*., 1987; Edna, 1987; Jones, 1974; Rutherford, Merrett, & McDonald, 1979; Wrightson & Gronwall, 1981). Alves *et al*. (1993) lost 68% of their patients by l-year follow-up, and they reported symptom frequency separately for patients successfully followed (60 %) and all patients including those lost to follow up (19%). Adapting the assumption that patients lost to follow up are asymptomatic (Alves *et al*., 1993), 7.0% of a total of 5316 patients from all studies reported symptoms 6 months or more after injury. If only patients successfully followed by Alves are included in the total, the figure increases to 7.4% of 4918 concussion patients.

In these studies, little effort has been made to separate continuation of pre-existing symptoms, the effects of negative expectation, misattribution of spontaneously occurring posttraumatic symptoms and the exaggeration of symptoms in a medico-legal context from persisting sequelae caused by the brain injury. Of particular relevance is that symptomatic patients after concussion in a study by Mittenberg *et al*. (1992) reported fewer premorbid symptoms than did normal controls.

There is evidence that question the causal relationship between late occurring symptoms and a concussion. Comparison of patients with symptoms of headache or dizziness of early onset (during hospitalization and immediately after discharge) with patients whose symptoms developed later (Cartlidge and Shaw, 1981) showed that late-onset symptoms were as common as symptoms with early onset. The groups were distinguished by the greater frequency of depression and compensation claims in the late-onset groups for both dizziness and headache. These authors and others (Rutherford *et al*., 1979) have concluded that psychosocial factors likely explained the late onset symptoms.

There are several factors that have been assumed to be possible risk factors for persisting symptoms after concussion such as advanced age, occupational status, low educational level, female gender, previous head injuries and, probably most important, premorbid psychological problems.

Advanced age is reported to be associated with poorer outcome after head injury (Denker, 1944; Rutherford *et al*., 1979; Dikmen *et al*., 1994). It may, however, well be that this is due to the susceptibility of older persons to more serious injuries as evidenced in a

study (Russell and Smith, 1961) that reported that age was related to longer posttraumatic amnesias which were, in turn, related to poorer outcome.

People with fewer years of education clearly have poorer outcomes neuropsychologically (Dikmen, Ross, *et al*., 1995) and occupationally (Dikmen *et al*., 1994; Rimel *et al*., 1981).

The relationship between occupational status and prognosis is more uncertain. Whereas a relationship between higher occupational status and better prognosis was found in Virginia (Rimel *et al*., 1981) and in Sweden (Lidvall *et al*., 1974), no relationship was found in two other studies (Denny-Brown, 1945; Wrightson & Gronwall, 1981).

The relationship between gender and prognosis is also unclear. Females had poorer outcomes in two studies in Belfast (Fenton *et al*., 1993; Rutherford *et al*., 1979) and in a Dutch study (Bohnen *et al*., 1994) whereas other studies did not show a relationship between gender and outcome (Denny-Brown, 1945; Rimel *et al*., 1981).

There is no clear evidence in the literature that two or three injuries are worse than one injury. In a population study with a large sample, there was a significant difference on some cognitive measures between men with multiple injuries as compared to those with single injuries, but the effect size was negligible (Carlsson *et al*., 1987). Since there appear to be no published data comparing premorbid characteristics of people with single mild head injuries with those with multiple mild head injuries it is possible that people who suffer multiple injuries are cognitive less able premorbidly. This, in turn, may be connected to greater accident proneness resulting in a larger number of injuries.

Most clearly, the recovery from concussion is associated with premorbid psychological health (Bohnen, *et al*.1994). Compared with controls, consecutive mild head trauma patients had double the number of adverse life events and four times the level of chronic social difficulty prior to their injury (Fenton *et al*., 1993). In a French study, symptoms associated with a diagnosis of PCS were 13 times more common in those with preexisting psychosocial problems than in those without premorbid problems (Cohadon, Richer, & Castel, 1991). In the same study, mild head trauma patients with premorbid psychosocial problems were almost 2.5 times more likely to be unemployed after injury than were mild head trauma patients without preexisting psychosocial problems. Only 5% of the premorbid problem-free subjects received a diagnosis of PCS. Dutch patients with preexisting emotional problems had more symptoms after mild head trauma than did uncomplicated cases (Bohnen *et al.*, 1992) and had more severe symptoms (Bohnen *et al*., 1994).

In summary, several studies seem to indicate that a significant minority of subjects who have had a concussion will develop a postconcussion syndrome with a direct causal relationship to the injury. However, there are also studies that show that PCS symptoms are not specific to head injury and several studies suggest that sociodemographic and pre-and/or postmorbid psychosocial factors may be of equal or even more importance for the causation of symptoms reported after concussion. There are few studies in which effort has been made to separate continuation of pre-existing symptoms, the effects of negative expectation, misattribution of spontaneously occurring posttraumatic symptoms and the exaggeration of symptoms in a medico-legal context from persisting sequelae caused by the brain injury.

V. Material and methods

The studies underlying the present thesis were performed in the Kaunas University Hospital and the Red Cross Hospital in Kaunas from September 1998 to February 1999 (historical cohort study) and from January 2001 to February 2004 (prospective cohort study).

In both studies an attempt was made to quantify the different symptoms associated with PCS both in terms of frequency and severity. Design of both studies made a more quantitative description of the impact of PCS possible. The first study had a historical cohort design, i.e. the study cohort was identified by going back in time. The advantage of this design was that the participants were not aware of the reason of the study when answering the first questionnaire. It was, however, not possible to estimate reliably the incidence, severity and duration of acute post-traumatic symptoms and their eventual evolution into chronicity. For such an analysis and in an attempt to look at the influence of sociodemographic factors on the development of PCS, a prospective controlled cohort study was performed with questionnaire based interviews shortly after concussion as well as 3 months and 1 year later. In contrast to the historical cohort study the participants would recognize the reason of the study when answering the first questionnaire and together with repetitive questionnaires they would thus be aware of the possibility of persistent PCS. Consequently, by comparing the symptoms reporting of both studies, the influence of expectation could be analysed.

The necessary sample size (concussion patients (CPAs) and controls) was difficult to calculate in view of diverging estimates of prevalence of the PCS, these ranging between 15% and 58% (Rutherford et al., 1978; Dicmen et al., 1986; Alexander, 1995; Bernstein, 1999; Bazarian and Atakaki, 2001). Furthermore, since there are several symptoms constituting the PCS, there is an uncertainty of which of the symptoms or which symptom combination one should choose as the basis for calculation of the desired power of the study. Since headache generally is considered to be the most prominent symptom of PCS it was decided to use this symptom to calculate the necessary number of participants.

The number of participants which could be recruited in the historical cohort study was limited to what one could detect in the medical records of the Red Cross Hospital and Kaunas University Hospital when taking into account the requirement of the study design that there should be an interval between concussion and the time of the interview of about 2 to 3 years, i.e. a difference between the maximal and minimal interval time of approximately 1 year. It was found that it was possible to identify 200 individuals with these interval times. A power

analysis programmed in Microsoft Excel® using the formula published by Lachin (1981) and based on the number of those who responded was then performed. Assuming a headache prevalence of 15% (or 20%) in the control group population, the historical cohort study had 80% power to detect a 5.1% (or 5.6%) additional risk of any headache following an accident (i.e. a true headache prevalence in a postconcussion population of at least 20.1% or 25.6% respectively).

The prospective cohort study did not have the limitation of recruitment as the historical cohort study. Here, one aimed at acquiring a number of participants similar or greater than the number that in previous whiplash studies in the Kaunas region (Schrader et al., 1996; Obelieniene et al., 1999) was estimated to have a sufficient power to detect significant differences in posttraumatic symptoms, i.e. 300. Assuming a prevalence of frequent headache (i.e., > 7 days per month) of 15% (or 20%) in the control group population, the prospective cohort study had 80% power to detect a 11% (or 12%) additional headache risk following an accident (i.e. a true headache prevalence in a postconcussion population of at least 26% or 32% respectively).

In order to increase the response rate and to encourage participation, all participants received an honorarium of 20 LTL for answering the questionnaires. In addition, they entered a raffle for a holiday trip.

The historical cohort study was approved by the Independent Ethics Committee of the Kaunas University of Medicine in 1998 (protocol number 16) and the prospective study was approved by the same Committee in 2001 (protocol number 35a).

1. Material and methods of the historical cohort study

The inception cohort consisted of 200 patients aged 18-67 years who were consecutively identified by reviewing the medical records from the general emergency ward of the Kaunas University Hospital (KUH) and the traumatological emergency ward of the Red Cross Hospital (RCH) in Kaunas, Lithuania, between 35 and 22 months before the study (between January 1996 and February 1997). First, the patients were identified by date of admittance, personal data and diagnosis in the general registration book. Then their full medical record was taken from the archive and reviewed. The patients had been consecutively admitted for the evaluation and treatment of a head trauma involving short lasting LOC (no longer than 15 minutes). There should be no focal neurological signs and other major injuries,

except for small skin lesions and bruises. The doctors in the emergency ward usually made notification of unconsciousness on the charts when there was a witness report. Witness reports were either directly from relatives, friends, ambulance staff, etc. or conveyed by the patient after having heard it from a witness. Particularly, in the latter situation amnesia and confusion may have resulted in inaccurate statements from the patients, leading to an overestimation of the injury severity.

A plain skull X-ray was peformed in all included patients. In no patient an imaging with CT or MRI was performed. This was due to the missing availability for CT and MRI in the participating hospitals in Kaunas at the time of the admission of the concussion patients. Since concussion needs to be defined not only clinically, as an injury leading to unconsciousness of less than 15 minutes, but also as leaving no morphological traces in the cerebral tissue as assessed by CT or MRI, an underestimation of injury severity may have occurred in some patients.

Patients who had any other major injury (defined as an injury requiring hospitalisation for more than 7 days) or loss of consciousness exceeding 15 minutes were excluded from the study.

An introductory letter, informed consent form and standard self-report questionnaire was sent by mail with questions about general health and detailed questions about headache (during the last year and during the last month before the inquiry) as well as about other symptoms attributable to the postconcussion syndrome. These included the presence and frequency of memory problems, concentration difficulties and dizziness. Concerning headache, it was asked about its frequency, duration, intensity, location, character and accompanying symptoms such as nausea, vomiting, phonophobia, and photophobia. In addition, the participants were asked to mark on a visual analogue scale (VAS) ranging from «no» to «much» (equivalent to a scale from 0 to 100) the degree of the following symptoms: headache, memory problems, concentration problems, dizziness, nausea, fatigue, tiredness, phonophobia, tinnitus, irritability, sleep problems, tendency to cry, depression, anxiety, intolerance to alcohol, neck pain, concern for health, and concern for brain injury. After having answered these first questionnaire a second questionnaire was sent by mail. The participants were now informed about the real reason of the contact and asked whether before or after the concussion they had had other head injuries with loss of consciousness. They were also asked if they could remember having had headache, memory problems and concentration difficulties before the concussion, and, if so, with what frequency. In addition, they were asked whether they could remember occurrence and total duration of acute posttraumatic

headache. The average interval between the concussion and the answering of the first questionnaire was 28.6 (SD 3.4) months.

The response rate among concussion patients was 66% (131 of 200).

There were 79 (60.3%) male CPAs with an average age of 34 years (SD 10) and 52 (39.7%) female CPAs with an average age of 38 years (SD 11).

Diagnoses of type of headache at the time of the interview were made according to the International Headache Society criteria using questions that allowed the establishment of the most frequent headache diagnoses such as migraine, episodic tension type headache, and chronic tension type headache. Possible cervicogenic headache (PCH) was diagnosed by using criteria published in 1990 (Sjaastad *et al*., 1990) and revised in 1998 (Sjaastad *et al*., 1998). Five criteria were used: 1) Precipitation of head pain by neck movement, 2) restriction of range of motion in the neck, 3) ipsilateral, shoulder and/or arm pain of a nonradicular nature, 4) unilaterality of the head pain, without sideshift, and 5) non-throbbing, moderate severe pain. Of these, criterion 1 was considered obligatory. Due to the purely questionnaire-based design of the present study, criteria such as precipitation of head pain by external pressure over the upper cervical or occipital region or confirmatory evidence by diagnostic anesthetic blockades could not be used.

There exists no precise definition of PCS concerning the presence and severity of complaints, but six symptoms are frequently mentioned in connection with the syndrome. In order to make a diagnosis of PCS in the present study, it was required that at least one of these symptoms should be present to a significant degree whereas the other symptoms could be of any severity. Significant complaints were arbitrarily defined as 1) frequent headache (more than seven days per month), 2) constant problems with concentration and 3) memory, 4) dizziness more than one day per week, 5) fatigue with a score of more than 50 on VAS and 6) irritability with a score of more than 50 on VAS.

Control group

For each patient with concussion (CPA) a sex- and age-matched control person was identified from the same medical sources. Inclusion criteria for the control person was a minor orthopedic injury (bruise, abrasion, tendon strain in the extremities, etc.), not involving the head and neck, causing admission to the emergency ward not more than two weeks before or two weeks after the matching CPA and age maximally three years more or less than their matching CPA. If several individuals fulfilled the criteria, the one admitted to the ward with the closest temporal relationship to the CPA was selected as the control. The controls received

an introductory letter, informed consent form and the same first questionnaire as the CPAs. The second questionnaire contained questions about the history of head traumas and those who on questioning reported any previous concussion were excluded (n = 20). A new control person was then drawn from the hospital charts.

The response rate of controls was 73% (146 of 200). There were 88 (60.3%) males with an average age of 35 years (SD 11) and 58 (39.7%) females with an average age of 39 years (SD 12) in the control group.

2. Material and methods of the prospective cohort study

The study population was consecutively recruited as an inception cohort from the emergency ward of KUH and RCH in Kaunas, Lithuania, and consisted of 300 patients aged 18-60 years who had been admitted for the evaluation and treatment of a head trauma involving LOC. A lower upper age than in the historical cohort study (i.e., 60 years) was chosen because of the greater demand on concentration when filling out several questionnaires during 1 year. Including people above 60 years would have the risk of a high drop out rate in this age group. The doctors in the emergency ward included patients only if a LOC of maximally 15 minutes could be documented and its duration being estimated by using all available information obtained by witness reports from relatives, friends, ambulance staff, etc., and self-report. Anterograde amnesia was estimated by careful interview of the patients and comparison of the patient's recollection of events with those of witnesses including the emergency personnel. Exclusion criteria were: 1) Prior history of alcohol abuse, drug abuse, epilepsy or significant psychiatric or neurological disorder; 2) previous concussion, 3) seizure associated with the concussion and 4) focal neurological signs and abnormal neurological status at admission except for amnesia and slight and transitory confusion; 5) significant other injury requiring hospitalisation; 6) duration of hospital stay exceeding one week.

Due to the missing RCH or limited KUH availability of imaging with CT and, in particular, MRI only 51 patients were investigated with a CT scan. A plain skull X-ray was performed in all included patients. In no case traumatic pathology was detected.

An introductory letter, informed consent form and standard self-report questionnaire was sent to the patients 7-14 days after the head trauma including questions about 1) general health; 2) headache in the last month; 3) various other symptoms and diseases; 3) headache, dizziness, memory problems and difficulties with concentration in the last year before the concussion; and 4) presence, character and duration of headache and dizziness after the

concussion. In addition, the participants were asked to fill out the Rivermead Postconcussion Symptoms Questionnaire (RPQ) and to mark the degree of different symptoms on the same VAS questionnaire that was used in the historical cohort. In the RPQ the patients were asked to rate the degree of 16 PCS symptoms (headache, dizziness, nausea and/or vomiting, noise sensitivity, sleep disturbance, fatigue/tiring more easily, being irritable/easily angered, feeling depressed or tearful, feeling frustrated or impatient, forgetfulness/poor memory, poor concentration, taking longer to think, blurred vision, light sensitivity, double vision and restlessness) compared with premorbid levels, using a range of values from 2 to 4 to indicate whether the symptoms experienced after trauma is a mild (2), moderate (3) or severe (4) problem compared with similar pre-injury complaints, when 0 is - no problem experienced at all and 1 - the same problem as before trauma.

After 3 months and after 1 year the patients answered questionnaires with questions about headache, dizziness, and cognitive dysfunction in the last month. Additionally, they were asked to mark on VAS the degree of the same symptoms as in the first questionnaire and to fill out a new RPQ. Once again they were questioned about occurrence and duration of headache and dizziness that appeared shortly after the trauma.

The average interval between the concussion and the answering of the first questionnaire was 20.4 days (SD 8.1).

The response rate among CPAs shortly after trauma was 72% (217 of 300), after 3 months – 67% (200 of 300) and after 1 year – 64% (192 of 300). There were 144 (66.4%) male CPAs with an average age of 33 years (SD 13) and 73 (33.6%) female CPAs with an average age of 38 years (SD 14).

A significant degree of core symptoms was defined in the same way as in the historical cohort study.

Control Group

For each patient with concussion (CPA) a sex and age-matched control person was identified 2 to 14 days after the admission of the CPA. Inclusion criteria for the control person was a minor injury, not involving the head and neck and age maximally three years more or less than their matching CPA. Exclusion criteria were: 1) Prior history of alcohol abuse, drug abuse, epilepsy or significant psychiatric or neurological disorder; 2) previous concussion; and 3) duration of hospital stay exceeding one week.

If several individuals fulfilled the criteria, the one admitted to the ward with the closest temporal relationship to the CPA was selected as the control.

The controls received the same questionnaires as the CPAs shortly after the trauma and 3 months and one year later including the RPQ questionnaires and excluding questions about acute posttraumatic headache and dizziness.

The response rate among controls shortly after trauma was 74% (221 of 300), after 3 months 70% (210 of 300) and after 1 year 72% (215 of 300). There were 145 (65.6%) males with an average age of 33 years (SD 13) and 76 (34.4%) females with an average age of 38 years (SD 14) in the control group.

3. Study End Points

In the historical cohort study, the main outcome variable was the number of patients with significant headache (more than seven days per months). The secondary end point variables were the number of patients with any or daily dizziness, constant or sporadic memory problems, constant or sporadic concentration problems, and the number of subjects who suffered from all six core symptoms simultaneously (i.e. headache, dizziness, concentration problems, memory problems, fatigue and irritability).

In the prospective study, the main outcome variable was also the number of patients with significant headache. The secondary end point variables were the VAS scores of all postconcussive symptoms, the number of patients with constant or sporadic cognitive dysfunction and the number of patients with any or daily dizziness.

4. Statistical Analysis of the Study

The data were presented as mean ± standard deviation (SD).

Prevalences of symptoms between groups (categorical data) were compared with the χ^2-test with Yates' correction using the statistical program STATMED by Nycomed Scandinavia. VAS scores were compared with two-sided Student's *t*-test for unequal variances using the statistical program of Microsoft Excel®. A p-value less than 0.05 was considered to be significant. The reason why the parametric Student's *t*-test was considered appropriate was that tests for distribution of the VAS scores of different symptoms showed relative moderate deviations from a normal distribution. The Student's *t*-test is relative robust when there are no great deviations and

gave p-values similar to those obtained by use of non-parametric tests like the Mann-Whitney or Wilcoxon test.

In the prospective study, in order to study the influence of duration of unconsciousness, anterograde amnesia and other variables on the severity of headache and cognitive dysfunction, for CPAs, multiple linear regression models with backward selection were constructed with VAS scores of headache and cognitive dysfunction at different times after the accident as the dependent variables and sex, age, height, weight, length of education, trauma mechanism (assault or other) duration of consciousness and anterograde amnesia as independent variables. In order to include categorical independent variables, general linear models (GLM) for this regression analysis were applied using the statistical software package SYSTAT version 10 .

First all variables were entered (no interaction terms). Then the variable with the highest p-value was removed sequentially until the model consisted of variables with $p < 0.20$.

Sex, age, height, weight length of education, trauma mechanism (assault or other) duration of consciousness and anterograde amnesia was entered as the first model.

In addition, for selected variables, univariate regression analyses were made.

The power and multiple regression analyses were performed by professor Trond Sand at the Norwegian University of Science and Technology, Department of Neuroscience, Trondheim, Norway.

VI. Results

1. Results of the historical cohort study

Of the 200 patients with concussion, 131 (66%) returned the questionnaires.

The average interval between the concussion and the answering of the questionnaire was 28.6 (SD 3.4) months. In 31% of cases the injury was the result of assault, in 31% due to car accident, in 29% caused by falling and in 8% due to other mechanisms. Twenty-two (17%) CPAs and 14 (10%) controls were reported to have been under the influence of alcohol at admission. According to the self-report in the questionnaire, only 4.6% of CPAs and 4.1% of the controls reported a weekly alcohol consumption of more than six standard units.

Of the selected control group of 200 subjects, 146 (73%) responded to the questionnaire.

Of the patients with concussion, 27 (21%) reported that they had had an additional concussion before the actual identified event.

1. 1. Demographic characteristics

The demographic characteristics of the CPAs and the controls are shown in table 1.1.1. The groups were similar except for differences in education and marital status. There were 79 (60.3%) male CPAs with an average age of 34 (SD 10) years and 52 (39.7%) female CPAs with an average age of 38 (SD 11) years. In the control group there were 88 (60.3%) males with an average age of 35 (SD 11) years and 58 (39.7%) females with an average age of 39 (SD 12) years. The age distributions of different age groups for CPAs and controls are given in figure 1.1.1 (males) and 1.1.2 (females). Both for males and females, the greatest age group was that from 18 to 27 years. Significantly more CPAs had secondary school education as compared to controls ($p = 0.03$) whereas more controls had university education (graduated and not graduated) although the difference did not reach statistical significance ($p = 0.10$). There were significantly more controls who were married ($p = 0.01$) and significantly more CPAs who were divorced ($p = 0.04$).

Table 1.1.1. Demographic characteristics of patients who have suffered a concussion and in non-head injured controls

Participants	Concussion (n = 131) n (%)	Controls (n = 146) n (%)	*p* Value[a]
Sex (*n*)			
Male	79 (60.3)	88 (60.3)	0.91
Female	52 (39.7)	58 (39.7)	0.91
Mean (SD) age (years)			
Men	34 (10)	35 (11)	0.60 [b]
Women	38 (11)	39 (12)	0.68 [b]
Education			
Primary school	9 (6.9)	7 (4.8)	0.63
Secondary school	49 (37.4)	36 (24.7)	0.03
Practical education/ Professional school	41 (31.3)	54 (37.0)	0.38
University graduate	22 (16.8)	30 (20.5)	0.52
University uncom-pleted	6 (4.6)	15 (10.3)	0.12
Other	4 (3.1)	4 (2.7)	0.83
Unemployment	28 (21)	23 (16)	0.29
Marital status			
Single	23 (17.6)	28 (19.2)	0.84
Living with partner	12 (9.2)	6 (4.1)	0.14
Married	61 (46.6)	91 (62.3)	0.01
Widowed	8 (6.1)	5 (3.4)	0.44
Divorced	27 (20.6)	16 (11.0)	0.04

[a] χ^2 – test with Yates' correction;
[b] two-sided Student's *t*-test.

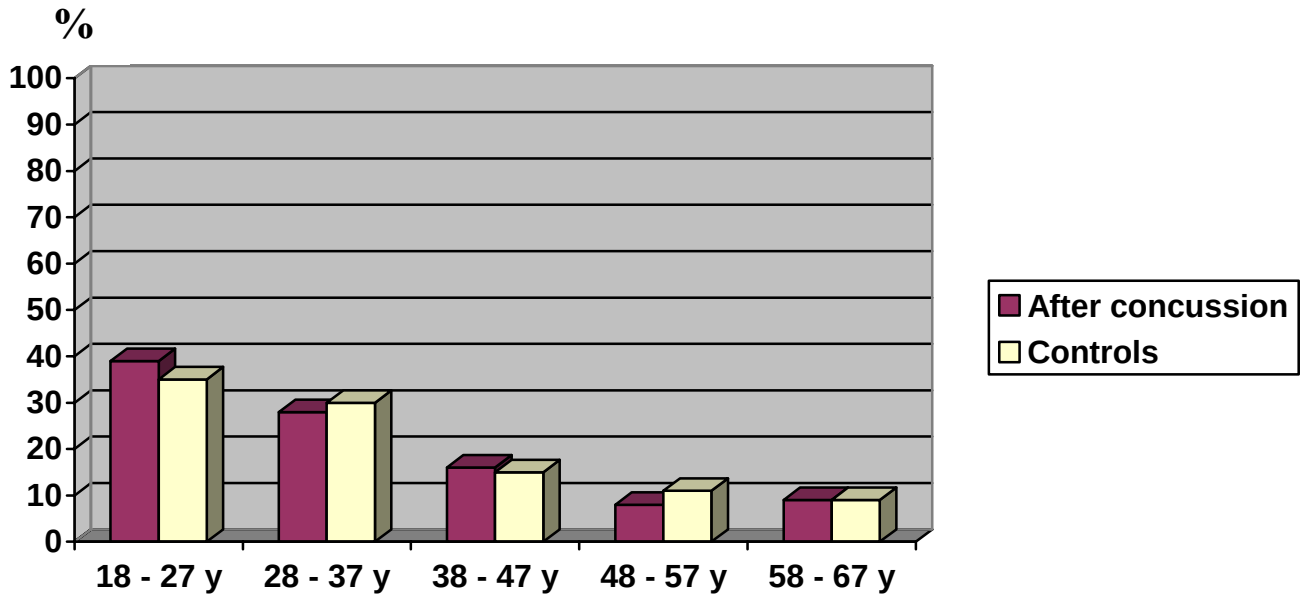


Fig. 1.1.1. Distribution of different age groups of male subjects after concussion and in controls.

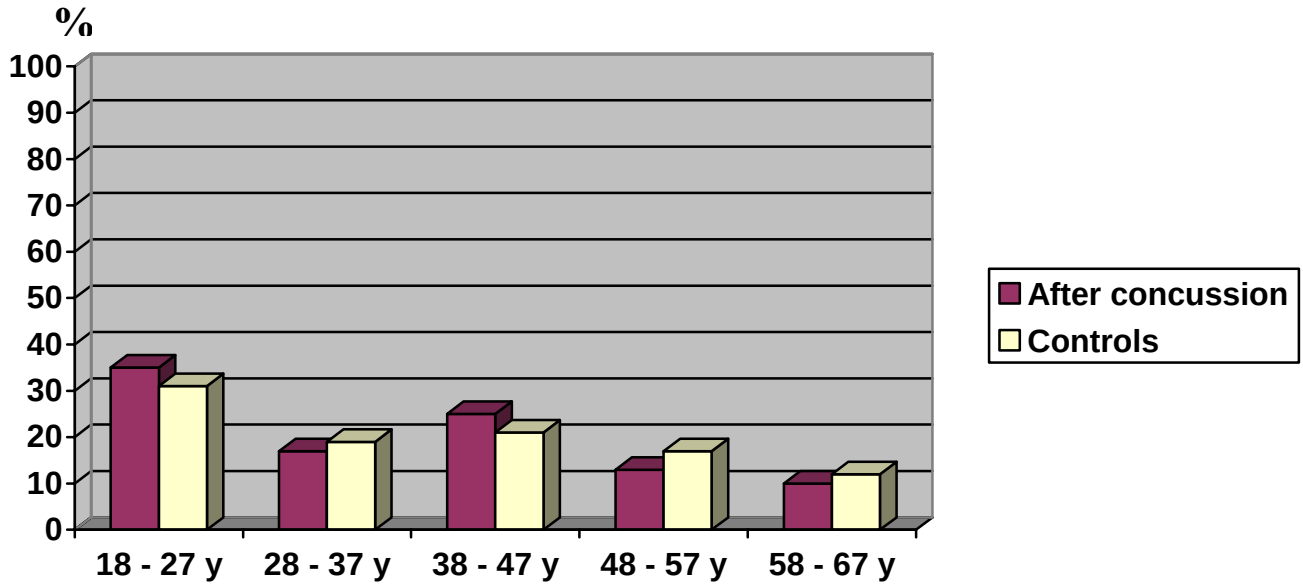


Fig. 1.1.2. Distribution of different age groups of female subjects after concussion and in controls.

1. 2. Headache

The prevalence of headache of any frequency during the last year was 78.6% (103 of 131) in CPAs and 78.8% (115 of 146) in controls ($p = 0.91$) (table 1.2.1). Frequent headache (more than seven days per month) during the last year was found in 19.1% (25 of 131) CPAs as compared to 18.5% (27 of 146) in controls ($p = 0.98$). Prevalence of headache occurring every day during the last year was 10.7% (14 of 131) in CPAs and 8.9% (13 of 146) in controls ($p = 0.77$). Significantly less CPAs reported on any headache before concussion as compared to after concussion (63.4% vs 78.6%; $p < 0.01$). There were however also significantly less CPAs who reported on any headache before the concussion as compared to controls (63.4% vs 78.8%; $p < 0.01$), thus supporting an underestimation of pretraumatic headache in CPAs. During the last month the prevalence of headache of any frequency was 61.1% (80 of 131) in concusion patients and 61% (89 of 146) in controls ($p = 0.92$). Frequent headache during the last month was found in 22.9% (30 of 131) CPAs as compared to 23.3% (34 of 146) in controls ($p = 0.95$). Prevalence of headache occurring every day during the last month was 11.5% (15 of 131) in CPAs and 12.3% (18 of 146) in controls ($p = 0.97$). CPAs had an average score of 41 (SD 29) of maximal 100 in VAS of headache and controls had an average score of 38 (SD 29) ($p = 0.47$) (table 1.5.1).

Table 1.2.1. Headache before and after concussion and in non-head injured controls

Frequency of headache	Before Concussion (n = 131) n (%)	After Concussion (n = 131) n (%)	Controls (n = 146) n (%)	*p* Value[a]
Headache during the last year				0.91[b]
No headache	48 (36.6)	28 (21.4)	31 (21.2)	
Headache				
< 1 day per month	25 (19.1)	27 (20.6)	38 (26.0)	
1-7 days per month	41 (31.2)	51 (38.9)	50 (34.2)	
8-15 days per month	6 (4.6)	7 (5.3)	5 (3.4)	
> 15 days per month	0 (0)	4 (3.1)	9 (6.2)	0.98[c]
Every day	11 (8.4)	14 (10.7)	13 (8.9)	
Headache during the last month				0.92[d]
No headache		51 (38.9)	57 (39.0)	
Headache				
1-7 days		50 (38.2)	55 (37.7)	
8-14 days		12 (9.2)	8 (5.5)	
> 14 days		3 (2.3)	8 (5.5)	0.95[e]
Every day		15 (11.5)	18 (12.3)	

[a] χ^2- test with Yates' correction, after concussion vs. controls;

[b] Any headache during the last year after concussion (103 of 131) vs. controls (115 of 146);

[c] Frequent headache (> 7 days per month) during the last year after concussion (25 of 131) vs. controls (27 of 146);

[d] Any headache during the last month after concussion (80 of 131) vs. controls (89 of 146);

[e] Frequent headache (> 7 days per month) during the last month after concussion (30 of 131) vs. controls (34 of 146).

All CPAs stated that they remembered that they had had acute headache after the trauma. This headache lasted less than 12 hours in 61.1%, from 12 hours to two days in 21.4%, from 2 days to one week in 9.2%, from 1 week to one month in 4.6% and for more than 1 month in 3.8%. Hence, acute headache had disappeared during the first week in 91.6% of cases (table 1.2.2).

Table 1.2.2. Duration of acute posttraumatic headache in patients who have suffered a concussion

Duration of acute postraumatic headache	Concussion patients (n = 131) n (%)
≤ 12 hours	80 (61.1)
> 12 hours - ≤ 48 hours	28 (21.4)
> 2 days - ≤ 1 week	12 (9.2)
> 1 week - ≤ 1 month	6 (4.6)
> 1 month	5 (3.8)

Analysis of different types of headache at the time of the interview showed that there were no significant differences in prevalence of migraine (9.9% versus 7.7%, p = 0.62), episodic tension type headache (33.6% versus 35.6%, p = 0.82), chronic tension type headache (2.3% versus 2.7%, p = 0.88), possible cervicogenic headache (0.8% versus 2.7%, p = 0.69) and unclassifiable headache (32.8% versus 22.6%, p = 0.10) between patients with concussion and controls (table 1.2.3).

Table 1.2.3. Headache diagnoses in patients who have suffered a concussion and in non-head injured controls (percentages in parentheses refer to the whole group of concussion patients (n = 131) and controls (n = 146))

Diagnosis	Concussion n = 103 n (%)	Controls n = 115 n (%)	p Value [a]
Migraine	13 (9.9)	11 (7.5)	0.62
Episodic tension type headache	44 (33.6)	52 (35.6)	0.82
Chronic tension type headache	3 (2.3)	4 (2.7)	0.88
Possible cervicogenic headache (criterion 1+2)	1 (0.8)	3 (2.1)	0.69
Unclassifiable	45 (34.4)	48 (32.9)	0.89
Total number of diagnoses	106*	118**	

a - Chi-squared test with Yates' correction;

* 3 patients qualified for 2 diagnoses (2 for migraine and episodic tension type headache and one for migraine and chronic tension type headache);

** 3 patients qualified for 2 diagnoses (2 for migraine and episodic tension type headache and one for migraine and possible cervicogenic headache).

1.3. Dizziness

The prevalence of dizziness of any frequency at the time of the interview was 64.9% (85 of 131) in CPAs and 63.0% (92 of 146) in controls (p = 0.84) (table 1.3.1). Daily dizziness was reported by 6.1% (8 of 131) CPAs and 6.2% (9 of 146) controls (p = 0.81). CPAs had an average VAS score for dizziness of 33 (SD 29) and controls 32 (SD 27) (p = 0.38) (table 1.5.1) .

Table 1.3.1. Dizziness in patients who have suffered a concussion and in non-head injured controls

Frequency of dizziness	Concussion (n = 131) n (%)	Controls (n = 146) n (%)	p Value [a]
No dizziness	46 (35.1)	54 (37.0)	0.84
Dizziness			
Once per week or Less	58 (44 .3)	67 (45.8)	0.88
Several times per Week	14 (10.7)	13 (8.9)	0.77
Daily	8 (6.1)	9 (6.2)	0.81
Other	5 (3.8)	3 (2.1)	0.61

[a] χ^2- test with Yates' correction.

1.4. Cognitive dysfunction

The prevalence of any memory problem after concussion was 68.7% (90 of 131) in CPAs and 58.9% (86 of 146) in controls (p = 0.12) (table 1.4.1).

Constant memory problems was reported by 8.4% (11 of 131) CPAs and 11% (16 of 146) controls (p = 0.61). Any concentration problem was reported by 67.2% (88 of 131) CPAs and 56.2% (82 of 146) controls (p = 0.08). Constant severe concentration problems was reported by 2.3% (3 of 131) CPAs and 2.7% (4 of 146) controls (p = 0.88). The corresponding figure for memory problems was a VAS score of 40 (SD 31) in CPAs and 36 (SD 30) in controls (p = 0.29) and for concentration problems 31 (SD 29) in CPAs and 30 (SD 24) in controls (p = 0.68) (table 1.5.1).

Table 1.4.1. Cognitive dysfunction before and after concussion, and in non-head injured controls

Subjective cognitive dysfunction	Before concussion (n = 131) n (%)	After concussion (n = 131) n (%)	Controls (n = 146) n (%)	*p* Value [a]
Memory				
No memory problems	85 (64.9)	41 (31.3)	60 (41.1)	0.12
Sporadic memory problems	40 (30.5)	79 (60.3)	70 (47.9)	0.05
Constant memory problems	6 (4.6)	11 (8.4)	16 (11.0)	0.61
Concentration				
No concentration problems	71 (54.2)	43 (32.8)	64 (43.8)	0.08
Sporadic concentration problems	51 (38.9)	74 (56.5)	71 (48.6)	0.24
Constant slight concentration problems	6 (4.6)	11 (8.4)	7 (4.8)	0.33
Constant severe concentration problems	3 (2.3)	3 (2.3)	4 (2.7)	0.88

[a] χ^2- test with Yates' correction, after concussion vs. controls.

Significantly more subjects reported that they did not have memory problems before the concussion (64.9%, 85 of 131) as compared to what they had after the concussion (31.3%, 41 of 131) ($p < 0.0001$) and when compared to controls (41.1%; 60 of 146) ($p = 0.0001$) supporting an underestimation of pretraumatic memory problems in CPAs. Significantly more subjects reported that they did not have concentration problems before the concussion (54.2%; 71 of 131) as compared to what they had after the concussion (32.8%, 43 of 131) ($p = 0.001$). There were also more subjects that reported that they did not have concentration problems before concussion (54.2%) as compared to controls (43.8%) but the difference did not reach statistical significance ($p = 0.11$).

1. 5. VAS scores of other symptoms of the postconcussion syndrome

There were no significant differences in VAS scores for fatigue (47 versus 42, p = 0.18) and irritability (60 versus 56, p = 0.33) between concussion patients and controls (table 1.5.1).

Table 1.5.1. Visual analogue scale (VAS) scores of different symptoms attributed to the postconcussion syndrome 2-3 years after the trauma in patients who have suffered a concussion and in non-head injured controls

Symptom	Concussion (n = 131) m (SD)	Controls (n = 146) m (SD)	*p* Value [a]
Headache	41 (29)	38 (29)	0.47
Memory problems	40 (31)	36 (30)	0.29
Concentration problems	31 (29)	30 (24)	0.68
Dizziness	33 (29)	32 (27)	0.38
Nausea	29 (29)	28 (28)	0.71
Fatigue	47 (28)	42 (28)	0.18
Tiredness	53 (31)	52 (29)	0.81
Phonophobia	53 (32)	49 (31)	0.26
Buzzing in the ears	26 (29)	22 (25)	0.23
Irritability	60 (34)	56 (33)	0.33
Sleep problems	36 (33)	37 (31)	0.96
Tendency to cry	36 (35)	41 (35)	0.29
Depression	46 (31)	36 (28)	0.002
Anxiety	44 (32)	40 (27)	0.28
Alcohol intolerance	38 (35)	29 (30)	0.04
Neck pain	29 (29)	25 (24)	0.17
Worried about complaints	41 (32)	39 (28)	0.62
Worried about brain injury	40 (33)	32 (30)	0.04

VAS scores between “no” and “much”: 0 – 100;

[a] Two-sided Student’s t-test (unequal variances).

Neither were there any significant differences for the other symptoms attributed to the postconcussion syndrome except for depression (p = 0.002), alcohol intolerance (p = 0.04) and worry about brain injury (p = 0.04). When those whose head injury was due to assault were excluded, no significant difference was seen concerning alcohol intolerance.

1. 6 Core symptoms of the postconcussion syndrome

Only one CPA and three controls had a combination of the six core symptoms of PCS, if the requirement was that all these symptoms had to be significant according to our definition. There was also no significant difference between CPAs and controls in prevalence of the symptom combination: 1) frequent headache (more than seven days per month), 2) any concentration problem, 3) any memory problem, 4) any dizziness 5) any fatigue and 6) any irritability (table 1.6.1) (11.5% versus 8.2%; p = 0.48).

Table 1.6.1. Prevalences of symptoms combinations in patients who have suffered a concussion and in non-head injured controls. Number and percentage (%) of subjects are given in whom one symptom is pronounced ("significant symptom") while the remainder symptoms are of any degree of severity

Significant symptom of symptoms combination	Concussion (n = 131) n (%)	Controls (n = 146) n (%)	*p* Value [a]
Headache (> 7 days per month)	15 (11.5)	12 (8.2)	0.48
Memory problems (constant)	10 (7.6)	13 (8.9)	0.87
Concentration problems (constant)	10 (7.6)	9 (6.2)	0.81
Dizziness (> one time per week)	18 (13.7)	16 (11.0)	0.60
Fatigue (> 50 on VAS)	22 (16.8)	15 (10.3)	0.16
Irritability (> 50 on VAS)	35 (26.7)	25 (17.1)	0.07

[a] - χ^2 test with Yates correction.

Likewise, analyses of prevalences of the same combination of symptoms but with one of the other symptoms being significant while the remaining symptoms could be any degree, showed only insignificant differences for all alternatives. Neither did adding to or substituting fatigue or irritability with other symptoms such as anxiety, sleep problems or tinnitus result in any significant difference. There was only a borderline significance for difference of prevalence of symptoms combination between CPAs and controls when irritability was a significant symptom ($p = 0.07$).

2. Results of the prospective cohort study

The response rate among CPAs shortly after trauma was 72% (217 of 300), after 3 months – 67% (200 of 300) and after 1 year – 64% (192 of 300). The average interval between the concussion and the answering of the first questionnaire was 20.4 days (SD 8.1).

In 66% of cases the injury was the result of assault, in 16% due to car accident, in 15% caused by falling and in 4% due to other mechanisms. No patient with concussion due to sporting activity was identified and enrolled. Only 2.8% of CPAs and 2.3% of the controls reported a weekly alcohol consumption of more than 6 standard units.

Of the 300 subjects eligible for the control group, 221 (74%) responded to the first questionnaire, 210 (70%) of these to the second and 215 (72%) to the last questionnaire sent after one year.

2. 1. Demographic characteristics

The demographic characteristics of the CPAs and the controls are shown in table 2.1.1. The groups were similar except for differences in marital status. There were 144 (66.4%) male CPAs with an average age of 33 years (SD 13) and 73 (33.6%) female CPAs with an average age of 38 years (SD 14). In the control group there were 145 (65.6%) males with an average age of 33 years (SD 13) and 76 (34.4%) females with an average age of 38 years (SD 14). The age distribution of different age groups for CPAs and controls are given in figure 2.1.1 (males) and 2.1.2 (females). As in the historical cohort study, both for males and females, the greatest age group was that from 18 to 27 years. Significant more controls were married than CPAs ($p = 0.03$).

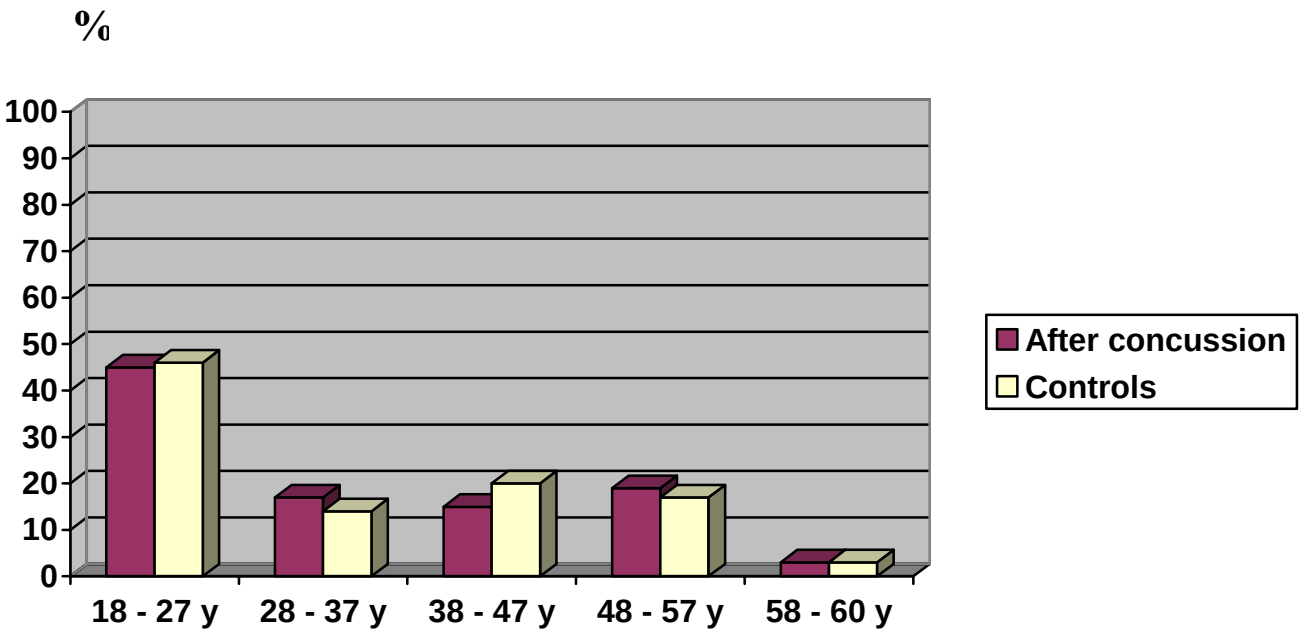


Fig. 2.1.1. Distribution of different age groups of male subjects after concussion and in controls.

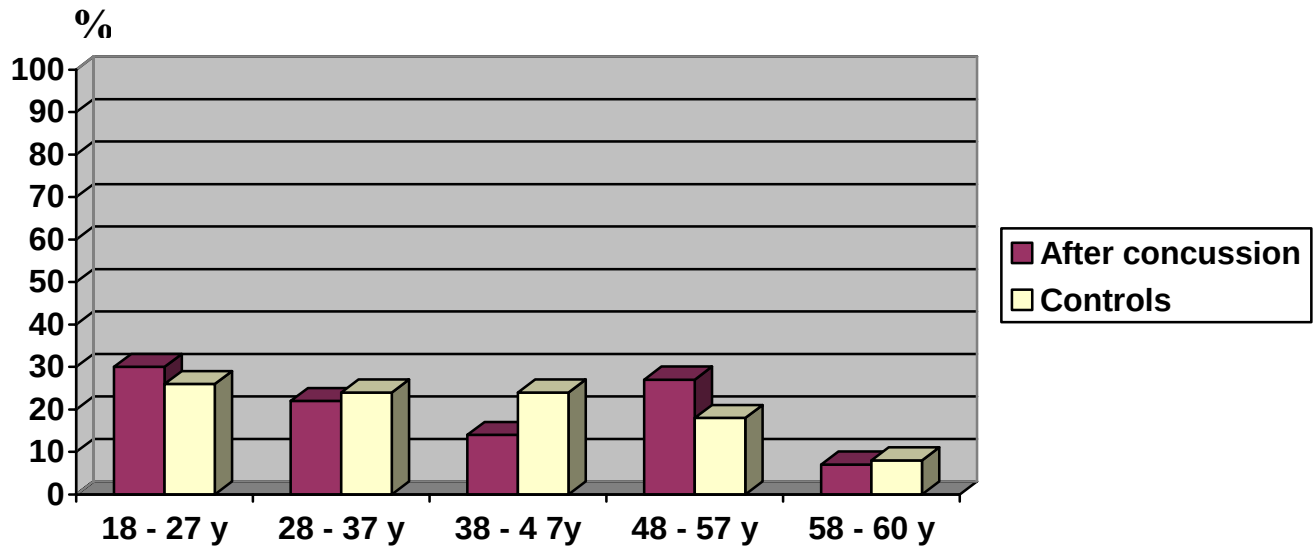


Fig. 2.1.2. Distribution of different age groups of female subjects after concussion and in controls.

Table 2.1.1. Demographic characteristics of patients who have suffered a concussion and in non-head injured controls

Participants	Concussion (n = 217) n (%)	Controls (n = 221) n (%)	*p*-Value[a]
Sex			
Male	144 (66.4)	145 (65.6)	0.95
Female	73 (33.6)	76 (34.4)	
Mean (SD), age (years)			
Men	33 (13)	33 (13)	0.87 [b]
Women	38 (14)	38 (14)	0.93 [b]
Education			
Primary school	10 (4.6)	8 (3.6)	0.78
Secondary school	60 (27.6)	61 (27.6)	0.92
Practical education/	81 (37.3)	78 (35.3)	0.73
Professional school			
University graduate	32 (14.7)	41 (18.6)	0.35
University uncompleted	22 (10.1)	16 (7.2)	0.36
Others	12 (5.5)	17 (7.7)	0.47
Unemployment	50 (23.0)	36 (16.3)	0.09
Marital status			
Single	59 (27.2)	44 (19.9)	0.09
Living with partner	16 (7.4)	17 (7.7)	0.96
Married	85 (39.2)	110 (49.8)	0.03
Widowed	7 (3.2)	8 (3.6)	0.97
Divorced	33 (15.2)	22 (10.0)	0.13
Other	17 (7.8)	20 (9.0)	0.78

[a] χ^2 – test with Yates' correction;

[b]Two-sided Student's t-test.

2. 2. Headache

Of the CPAs significantly less (44.2%; 96 of 217) stated that they had had headache in the year before the concussion compared to 71.9% (159 of 221) of the controls ($p < 0.02$). This difference related mainly to infrequent headache. Because of this considerable underreporting of pre-accident headache in the concussion group it was considered inappropriate by use of McNemar's test to evaluate the impact of concussion on occurence of any headache.

After concussion, acute headache was reported by 176 individuals (81.1%) (Fig 2.2.1). Of these, 54 (24.9% of all concussion patients) stated that this headache still was present at the time they answered the first questionnaire and 23 (11.5%) reported persisting headache after three months. Only 15 individuals (7.8%) that had reported persisting posttraumatic headache in the first questionnaire and after three months reported persisting headache also after one year. Elleven of them had had headache before the concussion. The other four who did not report any pretraumatic headache had only headache on 1-7 days per month.

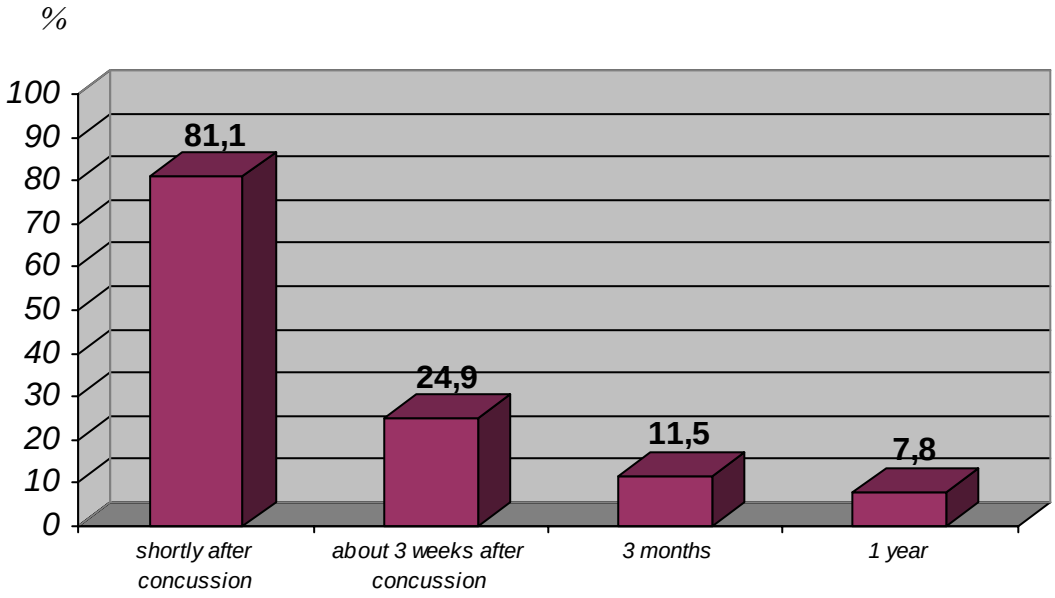


Fig. 2.2.1. Prevalence of posttraumatic headache appearing acute and persisting at different times after concussion.

Only one of the CPAs and one of the controls that did not report any headache in the year before the trauma reported daily headache after one year.

The prevalence of headache of any frequency after 3 months was 65.5% (131 of 200) in concussion patients and 59.5% (125 of 210) in controls (p = 0.25) (table 2.2.1). Frequent headache (more than seven days per month) was found in 21.0% (42 of 200) concussion patients as compared to 13.3% (28 of 210) in controls (p = 0.053). Prevalence of headache occurring every day was 7.0% (14 of 200) in concussion patients and 4.8% (10 of 210) in controls (p = 0.45). After 1 year, 64.6% (124 of 192) of concussion patients and 64.2% (138 of 215) of controls reported any headache (p = 0.98). Frequent headache was found in 20.8 % (40 of 192) concussion patients as compared to 14.9% (32 of 215) in controls (p = 0.15). Prevalence of headache occurring every day was after 1 year 4.2% (8 of 192) in concussion patients and 6.0% (13 of 215) in controls (p = 0.53). Concussion patients had after 3 months an average VAS score of 37 (SD 26) as compared to 34 (SD 27) in controls (p = 0.14) (table 2.5.1). After one year, the corresponding figure was a score of 38 (SD 27) versus 37 (SD 28) (p = 0.84).

Table 2.2.1. Headache 3 months and 1 year after the trauma in patients who have suffered a concussion and in non-head injured controls

Frequency of headache	Concusssion After 3 months (n = 200) n (%)	Controls After 3 months (n = 210) n (%)	*p* Value[a]	Concusssion After 1 year (n = 192) n (%)	Controls After 1 year (n = 215) n (%)	*p* Value[a]
Headache during last month	131 (65.5)	125 (59.5)	0.25	124 (64.6)	138 (64.2)	0.98
No headache	69 (34.5)	85 (40.5)		68 (35.4)	77 (35.8)	
Headache						
1-7 days	89 (44.5)	97 (46.2)		84 (43.8)	106 (49.3)	
8-14 days	21 (10.5)	15 (7.1)	0.053[b]	25 (13.0)	14 (6.5)	0.15[b]
> 14 days	7 (3.5)	3 (1.4)		7 (3.6)	5 (2.3)	
every day	14 (7.0)	10 (4.8)		8 (4.2)	13 (6.0)	

a χ^2- test with Yates' correction, after concussion vs. controls;

[b] - Frequent headache (> 7 days per month) during the last month.

2.3. Dizziness

In the first questionnaire, 77.0% of CPAs reported that they had experienced dizziness shortly after the concussion. Of these, 53 (24.4% of all CPAs) stated that this dizziness still was present and 23 (11.5%) reported persisting dizziness after three months. Only 13 individuals (6.7%) that had reported persisting posttraumatic dizziness in the first questionnaire and after three months reported persisting dizziness also after one year (fig.2.3.1).

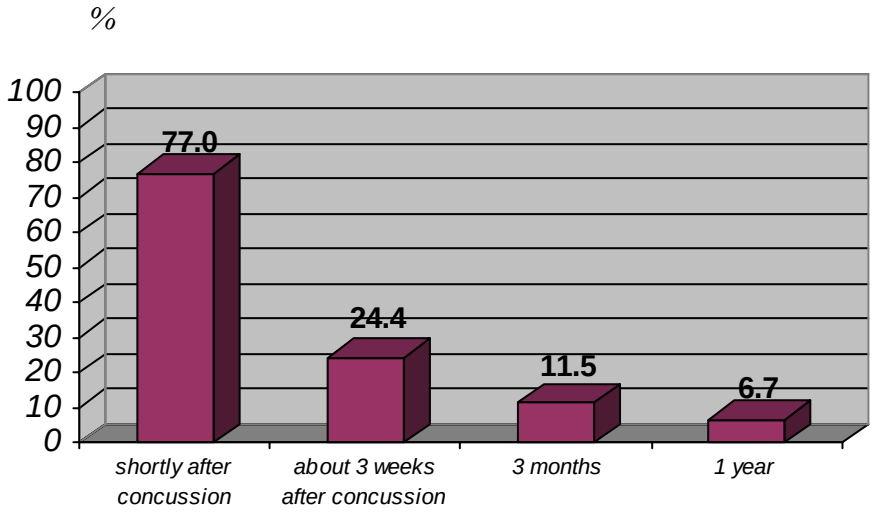


Fig. 2.3.1. Prevalence of dizziness appearing acute and persisting at different times after concussion.

Of the CPAs, 38.7% (84 of 217) stated that they had experienced dizziness in the year before the concussion compared to 54.3% (120 of 221) of the controls. This difference was statistically significant ($p < 0.002$). Because of this considerable underreporting of pre-accident dizziness in the concussion it was considered inappropriate by use of McNemar's test to evaluate the impact of concussion on occurrence of any dizziness.

The prevalence of any dizziness after 3 months was 63.0% (126 of 200) in concussion patients and 46.4% (97 of 209) in controls ($p = 0.001$ (table 2.3.1). Daily dizziness was found in 6.5% (13 of 200) of concussion patients as compared with 5.3% (11 of 209) of controls ($p = 0.75$). After 1 year, 62.0% (119 of 192) of concussion patients and 49.8% (107 of 215) of controls ($p = 0.02$) reported on any dizziness. Daily dizziness at the same time was reported by 6.8% (13 of 192) of concussion patients and 4.7% (10 of 215) of controls ($p = 0.48$). Concussion patients had after 3 months an average VAS score for dizziness of 38 (SD 28) as compared to 28 (SD 27) in controls ($p < 0.001$) (table 2.5.1). After one year, the corresponding figure was a score of 34 (SD 29) versus 29 (SD 27) ($p = 0.18$).

Table 2.3.1. Dizziness 3 months and 1 year after the trauma in patients who have suffered a concussion and in non-head injured controls

Frequency of dizziness	Concussion After 3 months (n = 200) n (%)	Controls After 3 months (n = 209) n (%)	*p* Value[a]	Concussion After 1 year (n = 192) n (%)	Controls After 1 year (n = 215) n (%)	*p* Value[a]
No dizziness	74 (37.0)	112 (53.6)	0.001	73 (38.0)	108 (50.2)	0.02
Dizziness						
Once per week or less	63 (31.5)	57 (27.3)	0.41	67 (34.9)	59 (27.4)	0.13
Several times per week	44 (22.0)	24 (11.5)	0.006	34 (17.7)	31 (14.4)	0.44
Daily	13 (6.5)	11 (5.3)	0.75	13 (6.8)	10 (4.7)	0.48
Others	6 (3.0)	5 (2.4)	0.94	5 (2.6)	7 (3.3)	0.92

a - χ^2 test with Yates' correction.

2. 4. Cognitive dysfunction

The prevalence of constant memory problems after 3 months was 5.6% (11 of 197) in concussion patients and 3.8% (8 of 208) in controls (p = 0.55) (table 2.4.1). After 1 year the corresponding figure was 11.5% (22 of 191) in concussion patients and 7.9% (17 of 215) in controls (p = 0.29). The prevalence of constant severe concentration problems after 3 months was 4.1% (8 of 197) in concussion patients and 2.9% (6 of 208) in controls (p = 0.71 (table 2.4.1). After 1 year, 5.2% (10 of 191) of concussion patients and 2.3% (5 of 215) of controls reported on constant severe concentration problems (p = 0.20). Concussion patients had after 3 months an average VAS score for memory problems of 46 (SD 32) as compared to 31 (SD 27) in controls (p < 0.001) (table 2.5.1). After one year, the corresponding figure was a score of 45 (SD 32) versus 35 (SD 30) (p = 0.01). Concussion patients had after 3 months an average VAS score for concentration problems of 41 (SD 28) as compared to 33 (SD 25) in controls (p = 0.01) (table 2.5.1). After one year, the corresponding figure was a score of 42 (SD 29) versus 34 (SD 26) (p = 0.01).

Table 2.4.1. Cognitive (memory and concentration) problems 3 months and 1 year after trauma in patients who have suffered a concussion and in non-head injured controls

Subjective cognitive dysfunction	Concussion After 3 months (n = 197) n (%)	Controls After 3 months (n = 208) n (%)	*p* Value[a]	Concussion After 1 year (n = 191) n (%)	Controls After 1 year (n = 215) n (%)	*p* Value[a]
Memory						
No memory problems	71 (36.0)	129 (62.0)	< 0.001	70 (36.6)	115 (53.5)	< 0.001
Sporadic memory problems	115 (58.4)	71 (34.1)	< 0.001	99 (51.8)	83 (38.6)	0.01
Constant memory problems	11 (5.6)	8 (3.8)	0.55	22 (11.5)	17 (7.9)	0.29
Concentration						
No concentration problems	57 (28.9)	88 (42.3)	0.006	55 (28.8)	84 (39.1)	0.04
Sporadic concentration problems	112 (56.9)	107 (51.4)	0.32	101 (52.9)	112 (52.1)	0.95
Constant slight concentration problems	20 (10.2)	7 (3.4)	0.01	25 (13.1)	14 (6.5)	0.04
Constant severe concentration problems	8 (4.1)	6 (2.9)	0.71	10 (5.2)	5 (2.3)	0.20

a - χ^2 test with Yates' correction, after concussion vs. controls.

2. 5. VAS scores of other symptoms of the postconcussion syndrome

Concerning the degree of other symptoms, after 3 months significant more complaints were reported by concussion patients for fatigue ($p = 0.002$), buzzing in the ears ($p = 0.001$), sleep problems ($p = 0.003$), depression ($p = 0.007$), anxiety ($p = 0.02$), alcohol intolerance ($p = 0.01$), worry about complaints ($p = 0.006$) and worry about brain injury ($p < 0.001$) (table 2.5.1). There were insignificant differences for irritability, nausea, tiredness, phonophobia, tendency to cry, and neck pain. After 1 year, significant more complaints were reported by concussion patients for tiredness ($p = 0.01$) and worry about brain injury ($p < 0.001$). There were insignificant differences for fatigue, irritability, nausea, phonophobia, buzzing in the ear, sleep problems, tendency to cry, anxiety, alcohol intolerance, neck pain, and worry about complaints. There was a borderline significance for difference in VAS score of depression ($p = 0,05$).

After three months, only two CPAs and three controls had a combination of the six core symptoms of PCS, if the requirement was that all these symptoms had to be significant according to our definition. After one year, one CPA and one control had this symptom combination

According to the first questionnaire four of the six core symptoms (headache, memory problems, concentration problems and dizziness) attributed to PCS had significantly higher VAS scores in CPAs than in controls whereas fatigue and irritability scores were not significantly different.

Table 2.5.1. Visual analogue scale of different symptoms attributed to the postconcussion syndrome 3 months and 1 year after the trauma in patients who have suffered a concussion and in non-head injured controls

Symptom	Concussion After 3 months (n = 200) m (SD)	Controls After 3 months (n = 210) m (SD)	*p* Value[a]	Concussion After 1 year (n = 192) m (SD)	Controls After 1 year (n = 215) m (SD)	*p* Value[a]
Headache	37 (26)	34 (27)	0.14	38 (27)	37 (28)	0.84
Memory problems	46 (32)	31 (27)	< 0.001	45 (32)	35 (30)	0.01
Concentration problems	41 (28)	33 (25)	0.01	42 (29)	34 (26)	0.01
Dizziness	38 (28)	28 (27)	< 0.001	34 (29)	29 (27)	0.18
Fatigue	50 (28)	41 (29)	0.002	50 (30)	44 (28)	0.08
Irritability	58 (32)	58 (32)	0.28	58 (31)	54 (29)	0.40
Nausea	25 (25)	23 (25)	0.39	27 (28)	25 (26)	0.88
Tiredness	54 (30)	51 (26)	0.25	55 (28)	49 (25)	0.01
Phonophobia	51 (31)	46 (28)	0.11	48 (31)	46 (28)	0.73
Buzzing in the ears	27 (27)	19 (23)	0.001	26 (27)	20 (22)	0.06
Sleep problems	43 (30)	34 (30)	0.003	42 (32)	37 (31)	0.15
Tendency to cry	37 (33)	36 (32)	0.78	40 (33)	33 (33)	0.12
Depression	46 (30)	38 (27)	0.007	49 (30)	40 (28)	0.05
Anxiety	43 (31)	36 (29)	0.02	43 (31)	37 (28)	0.18
Alcohol intolerance	33 (31)	25 (29)	0.01	31 (31)	26 (28)	0.17
Neck pain	32 (25)	32 (27)	0.97	33 (27)	29 (27)	0.57
Worried about complaints	47 (32)	38 (29)	0.006	44 (32)	38 (29)	0.34
Worried about brain injury	48 (32)	30 (30)	< 0.001	45 (33)	29 (30)	< 0.001

VAS scores between “no” and “much”: 0 – 100;

a - Two-sided Student’s t-test (unequal variances).

2. 6. Comparison of severity of symptoms 1 year after the trauma between concussion patients and controls in relation to marital status and education

After 1 year, unmarried and low educated people with concussion did not report significant more problems for any of the symptoms attributed to the postconcussion syndrome as compared to controls (tables 2.6.1 and 2.6.2). Married people with concussion reported a significant higher degree than controls of memory problems, concentration problems, dizziness, buzzing in the ear, tendency to cry, depression and worry about brain injury (table 2.6.1). Higher educated people with concussion reported a significant higher degree than controls of memory problems, concentration problems, dizziness, fatigue, nausea, tiredness, buzzing in the ear, tendency to cry, depression, anxiety, alcohol intolerance, worry about complaints and worry about brain injury (table 2.6.2).

Married people with concussion tended to worry more about brain injury than the unmarried, but the difference was insignificant ($p = 0.18$) (not in table).

Table 2.6.1. Visual analogue scale (VAS) scores of different symptoms attributed to the postconcussion syndrome in relation to marital status 1 year after the trauma in patients who have suffered a concussion and in non-head injured controls

Symptom	Concussion After 1 year married (n = 75) m (SD)	Controls After 1 year married (n = 108) m (SD)	*p* Value[a]	Concussion After 1 year unmarried (n = 117) m (SD)	Controls After 1 year unmarried (n = 107) m (SD)	*p V*alue [a]
Headache	41 (25)	34 (28)	0.10	37 (28)	39 (29)	0.47
Memory problems	49 (32)	33 (28)	< 0.001	43 (31)	37 (31)	0.18
Concentration problems	43 (30)	30 (23)	0.002	42 (29)	37 (28)	0.27
Dizziness	36 (27)	25 (26)	0.01	32 (29)	34 (28)	0.74
Fatigue	51 (30)	45 (27)	0.17	49 (30)	42 (29)	0.11
Irritability	59 (31)	53 (27)	0.17	58 (30)	56 (30)	0.59
Nausea	32 (28)	29 (26)	0.42	26 (29)	27 (28)	0.70
Tiredness	58 (27)	53 (23)	0.16	54 (30)	46 (27)	0.04
Phonophobia	52 (29)	48 (26)	0.34	45 (32)	44 (30)	0.86
Buzzing in the ears	28 (29)	19 (22)	0.02	25 (26)	20 (23)	0.17
Sleep problems	44 (33)	37 (29)	0.12	40 (31)	37 (33)	0.48
Tendency to cry	43 (33)	33 (33)	0.04	37 (34)	34 (34)	0.49
Depression	48 (31)	38 (27)	0.02	49 (30)	42 (29)	0.10
Anxiety	46 (31)	37 (29)	0.07	42 (31)	37 (27)	0.23
Alcohol intolerance	30 (28)	27 (28)	0.46	31 (33)	25 (29)	0.14
Neck pain	32 (28)	29 (26)	0.42	33 (27)	30 (28)	0.33
Worried about complaints	47 (32)	37 (29)	0.05	42 (33)	39 (29)	0.53
Worried about brain injury	48 (33)	28 (29)	< 0.001	43 (34)	30 (31)	0.003

VAS scores between “no” and “much”: 0 – 100;

a - two-sided Student’s t-test (unequal variances).

Table 2.6.2. Visual analogue scale (VAS) scores of different symptoms attributed to the postconcussion syndrome in relation to education 1 year after the trauma in patients who have suffered a concussion and in non-head injured controls

Symptom	Concussion After 1 year Higher education (n = 98) m (SD)	Controls After 1 year Higher education (n = 118) m (SD)	*p V*alue[a]	Concussion After 1 year Lower education (n = 94) m (SD)	Controls After 1 year Lower education (n = 97) m (SD)	*p* Value[a]
Headache	39 (26)	35 (26)	0.27	37 (28)	38 (30)	0.76
Memory problems	47 (30)	32 (28)	0.0001	43 (32)	39 (31)	0.42
Concentration problems	44 (29)	32 (26)	0.001	40 (30)	36 (26)	0.31
Dizziness	36 (26)	25 (25)	0.003	32 (30)	34 (29)	0.54
Fatigue	52 (30)	42 (27)	0.01	47 (30)	45 (29)	0.72
Irritability	60 (29)	54 (28)	0.13	57 (32)	55 (30)	0.68
Nausea	30 (29)	22 (24)	0.03	23 (28)	27 (28)	0.34
Tiredness	61 (28)	51 (25)	0.01	50 (28)	47 (26)	0.39
Phonophobia	50 (30)	48 (27)	0.71	46 (31)	44 (30)	0.67
Buzzing in the ears	28 (28)	17 (20)	0.001	24 (26)	22 (24)	0.72
Sleep problems	42 (31)	36 (30)	0.18	42 (33)	38 (33)	0.43
Tendency to cry	44 (32)	35 (34)	0.048	34 (34)	31 (32)	0.48
Depression	50 (29)	40 (29)	0.01	47 (31)	41 (27)	0.15
Anxiety	47 (30)	36 (27)	0.008	40 (31)	39 (28)	0.78
Alcohol intolerance	33 (31)	25 (29)	0.03	28 (30)	28 (28)	0.99
Neck pain	33 (28)	28 (24)	0.16	33 (26)	32 (29)	0.71
Worried about complaints	45 (31)	34 (29)	0.01	43 (34)	43 (29)	0.91
Worried about brain injury	45 (32)	26 (29)	< 0.0001	45 (34)	32 (31)	0.01

VAS scores between “no” and “much”: 0 – 100;

a - two-sided Student’s t-test (unequal variances).

2.7. Diagnosis of postconcussion syndrome by use of Rivermead postconcussion symptom questionnaire

The PCS has been considered to be present when 3 or more symptoms listed in the Rivermead postconcussion symptom questionnaire (RPQ) with the rating 2, 3 or 4 are present (WHO: ICD-9) (Ingebrigsten *et al*, 1998). Ratings of 1 are excluded because these indicate that the symptoms have resolved. When using this definition, 72% of the CPAs had a PCS diagnosis according to the first questionnaire which was sent 2 weeks after the trauma. According to the questionnaires sent after 3 months, 76% of CPAs had a PCS. After 1 year as many as 78% of CPAs had PCS. However, also the controls had high prevalences of PCS according to the RPQ criteria, although they had not suffered a concussion. According to the first questionnaire, 34% of controls reported on change in the symptoms that qualified them for the diagnosis of PCS. After 3 months, as many as 48% had a PCS according to the RPQ criteria. After 1 year, still 46% of controls had change of symptoms that qualified for a diagnosis of PCS.

2. 8. Influence of duration of unconsciousness, anterograde amnesia and other variables on the severity of headache and cognitive dysfunction

For multiple regression analysis on influence of duration of unconsciousness, anterograde amnesia and other variables on the severity of headache and cognitive dysfunction, the final model p-values are shown in the table 2.8.1.

R-squared is the proportion of variance explained by the model. R-squared is rather low in all models, thus only a small part of the variance in headache and cognitive dysfunction was explained by the chosen explanatory variables. Although the models for this reason can not be applied for prediction purposes, several associations are statistically significant. On the other hand, interpretation of the results must be made with caution. When multiple variable selection is performed in multiple regression (for example by backwards elimination), a risk of false positive findings (false significant predictors) is present due to multiple testing.

Full statistical printout of the final general linear regression models is given in Appendix 1: When no categorical variables are left in the model, Student's t-test is displayed instead of the F-test. Beta (regression coefficients) can only be estimated in models were all categorical models have been removed, see for example "Memory problems (1 yr)" below. In models with remaining categorical variables, the association between dependent and independent variables is measured by SYSTAT with the F-test. F values and degrees of freedom (sometimes requested by reviewers) have not been included in tables, however.

Univariate regression analysis printouts (including regression coefficients) are given in Appendix 2 for selected variables:

- concentration versus length of education
- memory versus length of education
- headache versus length of education
- headache versus duration of unconciousnesse

For the same selected variables scatter plots are presented in figures 2.8.1 - 4.

Headache shortly after the accident and after 3 months but not after one year seemed to be of less severity when duration of unconsciousness was longer. There was no significant association between the degree of cognitive dysfunction (memory and/or concentration problems) and duration of unconsciousness or anterograde amnesia at any time. Neither was there any correlation between headache or cognitive dysfunction and the type of trauma when comparing assault with other mechanisms except for headache after 3 months which was slightly more present ($p = 0.04$) in those who had a concussion caused by assault. There was no correlation with age except for memory problems after 1 year ($p = 0.01$). No association was found between length of education and cognitive dysfunction, but after 20 days and after 3 months, subjects with higher education had significantly less headache than subjects with shorter education ($p = 0.01$; $p = 0.003$). Headache and cognitive dysfunction correlated at each interview time with sex, females reporting more problems than males. There were, however, significant differences only for memory problems and concentration problems after 3 months ($p = 0.04$; $p = 0.01$) and for concentration problems after 1 year ($p < 0.01$). There were no significant associations between weight and headache or cognitive dysfunction except for significantly less memory problems after 1 year ($p = 0.01$) and significantly less concentration problems after 20 days ($p = 0.01$) in people with higher weight (coefficient of correlation (COC) for memory problems: ÷ 0.17 ($p = 0.02$) and COC for concentration problems: ÷ 0.15 ($p = 0.047$)).

Table 2.8.1. Backward multiple regression models for CPAs with R-squared-(italics) and p-values. Analysis was made for VAS scores of headache and cognitive dysfunction at different times after the accident as the dependent variables and sex, age, duration of unconsciousness, trauma mechanism (assault or other) length of education, height, weight, and anterograde amnesia as independent variables

Symtoms at different time periods after trauma	*R-squared*	Sex	Age	Unconsciousness (duration)	Trauma mechanism (assault/other)	Length of education	Weight
Headache (20 days)	*0.08*	0.03		0.03	0.12	0.01	
Headache (3 months)	*0.13*	0.001		0.02	0.04	0.003	
Headache (1 year)	*0.08*	0.001	0.14		0.14	0.06	
Memory problems (20 days)	*0.02*	0.08				0.14	
Memory problems (3 months)	*0.03*	0.04				0.10	
Memory problems (1 year)	*0.06*		0.01			0.16	0.01
Concentration problems (20 days)	*0.03*						0.01
Concentration problems (3 month)	*0.04*	0.01				0.06	
Concentration problems (1 year)	*0.06*	0.00					

Note: variables with $p > 0.20$ were removed by backward regression. Anterograde amnesia and height were associated with $p > 0.20$ in all regressions, hence these explanatory were dropped from every model and do not appear in the table.

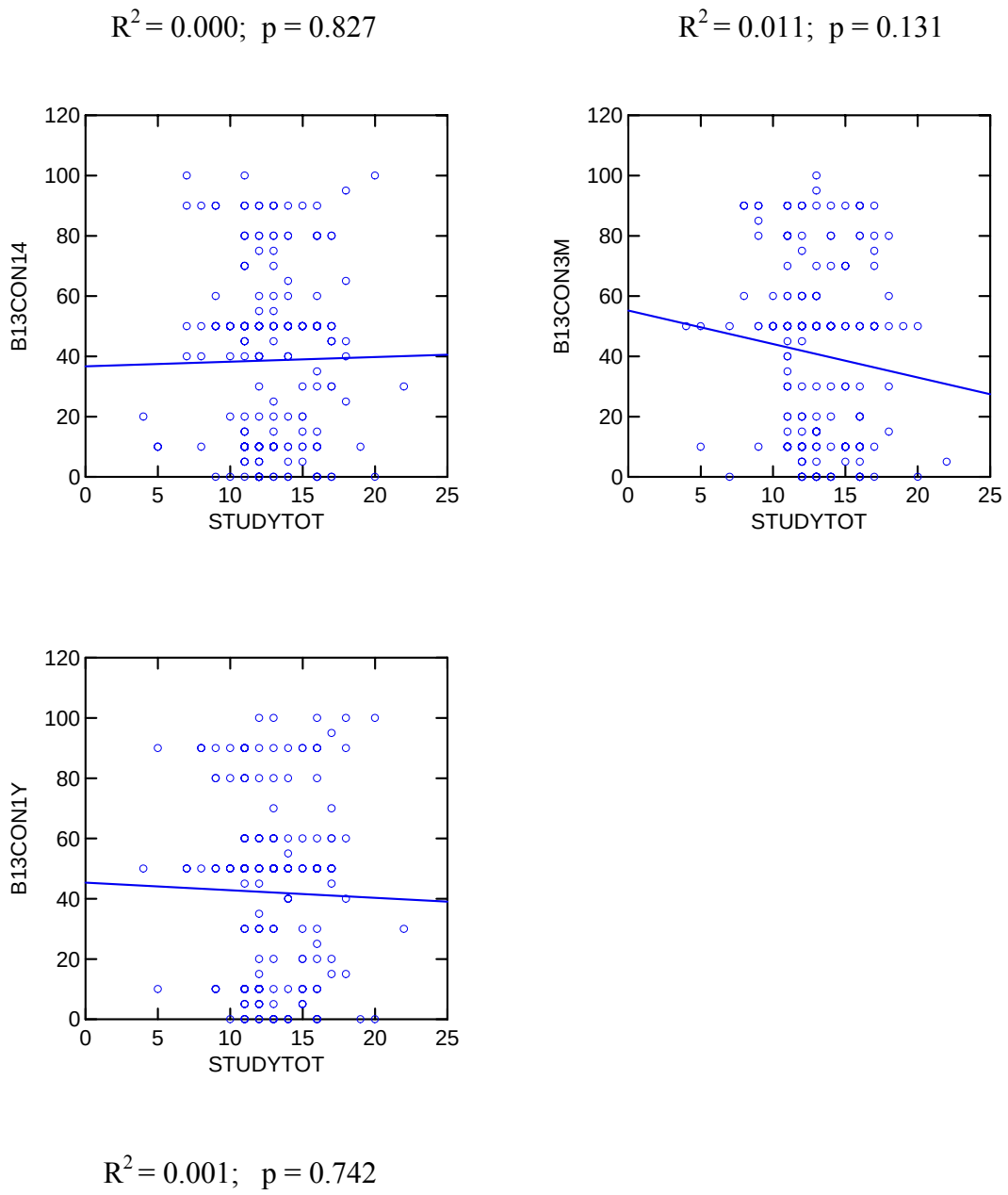
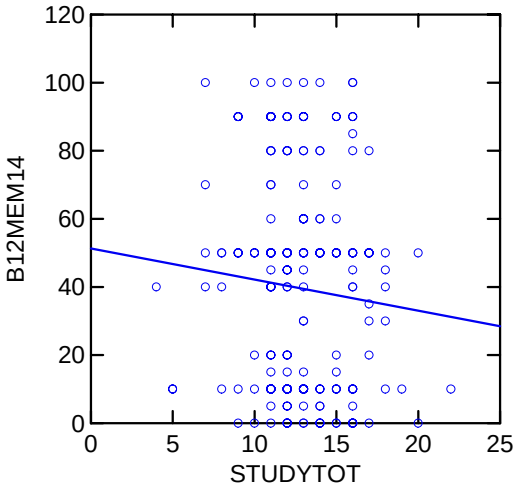


Fig. 2.8.1. Scatter plots with regression lines of severity of concentration problems versus length of education shortly after concussion (top left), after 3 months (top right) and after 1 year (below)

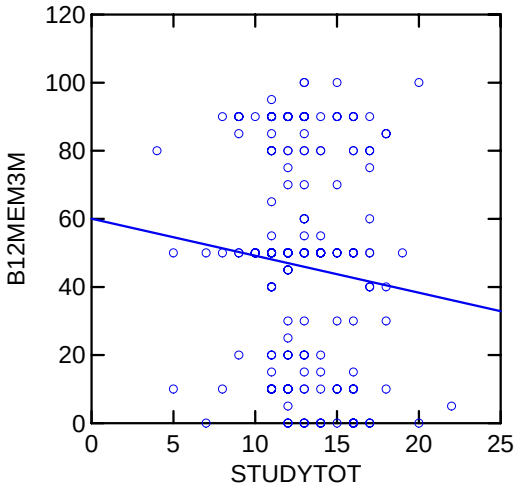
Y- Axis: Visual analogue scale scores of severity of concentration problems

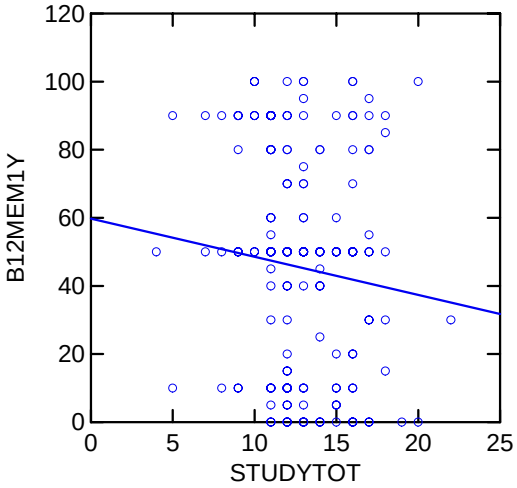
X- axis: Length of education in years

$R^2 = 0.007$; $p = 0.224$



$R^2 = 0.009$; $p = 0.185$





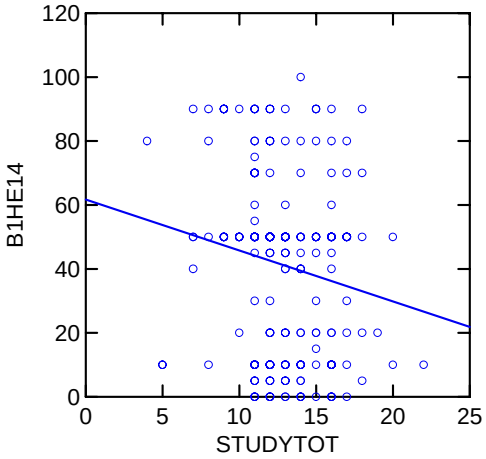
$R^2 = 0.010$; $p = 0.169$

Fig 2.8.2. Scatter plots with regression lines of memory problems versus length of education shortly after concussion (top left), after 3 months (top right) and after 1 year (below)

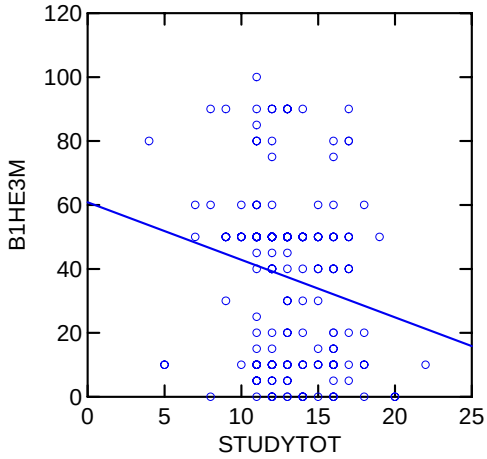
Y-axis: Visual analogue scale scores of memory problems

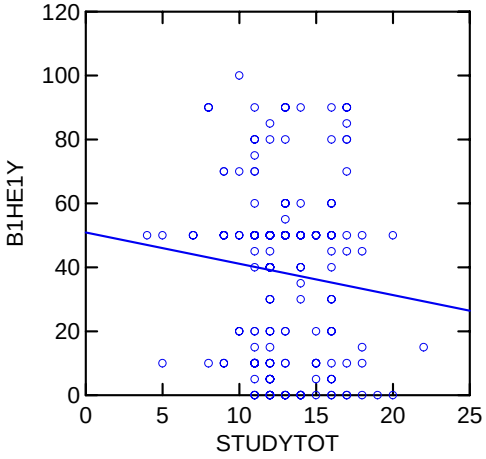
X-axis : Length of education in years

$R^2 = 0.027$; $p = 0.015$



$R^2 = 0.037$; $p = 0.006$





$R^2 = 0.011$; $p = 0.156$

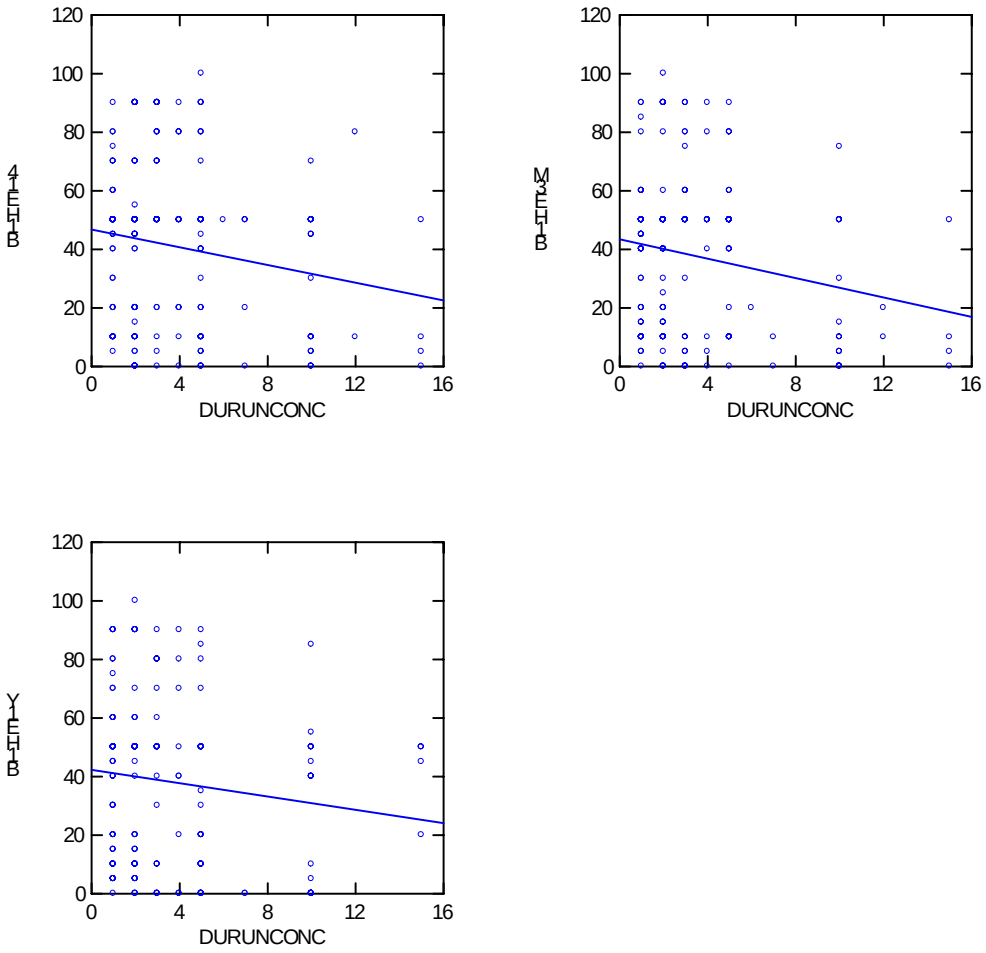
Fig. 2.8.3. Scatter plots with regression lines of headache versus length of education shortly after concussion (top left), after 3 months (top right) and after 1 year (below)

Y-axis: Visual analogue scale scores of headache

X-axis : Length of education in years

$R^2 = 0.031$; p=0.010

$R^2 = 0.040$; p = 0.005



$R^2 = 0.017$; p = 0.068

Fig. 2.8.4. Scatter plots with regression lines of headache versus duration of unconsciousness shortly after concussion (top left), after 3 months (top right) and after 1 year (below)

Y-axis: Visual analogue scale scores of headache

X-axis : Duration of unconsciousness in minutes

VII. Discussion

Historical cohort study

The main advantage of performing this study in Lithuania is that in this country few individuals expect persistent symptoms following a concussion. In a Lithuanian/Canadian cooperation study it was found that many Edmontonians anticipated symptoms of PCS to last months to years but considerably fewer Lithuanian subjects from Kaunas selected any symptoms as persisting in a chronic manner (Ferrari, Obelieniene *et al*., 2001). For example, headache was expected to last for months or years by 23% of Lithuanian subjects and 45% of Edmontonians. The corresponding figures for concentration difficulties were 10% versus 38%, for dizziness 19% versus 41% and for memory problems concerning different tasks 0-3% versus 9-17% (Ferrari, Obelieniene *et al*., 2001).

In Lithuania, there is also little possibility of financial compensation, the main reason being that the newly established insurance companies do not pay compensation for chronic subjective symptoms after concussion. Possibilities of receiving monetary compensation directly from an usually equally poor offender are minimal and none of the Lithuanian researchers who participated in the studies can remember having heard of a case where money was paid to a concussion victim because of chronic postconcussive symptoms. For this reason, the already extensive questionnaires in both the historical and prospective study did not contain questions whether the traumatized patients were seeking and/or awarded economical compensation.

A problem in the historical study was that no imaging studies such as CT and MRI were done which could document that there were no morphological lesions in addition to the clinical entity of concussion.

According to the Swedish Council on Technology Assessment in Health Care (SBU report, 2000) about 9% of all patients that attend to the hospital with concussion have pathological findings on CT. Thus an estimated maximum of about 18 patients in the present study would be expected to have morphological traces in the cerebral tissue on

CT. Conceivably, the inclusion of these patients in our study could introduce a bias if they developed more chronic subjective symptoms than patients without visible lesions on CT. Such bias could then significantly increase the symptom-pool in the concussion group compared to non-head injured controls. This was, however, not the case. Furthermore, we are not aware of any earlier study that has shown a consistent dose-response relationship between the degree of brain injury and the set of chronic subjective symptoms connected with PCS.

The results of our study show that the majority of subjective symptoms attributed to PCS are found at similar rates in subjects who had a concussion and in a control group with mild non-head injuries. Notably, headache, the most common and predominant symptom of persistent PCS (Alexander, 1995; Martelli *et al*., 1999; Packard, 1999) had almost identical prevalence and frequency distribution. These results are in line with the results in a recent Lithuanian study on the prevalence, course and clinical features of PCS in children (Nečajauskaitė *et al*., 2005). In this study, the symptoms in 102 matched pairs of a group of children who had experienced a single concussion and a control group of children with other mild body injury without a head trauma were analyzed one to 5 years after the trauma (median: 27 months). The results showed that the prevalence of headache, irritability, fears, sleep disorders, learning difficulties, as well as concentration and memory problems did not differ significantly between the groups.

It is interesting that all patients with concussion remembered that they had acute posttraumatic headache, but this headache had in 96% of cases disappeared within one month. Disappearance of posttraumatic headache was even reported by patients who had frequent headache at the time of the interview, indicating that the patients could differentiate the acute trauma-induced headache from their spontaneous headache. On the basis of these results, one must question the assumption that chronic posttraumatic headache with reported incidences as high as 44% after 6 months (de Benedittis and Santis, 1983) and 20% after 4 years (Keidel and Diener, 1997) in western countries is causally related to the head trauma.

In both groups, headache was more prevalent and frequent than headache reported by control groups taken at random from the general population register of the Kaunas region in previous whiplash studies (Schrader *et al*., 1996; Obelieniene *et al*., 1999). In

theses studies the prevalence of headache occurring in more than seven days per month was 6% in the general population, whereas it was 19% and 18% in the present patients and control groups. This underscores the necessity of using an adequate comparison group and the importance of not restricting comparisons to uninjured controls (Satz *et al.*, 1999). Hypothetical explanations for the difference are general effects of injury, or alternatively, that subjects having an accident as a group have different personality characteristics as compared to other populations. The fact that headache seems to be more prevalent in people with lower socio-economic status (Stewart *et al*., 1992; Hasvold *et al*., 1996; Hagen *et al.*, 2002) and that the educational level in both groups of the present study was lower than that in the uninjured controls in the whiplash studies would favor the latter hypothesis. Another supportive reason is that psychopathology may predispose to injuries (Jin *et al*., 1991; Poole *et al*., 1997; Ponzer *et al.*, 1999) and that there is comorbidity for psychiatric diseases and headache (Guidetti *et al*., 1998; Lake *et al.*, 2005). However, as the design of the present study did not allow for an assessment of premorbid psychiatric problems, a definite answer concerning the causes for the observed high prevalence and frequency of headache in both injury groups can not be given.

In previous studies in western countries little effort has been made to quantify posttraumatic headache. This precludes a direct comparison between the prevalence of various headache frequencies found in the present study and that reported. It seems, however, that reported high incidences of posttraumatic headache (de Benedittis and Santis, 1983; Mittenberg *et al*, 1992; Keidel and Diener, 1997) in western societies are of similar magnitude as in Lithuania. It is thus likely that the headache has the same non-traumatic etiology (i.e. no evidence of cranial damage) in Lithuania as, for example, in North America. In western societies, however, the headache is frequently attributed to the head injury. This may be explained by underreporting or underestimation of pre-injury headache (Mittenberg *et al*., 1992), or by amplification of symptoms due to fear, negative expectation and the possibilities of secondary gain. Underestimation of pre-injury symptoms may also have occurred in the injured subjects of the present study (cf. Tables 1.2.1 and 1.4.1), but with regard to headache and cognitive dysfunction considerably less than in a North American head-injury population (Mittenberg *et al*., 1992). The reason for this difference in underestimation or underreporting of pre-injury symptoms between

Lithuanians and North Americans is uncertain. Hypothetically, in traumatized Lithuanians underestimation may be due to recall bias only whereas additional factors including possibilities for secondary gain may be involved when North Americans report their pre-injury symptoms.

There is an ongoing discussion about the etiology of chronic headache after head trauma (Warner, 2000; Saper, 2000; Hachinski, 2000; Evans, 2004) and whether the features of posttraumatic headaches are different from or identical to those of the natural occurring headaches (Haas, 1996; Couch and Bearss, 2001; Haas *et al.*, 2004). Analyses of headache types in the present study showed no difference for any headache category between those who sustained a concussion and the non-head-injured controls. This is in agreement with a study in which characteristics and accompaniments of chronic posttraumatic headache within each diagnostic group were compared to those in a control group (Haas, 1996). No notable differences between the posttraumatic and control group was found. The same author later performed a study in which it was demonstrated that even chronic headaches related to physically injurious traumatic events that did not include head trauma were, as a group, similar to those after head trauma (Haas, 2004).

According to the VAS scores, the head-injured subjects reported more depression than the controls. Depression is frequently reported following minor head or brain injury (Busch and Alpern, 1998, Levin *et al.*, 2005; Ruttan and Heinrich, 2003) and major depression has been reported to occur in as many as 15% of mild head injured subjects. While the observed difference between the head-injured subjects and controls in the present study may suggest an aetiological role of the brain injury itself, it may also be accounted for by greater psychosocial problems in the head-injury group, cf. the higher rate of unemployment, divorcees, widowed subjects and higher alcohol consumption, and the lower rate of unmarried individuals. It might be argued that differences in psychosocial problems relate to sequelae of brain injury. As the used questionnaires did not contain questions about the temporal relationship between marital status, unemployment and alcohol consumption on one side and time of injury on the other, no definite conclusions can be made. However, as there was no difference between the groups with regard to the majority of other symptoms attributed to the PCS, it seems unlikely that sequelae of head-injury were a major cause for the observed differences.

Another argument for that head injury itself is not responsible for differences in depression between the groups is the finding that patients with concussion are more likely to have a history of substance abuse, have a personality disorder, and be more aggressive and hostile compared with subjects without concussion and that the hostility and agression they had before concussion continue to be risk factors for suicidal behavior after their head trauma (Oquendo *et al.*, 2004).

Despite the fact that we tried various definitions and different constellations of core symptoms in order to make a diagnosis of PCS, no specific effect of the head injury was detected in the present study. Only one subject in the head injury group and three individuals in the control group satisfied a definition of persistent PCS as a cluster of significant symptoms, a fact that makes it doubtful that this condition is a clinical disease entity.

It must nevertheless be emphasized that this study does not rule out the possibility of permanent clinical consequences of mild traumatic brain injury due to concussion.

It must also be emphasized that with a historical cohort study such as the present one, one cannot precisely and reliably estimate the incidence, severity and duration of acute posttraumatic symptoms and their eventual evolution into chronicity. For such an analysis, large prospective controlled cohort studies in litigation-poor societies are needed. In studies with this design, it should be possible to determine if there are permanent sequelae. According to the results of the present study it seems probable that these sequelae have to be defined by a set of symptoms different from the traditional symptom criteria.

Prospective cohort study

As in the historical cohort study also in the prospective study an attempt was made to estimate the different symptoms associated with the PCS both in terms of frequency and severity. The majority of earlier epidemiological studies have limited their evaluation to the registration of presence and persistence of symptoms that reportedly have not been present before the concussion. Even the Rivermead Post Concussion Symptoms Questionnaire (RPQ) (King *et al*., 1995 ; Ingebrigsten *et al.,* 1998; Smith-Seemiller *et al*.,

2003) used by several investigators has a limited ability for quantification. The patients are asked to rate the degree of 16 PCS symptoms compared to premorbid levels, using only a range of values from 2 to 4 to indicate whether the symptoms experienced after the trauma is a mild, moderate or severe problem compared to similar pre-injury complaints (King *et al*., 1995). In addition, the comparison design of the RPQ makes it vulnerable to overestimation of injury effect through possibilities of negative expectation of symptoms and underestimation of pre-injury complaints. According to the RPQ results in this prospective study, an incidence of 78% of PCS was found 1 year after the concussion contrasting with the other methods used in the study to grade symptoms and to determine the incidence of PCS. As many as 47% of controls qualified for a diagnosis of PCS 1 year after a minor non-head injury underscoring that PCS symptoms are not unique to concussion. This is in line with a study in which comparison was made between patients with chronic pain and mild traumatic brain injury on the RPQ and in which no group differences were found for total RPQ scores (Smith-Semiller *et al*., 2003).

The most important observation in the prospective study was that headache, the most common and predominant symptom of persistent PCS (Alexander, 1995; Martelli *et al*., 1999), both after 3 months and after 1 year did not differ significantly in prevalence and frequency as well as in the VAS score between the head-injured participants and the non-head injured controls. An additional observation was that there was no positive dose-response relationship between the severity of the trauma (as judged by duration of unconsciousness and anterograde amnesia) and headache. On the contrary, a somewhat unexpected finding was an inverse correlation between severity of headache and the duration of these symptoms shortly after the trauma and after 3 month but not after 1 year. The reason for this inverse correlation remains unexplained.

Despite slight and insignificant differences in headache between the groups already 3 months after the accident, as many as 11.5% of the concussion patients reported persisting headache due to the head trauma after 3 months and still 7.8% after one year suggesting a possible misattribution of headache to the event. A contributing factor for misattribution may have been that the concussion patients in comparison to the controls had an underestimation of infrequent headache in the year before the accident. Also concerning dizziness, CPAs underestimated its presence before the trauma. This

underestimation of pre-injury symptoms is in accordance with the results of Mittenberg *et al*. in a North American head trauma population (Mittenberg *et al*., 1992). They administered a check-list of symptoms of the PCS to subjects who had no personal experience or knowledge of head injury. Subjects indicated their present symptoms, then imagined having suffered a mild head injury in a motor vehicle accident, and endorsed symptoms they expected to experience six months after the injury. The checklist of symptoms was also administered to a group of patients with head injuries for comparison. Imaginary concussion reliably showed expectations in controls of a coherent cluster of symptoms virtually identical to the PCS reported by patients with head trauma. Patients consistently underestimated the premorbid prevalence of these symptoms compared with the base rate in controls. The authors therefore concluded that symptom expectations appear to share as much variance with postconcussion syndrome as head injury itself. In a later study, Gunstad and Suhr (2004) corroborated the results of Mittenberg *et al.* by showing that head-injured persons and headache sufferers underestimated premorbid symptom rates relative to the baseline of controls. In both studies, underestimation of pre-injury symptoms was more pronounced than in the present investigation.

How can the phenomenon of expectation which is far more prominent in North-America compared to Lithuania, contribute to the production of PCS symptoms in Western countries? One possibility is that expectation of symptoms after concussion leads to underestimation of pre-accident complaints. Due to this underestimation, the head-injured subject erroneously experiences additional and more pronounced symptoms post-accident and consequently attributes them to the head trauma. This may happen, although, in reality, the presence and degree of postconcussional symptoms may be no more than what the person had before the trauma. Alternative possibilities and/or contributions are described in the biopsychosocial model of posttraumatic symptoms (Ferrari and Schrader, 2001). In this model, expectation will lead the injured person to become hypervigilant for symptoms, to register normal bodily sensations as abnormal, and to react to bodily sensations with affect and cognitions that intensify them and make them more alarming, ominous, and disturbing. The consequence is symptom amplification. In the setting of amplification, previously unintrusive symptoms, largely

ignored in daily life, become far more intrusive after the trauma. The patient regards them as new and attributes them to the trauma.

The second principal observation in the present study was that also several of the other symptoms attributed to PCS did not differ significantly between the groups after 3 months. After 1 year, the vast majority of symptoms did not differ significantly, corroborating the findings in the historical cohort study and once more questioning the concept of the PCS as a disease entity, at least in a persisting form. Exceptions after 1 year were slightly significant differences concerning sporadic memory problems, slight constant concentration problems and any dizziness. This contrasts with the results of the historical cohort study in which no significant differences for the same symptoms were found. In this study, presumably less awareness of symptoms after concussion was present than in the prospective study in which the participants had to be informed of the reason of the interview already from the beginning. The use of repetitive questionnaires conceivably contributed to awareness of symptoms. It is therefore suggested that negative expectation for symptoms rather than the effect of an organic brain injury was responsible for reporting of more cognitive dysfunction and dizziness by the subjects exposed to concussion. The other symptoms connected to the PCS, in particular headache and irritability, seemed to be more resistant to the effects of expectation. It may also be possible that expectation increased the experience of symptoms in both groups to a similar level except for subjective cognitive dysfunction and dizziness. These are symptoms that even laypersons would hardly attribute to minor non-head injuries. Results of a study on postconcussion syndrome symptom reporting in athletes, headache sufferers, and depressed individuals support such possibility (Gunstad and Suhr, 2001). These results suggested that the ”expectation as etiology” hypothesis may not only be applicable in the context of concussion but that, following any negative event, people may attribute all symptoms to that negative event.

One limitation for using the results of the historical cohort study for comparison of reported symptoms with those of the prospective study is that the former was conducted between 35 and 22 months after the concussion whereas the prospective study ended after 1 year. For this reason, one cannot by comparison alone exclude that persisting differences in cognitive dysfunction and, in part, dizziness, after one year was due to

organic brain injury and that these symptoms would have dissipated with time. There are, however, other results that make it questionable that persisting symptoms after 1 year indicate organic brain injury. Firstly, there was no correlation to the duration of unconsciousness or anterograde amnesia, i.e. no dose-response relationship. Secondly, reporting of cognitive dysfunction seemed to be dependent upon marital status and/or educational level as unmarried people and/or people on a lower educational level did not have significant differences for these symptoms. The reason for this is uncertain. Since married people after concussion according to the prospective study tended to worry more about brain injury it may, however, be speculated that communication and mutual reinforcements of worries with a spouse as well as concerns induced by the questionnaire may have amplified the reporting of cognitive dysfunction in these people.

When judged by differences in severity of symptoms after 1 year and comparing these differences with the results in the historical cohort study, the effect of expectation on symptom amplification induced by repetitive questionnaires was moderate at the most all CPAs taken together. Thus, an effect was only possible for concentration problems, memory problems and tiredness. When judged by prevalence of symptoms, a moderate amplification due to expectation was also possible for dizziness. Since unmarried CPAs and CPAs with lower education had no significant differences in symptoms there was with all probability no effect of expectation on symptom amplification in these subjects.

Although the dependence of significant effects of the concussion on certain sociodemographic characteristics rather than on the severity of the trauma is an argument against a causal relationship between the concussion and persisting symptoms for up to one year, the possibility of such a causality cannot be entirely dismissed, at least concerning cognitive dysfunction and dizziness. The investigative instruments employed in the prospective study may simply have been too crude and the number of participants enrolled too low to detect subtle sequelae of the concussion. Even in a highly critical meta-analytic review of neuropsychological studies of mild head trauma an effect was found, although the maximum prevalence of persistent neuropsychological deficit was considered to be small and neuropsychological assessment is likely to have positive predictive value of less than 50% (Binder *et al*., 1997). It was therefore concluded that clinicians will more likely be correct when not diagnosing brain injury than when

diagnosing a brain injury in cases with chronic disability after MHT. With such a small effect size it may well be that only educated (i.e. probably more observant) people communicating with and being observed by a spouse are able to recognize any cognitive dysfunction. Recent investigations using positron emission tomography (PET) and functional MRI (fMRI) have confirmed that effects of mild traumatic head injury on memory function is indeed subtle at the most. In a PET study on regional cerebral blood flow and regional 2- [^{18}F] fluoro-2-deoxy-D-glucose (FDG) uptake no difference was found between mild head trauma patients and controls in the resting state (Chen *et al*, 2002). However, during the spatial working memory task, patients had a smaller increase in rCBF than controls in the right prefrontal cortex. A limitation of the study was the patients and controls were significantly different in their recognition memory performance on the list learning task. Delayed list recognition is considerably easier than free recall, and poor performance on this task has been described as reflective of malingering cognitive performance on similar paradigms. On the other side, the average recognition performance was higher than that thought to be reflective of malingering (Suhr *et al*., 1997). Studies in which patterns of regional brain activation in response to varying working memory (WM) loads shortly after mild traumatic brain injury (MTBI) were assessed with fMRI (McAllister *et al*., 1999, 2001) showed that task performance did not differ significantly between the traumatized group and a control group on any task condition. However, whereas the controls maintained their ability to increase activation of WM circuitry with each increase in WM prosessing load the MTBI patients showed disproportionate increased activation during the moderate processing load condition, but very little increase in activation associated with the highest processing load condition. Such subtle memory deficits may only be detected under certain conditions, i.e. when people have higher demands on intellectual performance and live with a spouse. The subtle deficits may then by repair processes diminish or disappear in an observation time of 2 to 3 years and this may have been the reason why they were not detectable in the earlier historical cohort study.

One limitation of the PET and fMRI studies was that they were performed in a society with great possibilities of economic compensation and that no controls were investigated who voluntarily in one or another way used a different strategy on the

working memory tasks. Additional studies using these investigative instruments and including adequate control groups, preferably outside the medicolegal context, are therefore needed.

A prerequisite for the concept and validity of the PCS as an organic sequelae after concussion is that this trauma is capable to produce significant and permanent morphological traces and/or functional disturbances in the brain. This is, however, still uncertain and Margulies (2000) in a review article on this topic concludes that the evidence for permanent traumatic brain damage as cause of PCS is weak.

Short lasting loss of consciousness (LOC) is the predominat symptom of concussion. How a blow to the head causes LOC is still not completely understood, but according to the hitherto most extensive review on the pathophysiological basis of concussion (Shaw, 2002), only the convulsive theory (i.e., a trauma induced epileptic seizure) seems compatible with the neurophysiological data and can provide a totally viable explanation for concussion. There is no evidence, that a single epileptic seizure should be capable to produce persisting symptoms beyond those which can be attributed to the postictal state that lasts from minutes to maximally a few weeks. Even after a provoked epileptic seizure caused by electroconvulsive treatment (ECT), the types of memory problems ensuing from this procedure are discussed, and most evidence suggests that most of the deficits are transitory and that modern ECT is not causing brain damage (Reisner, 2003).

Diffuse axonal injury (DAI) has been proposed as the type of brain damage caused by concussion (Symonds, 1963; Alexander, 1995). However, in a frequently cited experimental study in which head injury was induced in primates (which best replicates brain injury in humans), all the 15 concussed monkeys with coma of less than 15 minutes had good recovery and none had DAI (Gennarelli *et al*., 1982). There are only few anectdotal human pathological data from individuals who had a concussion and then died from other causes (Oppenheimer, 1968; Blumbergs,1994). These studies suggest that axonal injury can occur in a number of axons after concussion, but they have not demonstrated the presence of the hallmark of DAI, i.e. diffuse axonal retraction balls. Whether these axonal changes are permanent or clinically significant is unknown. Persistence of such subtle pathology and signficant clinical symptoms related to it, is,

however, doubtful, taken the plasticity and repair ability of the brain into account. Especially, there is no scientific evidence to relate these microscopic axonal changes to chronic headache, the most prominent symptom of the PCS (Warner, 2000). There are no pain receptors deep in the brain where these axonal changes have been described. Neuroradiological strudies give only weak support for permanent brain damage since the majority of subjects that have sustained a concussion do not have lesions shown by conventional structural neurodiagnostic techniques such as CT and MRI. In those who have true traumatic abnormalities, these will in most cases resolve or diminish within 3 months consistent with the results of the present study that shows a disappearance of several symptoms attributed to PCS (including headache) after 3 months and of the vast majority of these symptoms after 1 year.

VIII. Conclusions

1. On the average of 28 months after concussion, there were no significant differences for the prevalence of headache between concussion patients and controls. In both groups, nearly two thirds of subjects had headache of any frequency and one fifth reported on frequent headache during the last month. There was also no significant difference in the severity of headache, the prevalence of different headache diagnoses, or the prevalence and severity of any dizziness and any cognitive dysfunction among concussion patients and controls.

2. There were insignificant differences in severity between concussion patients and controls for all other symptoms of the postconcussion syndrome except for depression (VAS score 46 vs 36, respectively, p = 0,002, alcohol intolerance (VAS score 38 vs 29, respectively, p = 0,04) and worry about brain injury (VAS score 40 vs 32, respectively, p = 0,04).

3. In the historical cohort study, all concussion patients stated that they had had acute headache immediately after the trauma, while in the prospective study the corresponding figure was 81%. According to the results of the historical cohort study, headache had disappeared during the first two days in 82% of cases and during the first week in 92% of cases. In the prospective study, headache had disappeared during the first 3 weeks just in 75% of cases and during the first 3 months in 88% of cases.

4. The prevalence of any headache among concussion patients was not significantly greater than in controls 3 months (66% vs 60%, respectively) and 1 year (65% vs 64%, respectively) after concussion. There was also no significant difference in the severity of headache.

The prevalence and severity of any dizziness after 3 months was significantly greater in concussion patients as compared to controls (63% vs 46% and VAS score 38 vs 28, respectively). After 1 year, there was still a slightly significant difference of prevalence of

any dizziness between concussion patients and controls (62% vs 50%), but at that time there was no significant difference in severity of this symptom (VAS score of 34 vs 29, respectively).
The prevalence of more severe cognitive problems after 3 months and after 1 year among concussion patients was not significantly greater than in controls. The severity of memory and concentration problems for concussion patients after 3 months (VAS scores 46 vs 39 and 41 vs 33, respectively) and after 1 year (VAS scores 45 vs 35 and 42 vs 34, respectively) was significantly higher than in controls. In addition, after 1 year, significant more complaints were reported by concussion patients for tiredness and worry about brain injury.

5. One year after concussion, married concussion patients reported significantly more memory problems, concentration problems, dizziness, buzzing in the ear, tendency to cry, depression and worry about brain injury than controls. Higher educated concussion patients reported significantly more memory problems, concentration problems, dizziness, fatigue, tiredness, buzzing in the ear, tendency to cry, depression, anxiety, alcohol intolerance, worry about complaints and worry about brain injury than controls.
Unmarried and lower educated concussion patients did not report significant more problems for any of the symptoms attributed to the postconcussion syndrome as compared to controls.

6. Severity of headache shortly after the accident and after 3 months but not after one year was significantly correlated to duration of unconsciousness. However, there was an inverse relationship, i.e. headache severity decreased with increasing duration of unconsciousness. No significant correlation between severity of headache and duration of anterograde amnesia was found at any time. Neither was there at any time a significant correlation between the severity of cognitive dysfunction and duration of unconsciousness or anterograde amnesia.

IX. Practical considerations

1. Neurosurgeons, neurologists and other health care providers who evaluate and treat patients after concussion should inform them about the good prognosis. In particular, they should reassure them that eventual postconcussive symptoms such as headache, dizziness, concentration problems and memory disturbances usually will last up to a few weeks and seldom longer than 3 months.
2. Patients who complain of persisting symptoms for more than 1 year after the accident and are worried about the possibility of a permanent brain damage should be told that these symptoms usually are unrelated to the trauma. To help them to accept and understand this information it is important to tell them about the frequent occurrence of such symptoms also in people who never had had a brain injury. They should be informed about the benign nature of the complaints and that the possibility that these symptoms may abate or disappear again is equally good as for any other non-traumatized patient with the same problems.
3. Physicians who treat headache in patients after concussion should be aware of that headache that is present more than 3 months after concussion usually represents a primary headache type. Consequently, the principles for treating these headaches are the same as for primary headaches in non-traumatized patients.
4. In an expert witness declaration made in a medico-legal proceeding or for disability claims against the social security system it should be emphasized that there is no documentation in controlled studies for a causal relationship between concussion and symptoms lasting more than 1 year. Neither is there documentation for a significant permanent brain damage caused by concussion.

X. The doctoral dissertation was based on the following publications:

1. Mickevičienė D, Schrader H, Nestvold K, Šurkienė D, Kunickas R, Stovner LJ, Sand T (2002) A controlled historical cohort study on the post-concussion syndrome. Eur J Neuro l9 (6): 581-7.

2. Mickevičienė D, Schrader H, Obelienienė D, Surkienė D, Kunickas R, Stovner LJ, Sand T (2004) A controlled prospective inception cohort study on the post-concussion syndrome outside the medicolegal context. Eur J Neurol 11 (6): 411-9.

Other publications:

1. Schrader H, Obelienienė D, Bovim G, Šurkienė D, Mickevičienė D, Misevicienė I, Sand T (1996) Natural evolution of late whiplash syndrome outside the medicolegal context. Lancet 4; 347(9010): 1207-1211.

2. Schrader H, D.Mickevičienė D, Šurkienė D (2000). The postconcussion syndrome. 3rd Baltic congress of neurology: Final program and abstracts. Kaunas, Lithuania May, 25 - 27, p.88.

3. Mickevičienė D, Schrader H, Šurkienė D, Kunickas K, Stovner LJ, Sand T. A historical cohort study on posttraumatic headache outside the medico-legal context.- (Poster session N3) Cephalalgia:An international journal of headache,-2001, vol.2, N4, May:The 10th congress of International headache society: IHC 2001: Liberty from headache: abstracts, June 29-July 2, 2001, New York City, New York6 USA, p.524, abstr. N P3-U6.-ISSN 0333-1024. -www. cephalalgia.org.

4. Mickevičienė D, Schrader H, Stovner LJ, Sand T (2005) Reply to Dr. R. W. Evans. Comment on: Eur J Neurol Feb;12(2):160. Eur J Neurol. 2005 Apr;12(4): 324-5.

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6. Stovner LJ, Schrader H, Obelienienė D, Šurkienė D, Mickevicienė D, Bovim G, Sand T (2005) Headache after whiplash is likely to represent stress-induced primary headache (Abstract/Poster Poster IHC Kyoto Okt 2005). Cephalalgia 25:1000.

7. Schrader H, Stovner LJ, Obelienienė D, Šurkienė D, Mickevičienė D, Bovim G, Sand T (2006) Examination of the diagnostic validity of "headache attributed to whiplash injury": A controlled, prospective study. Accepted for publication in Eur J Neurol..

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XIII. Addendum

Questionnaires

First questionnaire for concussion patients and controls in historical cohort study

Please answer the questions by putting a circle around the appropriate alternative.
Unless otherwise indicated, never encircle more than one possibility!

1-4 Running no.....

5-10 Date today:
dd mm yy

Personalia :

Name:.....

Address: .....

Phone no. .....

11 Sex: 0 Male
1 Female

12-13 Age: ..... years

14-15 Height (cm) .....

16-17 Weight .....

18 *Highest education:*
1 Primary school
2 Secondary school
3 Professional school or special practical education
4 University graduate
5 University, uncompleted
6 Others, please specify.....

19-20 *How many years did you study in total (include schools, University)?* .....

21-26 *Profession* .....

27-28 *Present job:*

29 *Civil status:*
1 Single, living alone
2 Single, living together with a partner
3 Married
4 Widow(er)
5 Divorced
6 Other, please specify .....

GENERAL HEALTH STATUS:

30 *How do you estimate your health status?*
0 I feel healthy
1 I feel unhealthy

Please encircle if you have any of the following diseases/complaints (more than one if necessary):

31 *Diabetes mellitus*
0 No
1 Yes, on medication (please specify:.....)
2 Yes, without medication

32 *Hypertension* (please specify your blood pressure, if you know ..... mm Hg)
0 No
1 Yes, on medication (please specify: .....)
2 Yes, without medication

33 *Rheumatic disease, please specify.....*
0 No
1 Yes, on medication (please specify: .....)
2 Yes, without medication

34 *Heart infarction:*
0 No
1 Yes, once
2 2-3 times
3 More than 3 times

35 *Psychological problems, please specify.....*
0 No
1 Yes, on medication (please specify.....)
2 Yes, without medication

36 *Low back pain in the last month*
0 No
1 Less than 1 day
2 One day to 7 days
3 8 - 15 days
4 More than 15 days
5 Every day

37 *Neck pain in the last month*
0 No
1 One day to 7 days
2 8 - 14 days
3 More than 14 days
4 Every day

38 *Headache in the last month*
0 No
1 One day to 7 days
2 8 - 14 days
3 More than 14 days
4 Every day

39 *Other diseases or complaints*
0 No
1 Yes, please specify .....

Please encircle any chronic disease that members of your family (parents, siblings, children) suffer from (more than one if necessary):

40 *Diabetes mellitus*
0 No
1 Yes

41 *Hypertension*
0 No
1 Yes

42 *Rheumatic disease, please specify.....*
0 No
1 Yes

43 *Heart infarction, Angina pectoris*
0 No
1 Yes

44 *Psychological problems, please specify.....*
0 No
1 Yes

45 *Low back pain*
0 No
1 Yes

46 *Neck pain*
0 No
1 Yes

47 *Headache*
0 No
1 Yes

48 *Other diseases or complaints*
0 No
1 Yes

49 *Smoking habits:*
0 Never
1 Smoked, but gave it up
2 Sporadically smoking (less than 1 per day)
3 Regularly 1-5 cigarettes per day
4 More than 5 cigarettes per day

50 *Alcohol habits* (1 "drink" = 1 glass of wine = 1 small beer = 15 g alcohol):
0 Never
1 Used to, but gave up
2 A few drinks per year
3 One drink per month
4 A few drinks per month
5 1 drink per week
6 1-6 drinks pr week
7 More than 6 drinks pr week

SPECIFIC HEALTH SITUATION

51 *Have you had headache in the last year ?*
0 No
1 Yes

If you did not have any headache in the last year please go to the questions concerning other complaints (questions 93 to 108)

52 *How often did you have headache the last year ?*
0 Less than one day per month
1 1-7 days per month
2 8-15 days per month
3 More than 15 days per month
4 Every day or almost so
+ Other, please specify .....

53 *What is the usual duration of a headache attack/period?*
1 Less than 4 hours
2 4-72 hours
3 More than 72 hours, but still clearly separate episodes
4 Continuous headache with varying intensity
5 Continuous constant headache
6 Changing pattern; short- and long-lasting attacks
7 Other, please specify .....

54 *What is the usual intensity of the headache?*
1 Mild (can continue any activity)
2 Moderate (cannot continue activity, but can stay out of bed)
3 Severe (must go to bed)
4 Excruciating

55 *What is the location of the headache?*
1 One-sided, always right side
2 One-sided, always left side
3 One-sided, changing side
4 Both sides
5 Sometimes One-sided (always same side), sometimes both sides
6 Others, please specify .....

56 *Where does a pain attack or a worsening of the pain, start?*
1 Neck
2 Forehead
3 Another specific place, please specify .....

57 *Does the pain subsequently spread to other areas of the head?*
0 No
1 Yes, from the neck to the forehead
2 Yes, from the forehead to the neck
3 Yes, other patterns, please specify .....
4 Unknown

58 *Do you regularly have pain in areas outside the head together with your headache?*
0 No
1 Yes

59 *Do you regularly have pain in both shoulders together with your headache?*
0 No
1 Yes

60 *Do you regularly have pain in one shoulder (same side as pain maximum) together with your headache?*
0 No
1 Yes

61 *Do you regularly have pain in both arms together with your headache?*
0 No
1 Yes

62 *Do you regularly have diffuse pain in one arm (same side as headache maximum)*?
0 No
1 Yes

63 *Do you regularly have pain in one arm (same side as headache maximum) and spreading to one or more fingers?*
0 No
1 Yes

64 *Do you in connection with your headache regularly have pain in other places. Please specify* .....
0 No
1 Yes

65 *What is the character of the headache?*
1 Pressing
2 Pounding (pulsating)
3 Usually pressing, but pounding when maximal
4 Other, please specify .....

66 *Does nausea accompany your headache?*
0 No
1 Yes

67 *Does vomiting accompany your headache?*
0 No
1 Yes

68 *Does dizziness accompany your headache?*
0 No
1 Yes

69 *Does swelling around one eye accompany your headache?*
0 No
1 Yes

70 *Does increased sensitivity to sounds accompany your headache?*
0 No
1 Yes

71 *Does increased sensitivity to light accompany your headache?*
0 No
1 Yes

72 *Does blurred vision in one eye accompany your headache?*
0 No
1 Yes

73 *Does difficulty in swallowing accompany your headache?*
0 No
1 Yes

74 *Do you feel aggravation of headache when using stairs or bending forward?*
0 No
1 Yes

75 *Do other symptoms accompany your headache?*
0 No
1 Yes, please specify .....

76 *Does eating cheese provoke your headache?*
0 No
1 Yes, please specify .....

77 *Does turning your head to one side and keeping this position provoke your headache?*
0 No
1 Yes

78 *Does bending the head backwards provoke your headache?*
0 No
1 Yes

79 *Does external pressure towards the upper neck region provoke your headache?*
0 No
1 Yes

80 *Does drinking alcohol provoke your headache?*
0 No
1 Yes

81 *Do coughing, sneezing or bowel movements provoke your headache?*
0 No
1 Yes

82 *Does mental stress provoke your headache?*
0 No
1 Yes

83 *Does irregular sleep provoke your headache?*
0 No
1 Yes

84 *Are there other reasons provoking your headache?*

0 No
1 Yes, please specify .....

85 *At what age did your headache start?*

1 Less than 20 years old, specify if possible ....
2 20-30 years old, specify if possible ....
3 31-40 years old, specify if possible ....
4 More than 41 years old, specify if possible ....
5 Unknown

86 *Has your headache problem changed character since it started?*

0 No
Yes, increased
1 gradually over months/years
2 over days, please specify .....
3 abruptly (in one day), please specify .....
Yes, decreased
4 gradually over months/years
5 over days, please specify.....
6 abruptly (in one day), please specify.....

87 *Have you treated your headache with:*

Usual analgesics (please specify .....)

0 No
1 Yes, with no effect
2 Yes, with some effect
3 Yes, with complete effect

88 *Have you treated your headache with ergotamine, dehydroergotamine?*

Please specify .....

0 No
1 Yes, with no effect
2 Yes, with some effect
3 Yes, with complete effect

89 *Have you treated your headache with physiotherapy?*

0 No
1 Yes, with no effect
2 Yes, with some effect
3 Yes, with complete effect

90 *Have you treated your headache with general physical training?*

0 No
1 Yes, with no effect
2 Yes, with some effect
3 Yes, with complete effect

91 *Have you used other medication?*

If yes, please specify .....

0 No
1 Yes, with no effect
2 Yes, with some effect
3 Yes, with complete effect

92 *Have you used any other treatment?*

0 No
Yes, please specify .....

1 with no effect
2 with some effect
3 with complete effect

Other complaints:

93 *Have you had neck pain in the last year ?*
- 0 No
- 1 Less than one day per month
- 2 One to 7 days per month
- 3 8 - 14 days per month
- 4 More than 14 days per month
- 5 Every day or almost every day

94 *Have you had pain irradiating from the neck ?*
- 0 No
- 1 To one shoulder
- 2 To both shoulders
- 3 To one arm
- 4 To both arms
- 5 Up to the head
- 6 Down to the back
- 7 Other,please specify

95 *Have you had reduced neck mobility ?*
- 0 No
- 1 Constant moderately reduced
- 2 Constant severely reduced
- 3 Only in periods
- 4 Only if I have headache
- Other, please specify.....

96 Do you h*ave you headache and neck pain at the same time ?*
- 0 Yes
- 1 No

97 *If yes, what is more bothersome ?*
- 0 The neck pain
- 1 The headache
- 2 Both pains are equally bothersome
- 3 Other, please specify.....

98 *Do you have problems with your memory?*
- 0 No
- 1 Yes, sporadically
- 2 Yes, regularly

99 *Do you have concentration problems?*
- 0 No
- 1 Yes, sporadically
- 2 Yes, regularly but slight
- 3 Yes, regularly and severe

100 *Do you have ringing or other strange noises in the ear (s)?*
- 0 No
- 1 Sporadically less than 15 days per month
- 2 Sporadically more than 15 days per month
- 3 Every day, but not constantly
- 4 Every day all the time

101 *If you have noises in your ear(s), what kind of noises do you have ?*
- 0 Peep
- 1 Buzzing
- 2 Drone
- 3 Others, please specify .....

102 *Have you been dizzy the last year ?*
- 0 No
- 1 Yes

103 *If yes, what type of dizziness have you had ?*
- 0 Feeling like being in a carrousell
- 1 Feeling like being on board of a ship
- 2 Unsteadiness

3 Other type, please specify.....

104 *How often are you dizzy ?*
0 Less than once a month
1 One time in a week
2 Several times in a week
3 Several times a day
4 Daily
5 Other, please specify.....

105 *What makes you dizzy ?*
0 The dizziness appears without obvious reason
1 Physical efforts
2 Change of position (e.g. turning round in the bed, getting up quickly)
3 Psychological stress
4 Other, please specify.....

106 *If you have been dizzy the last year, can you go without support ?*
0 Yes
1 No
If no, please describe what kind of aid you need .....

.....

107 *Have you together with dizziness had nausea ?*
0 Yes
1 No

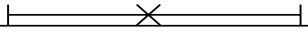
108 *Have you together with dizziness had vomiting ?*
0 Yes
1 No

After having finished this questionnaire, please go to questionnaire B where you have to indicate on a line the degree of your present symptoms.

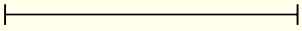
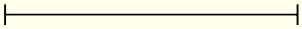
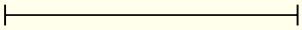
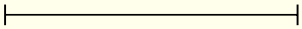
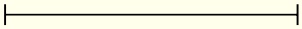
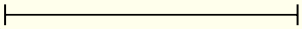
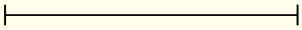
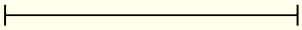
Questionnaire B with use of VAS scale for historical cohort and prospective cohort study

SOME QUESTIONS ABOUT HEALTH PROBLEMS

Below there are series of questions about health problems. You are kindly asked to answer whether you have some of these complaints or not. You have to make a cross on a line. In case you make the cross at the border on the left side it means that you do not have complaints; if you put the cross on the border of the right side you have very great complaints. If you have complaints with a medium magnitude, you put a cross like this :

No complaints  Great complaint

Please answer all questions. Put only one cross on each line.

1	Do you have headache?	have no headache		have much headache
2	Do you have neck pain?	have no neck pain		have much neck pain
3	Are you dizzy ?	do not experience dizziness		I am very dizzy
4	Do you have nausea/feel unwell?	do not have nausea or feel unwell		have much nausea and feel much unwell
5	Do you usually feel exausted and tired?	do usually not feel exausted and tired		do usually feel very exausted and tired
6	How exausted and tired do you get on physical or psychological strain?	do not get particularly ex-austed and tired on physical and psychological strain		do get very exausted and tired on physical and psycholo-gical strain
7	Do you react on noise and high sounds?	do not react on noise and high sounds		do react strongly on noise and high sounds
8	Do you get easily irritated?	do not get easily irritated		do very easily get irritated

page 2

9	Do you cry easily?	do not cry easily	⊢——⊣	do very easily cry
10	Do you feel depressed or down?	I am not depressed or down	⊢——⊣	I am very depressed or down
11	Do you have anxiety?	do not have anxiety	⊢——⊣	do have much anxiety
12	Do you have reduced memory?	do not have reduced memory	⊢——⊣	do have very much reduced memory
13	Do you have concentration problems?	do not have concentration problems	⊢——⊣	do have very great concentration problems
14	Do you have sleep problems?	do not have sleep problems	⊢——⊣	do have big sleep problems
15	Do you react different to alcohol?	do not react different to alcohol compared to earlier times	⊢——⊣	do react very different to alcohol compared to earlier times
16	Do you have sounds in your ear/s?	do not have sounds in my ear/s	⊢——⊣	do have much sound in my ear/s
17	Are you worried about your condition/ complaints?	I am not worried about my complaints	⊢——⊣	I am very worried about my complaints
18	Are you afraid of having a brain injury?	I am not afraid of having a brain injury	⊢——⊣	I am very afraid of having a brain injury

Second questionnaire for concusion patients in historical cohort study

Questions related to a head trauma with loss of consciousness:

109 *Have you had a head trauma with loss of consciousness ?*
0 No
1 Yes, one time
2 Yes, two times
3 More times, please specify.....

110 *Year of the first head trauma with loss of consciousness: .....*
Year of eventual second head trauma with loss of consciousness.....
Years of eventual later head traumas with loss of consciousness.....

111 *Todays date: .....*

Questions related to the situation BEFORE the head trauma with loss of consciousness

112 *Did you have headache before the last head trauma with loss of consciousness ?*
0 No, never
1 Yes

Headache before the last head trauma with loss of consciousness:

113 *How often did you have headache?*
0 Less than one day per month
1 1-7 days per month
2 8-14 days per month
3 More than 14 days per month
4 Every day or almost so
+ Other, please specify .....

114 *What was the usual duration of a headache attack/period?*
1 Less than 4 hours
2 4-72 hours
3 More than 72 hours, but still clearly separate episodes
4 Continuous headache with varying intensity
5 Continuous constant headache
6 Changing pattern; short- and long-lasting attacks
+ Other, please specify

115 *What was the usual intensity of the headache?*
1 Mild (can continue any activity)
2 Moderate (cannot continue activity, but can stay out of bed)
3 Severe (must go to bed)
4 Excruciating

Other complaints:

116 *Did you have problems with your memory before the last head trauma with loss of consciousness?*
0 No
1 Yes, sporadically
2 Yes, regularly

117 *Did you have concentration problems before this head trauma?*
0 No
1 Yes, sporadically
2 Yes, regularly but slight
3 Yes, regularly and severe

The situation AFTER the accident:

118 *Have you had headache after the last head trauma with loss of consciousness ?*
0 No
1 Yes, but less than before
2 Yes, of the same character and magnitude as I have had before
3 Yes, of the same character, but worse than before
4 Yes, of the same magnitude, but of different character
5 Yes, of different character and worse than before

119 *When did the headache after this last head trauma occur for the first time?*
1 Immediately (<30 minutes after the accident)
2 Between 30 minutes and 24 hours
3 1-3 days after the accident
4 4-7 days after the accident
5 1-4 weeks after the accident
6 >4 weeks after the accident, please specify.....
- Unknown

120 *How long did the headache last ?*
1 Less than 12 hours
2 From 12 to 48 hours
3 From 2 days to one week
4 1 week to 1 month
5 More than 1 month. How long, please specify .....

Second questionnaire for controls in historical cohort study

Questions related to a head trauma with loss of consciousness:

109 *Have you had a head trauma with loss of consciousness ?*
0 No
1 Yes, one time
2 Yes, two times
3 More times, please specify.....

110 *Year of the first head trauma with loss of consciousness: .....*
Year of eventual second head trauma with loss of consciousness.....
Years of eventual later head traumas with loss of consciousness.....

111 *Todays date: .....*

First questionnaire for concussion patients in prospective study

Please answer the questions by putting a circle around the appropriate alternative.
Unless otherwise indicated, never encircle more than one possibility!

1-4 Running no.....

5-10 Date today:
dd mm yy

Personalia :

Name:.....

Address: .....

Phone no. .....

11 Sex: 0 Male 12-13 Age: ..... years
1 Female

14-15 Height (cm) .....

16-17 Weight .....

18 *Highest education:*
1 Primary school
2 Secondary school
3 Professional school or special practical education
4 University graduate
5 University, uncompleted
6 Others, please specify.....

19-20 *How many years did you study in total (include schools, University)?* .....

21-26 *Profession* .....

27-28 *Present job:*

29 *Civil status:*
1 Single, living alone
2 Single, living together with a partner
3 Married
4 Widow(er)
5 Divorced
6 Other, please specify .....

GENERAL HEALTH STATUS

30 *How do you estimate your health status?*
0 I feel healthy
1 I feel unhealthy

Please encircle if you have any of the following diseases/complaints (more than one if necessary):

31 *Diabetes mellitus*
0 No
1 Yes, on medication (please specify:.....)
2 Yes, without medication

32 *Hypertension* (please specify your blood pressure, if you know
..... mm Hg)
0 No
1 Yes, on medication (please specify: .....)
2 Yes, without medication

33 *Rheumatic disease, please specify.....*
0 No
1 Yes, on medication (please specify: .....)
2 Yes, without medication

34 *Heart infarction:*
0 No
1 Yes, once
2 2-3 times
3 More than 3 times

35 *Psychological problems, please specify.....*
0 No
1 Yes, on medication (please specify.....)
2 Yes, without medication

36 *Low back pain in the last month*
0 No
1 Less than 1 day
2 One day to 7 days
3 8 - 15 days
4 More than 15 days
5 Every day

37 *Neck pain in the last month*
0 No
1 One day to 7 days
2 8 - 15 days
3 More than 15 days
4 Every day

38 *Headache in the last month*
0 No
1 One day to 7 days
2 8 - 15 days
3 More than 15 days
4 Every day

39 *Other diseases or complaints*
0 No
1 Yes, please specify .....

40 *Your smoking habits:*
0 Never
1 Smoked, but gave it up
2 Sporadically smoking (less than 1 per day)
3 Regularly 1-5 cigarettes per day
4 More than 5 cigarettes per day

41 *Your alcohol habits* (1 "drink" = 1 glass of wine = 1 small beer = 15 g alcohol):
0 Never
1 Used to, but gave up
2 A few drinks per year
3 One drink per month
4 A few drinks per month
5 1 drink per week

Please encircle any chronic disease that members of your family (parents, siblings, children) suffer from (more than one if necessary):

42 *Psychological problems, please specify.....*
0 No
1 Yes

43 *Neck pain*
0 No
1 Yes

44 *Headache*

0 No
1 Yes

SPECIFIC HEALTH SITUATION

45 *Have you had headache in the last year before your head trauma with loss of consciousness ?*

0 No
1 Yes

If you did not have any headache in the last year before your head trauma please go to the questions concerning other complaints (questions 68 to 93)

46 *How often did you have headache the last year before your head trauma ?*

0 Less than one day
1 1-7 days
2 8-15 days
3 More than 15 days
4 Every day or almost so
+ Other, please specify .....

47 *What was the usual duration of a headache attack/period?*

1 Less than 4 hours
2 4-72 hours
3 More than 72 hours, but still clearly separate episodes
4 Continuous headache with varying intensity
5 Continuous constant headache
6 Changing pattern; short- and long-lasting attacks
7 Other, please specify .....

48 *What was the usual intensity of the headache?*

1 Mild (can continue any activity)
2 Moderate (cannot continue activity, but can stay out of bed)
3 Severe (must go to bed)
4 Excruciating

49 *What was the location of the headache?*

1 One-sided, always right side
2 One-sided, always left side
3 One-sided, changing side
4 Both sides
5 Sometimes One-sided (always same side), sometimes both sides
6 Others, please specify .....

50 *Where did a pain attack or a worsening of the pain, start?*

1 Neck
2 Forehead
3 Another specific place, please specify .....

51 *Did the pain subsequently spread to other areas of the head?*

0 No
1 Yes, from the neck to the forehead
2 Yes, from the forehead to the neck
3 Yes, other patterns, please specify .....
4 Unknown

52 *What was the character of the headache?*

1 Pressing
2 Pounding (pulsating)
3 Usually pressing, but pounding when maximal
4 Other, please specify .....

53 *Did nausea accompany your headache?*
0 No
1 Yes

54 *Did vomiting accompany your headache?*
0 No
1 Yes

55 *Did swelling around one eye accompany your headache?*
0 No
1 Yes

56 *Did increased sensitivity to sounds accompany your headache?*
0 No
1 Yes

57 *Did increased sensitivity to light accompany your headache?*
0 No
1 Yes

58 *Did blurred vision in one eye accompany your headache?*
0 No
1 Yes

59 *Did you feel aggravation of headache when using stairs or bending forward?*
0 No
1 Yes

60 *Did other symptoms accompany your headache?*
0 No
1 Yes, please specify .....

61 *Did turning your head to one side and keeping this position provoke your headache?*
0 No
1 Yes

62 *Did bending the head backwards provoke your headache?*
0 No
1 Yes

63 *Did external pressure towards the upper neck region provoke your headache?*
0 No
1 Yes

64 *Did coughing, sneezing or bowel movements provoke your headache?*
0 No
1 Yes

65 *Did mental stress provoke your headache?*
0 No
1 Yes

66 *At what age did your headache start?*
1 Less than 20 years old, specify if possible ....
2 20-30 years old, specify if possible ....
3 31-40 years old, specify if possible ....
4 More than 41 years old, specify if possible ....
5 Unknown

67 *Has your headache problem changed character since it started?*
0 No
Yes, increased
1 gradually over months/years
2 over days, please specify .....
3 abruptly (in one day), please specify .....
Yes, decreased
4 gradually over months/years
5 over days, please specify.....
6 abruptly (in one day), please specify.....

Other complaints in the last year before your head trauma with loss of consciousness:

68 *Have you had neck pain in the last year before your head trauma ?*
- 0 No
- 1 Less than one day per month
- 2 One to 7 days per month
- 3 8 - 15 days per month
- 4 More than 15 days per month
- 5 Every day or almost every day

69 *Did you have problems with your memory in the last year before your head trauma ?*
- 0 No
- 1 Yes, sporadically
- 2 Yes, regularly

70 *Did you have concentration problems in the last year before your head trauma ?*
- 0 No
- 1 Yes, sporadically
- 2 Yes, regularly but slight
- 3 Yes, regularly and severe

71 *Did you have ringing or other strange noises in the ear (s) in the last year before your head trauma ?*
- 0 No
- 1 Sporadically less than 15 days per month
- 2 Sporadically more than 15 days per month
- 3 Every day, but not constantly
- 4 Every day all the time

72 *If you did have noises in your ear(s), what kind of noises did you have ?*
- 0 Peep
- 1 Buzzing
- 2 Drone
- 3 Others, please specify .....

73 *Have you been dizzy the last year before your head trauma ?*
- 0 No
- 1 Yes

74 *If yes, what type of dizziness did you have ?*
- 0 Feeling like being in a carrousell
- 1 Feeling like being on board of a ship
- 2 Unsteadiness
- 3 Other type, please specify.....

75 *How often were you dizzy ?*
- 0 Less than once
- 1 One time in a week
- 2 Several times in a week
- 3 Several times a day
- 4 Daily
- 5 Other, please specify.....

76 *What made you dizzy ?*
- 0 The dizziness appears without obvious reason
- 1 Physical efforts
- 2 Change of position (e.g. turning round in the bed, getting up quickly)
- 3 Psychological stress
- 4 Other, please specify.....

77 *Did you together with dizziness have nausea ?*
- 0 Yes
- 1 No

78 *Did you together with dizziness have vomiting ?*
- 0 Yes
- 1 No

Questions related to your head trauma with loss of consciousness

79 *Did you have headache after your head trauma with loss of consciousness ?*
0 No
1 Yes

If you did not have any headache after your head trauma then go to question nr. 90

80 *If yes, when did the headache after this head trauma occur for the first time?*
1 Immediately (less than 30 minutes after the trauma)
2 Between 30 minutes and 2 hours after the trauma
3 Between 2 hours and 4 hours after the trauma
4 Between 4 hours and 6 hours after the trauma
5 Between 6 hours and 24 hours after the trauma
6 1- 4 days after the trauma
7 5 - 7 days after the trauma
8 8 - 15 days after the trauma

81 *How long did the headache you got after the trauma last ?*
1 Less than one hour
2 Between 1 and 2 hours
3 Between 2 and 4 hours
4 Between 4 and 6 hours
5 Between 6 and 24 hours
6 1 - 2 days
7 2 - 4 days
8 5 - 7 days
9 8 - 10 days
10 11 - 13 days
11 14 - 15 days
12 I still have the headache that I got after the trauma

82 *If you got a headache after the trauma, what was its character ?*
1 Pressing
2 Pounding (Pulsating)
3 Both pressing and pulsating
4 Stabbing

83 *Where was the headache located most of the time ?*
1 In the whole head
2 In one half of the head
3 In the forehead on both sides
4 In the forehead on one side
5 In the occipital area on both sides
6 In the occipital area on one side
7 Shifting locations

84 *In case you got a headache after the trauma and this headache lasted more than one day, how long was its average duration during 24 hours ?*
1 Less than 4 hours
2 4 - 6 hours
3 6 - 12 hours
4 The whole day

85 *What was the usual intensity of the headache you got after the trauma ?*
1 Mild (can continue any activity)
2 Moderate (cannot continue activity, but can stay out of bed)
3 Severe (must go to bed)
4 Excruciating

86 *Did nausea accompany the headache you got after the head trauma ?*
0 No
1 Yes

87 *Did vomiting accompany the headache you got after the head trauma ?*

0 No
1 Yes

88 *Did increased sensitivity to sounds accompany the headache you got after the head trauma?*

0 No
1 Yes

89 *Did increased sensitivity to light accompany the headache you got after the head trauma ?*

0 No
1 Yes

90 *Did you have dizziness after your head trauma ?*

1 No
2 Yes

91 *If yes, when did the dizziness after the head trauma occur for the first time?*

1 Immediately (less than 30 minutes after the trauma)
2 Between 30 minutes and 2 hours after the trauma
3 Between 2 hours and 4 hours after the trauma
4 Between 4 hours and 6 hours after the trauma
5 Between 6 hours and 24 hours after the trauma
6 1- 4 days after the trauma
7 5 - 7 days after the trauma
8 8 - 15 days after the trauma

92 *In case you got a dizziness after the head trauma, how long did it last ?*

1 Less than one hour
2 Between 1 and 2 hours
3 Between 2 and 4 hours
4 Between 4 and 6 hours
5 Between 6 and 24 hours
6 1 - 2 days
7 2 - 4 days
8 5 - 7 days
9 8 - 10 days
10 11 - 13 days
11 14 - 15 days
12 I still have the dizziness that I got after the trauma

93 *If you got dizziness after the head trauma, what type of dizziness did you have ?*

0 Feeling like being in a carrousell
1 Feeling like being on board of a ship
2 Unsteadiness
3 Other type, please specify.....

After having finished this questionnaire, please go to questionnaire B where you have to indicate on a line the degree of your present symptoms.

Questionnaire after 3 months and 1 year for concussion patients in prospective study

Please answer the questions by putting a circle around the appropriate alternative.
Unless otherwise indicated, never encircle more than one possibility!

1-4 Running no.....

5-10 Date today:
dd mm yy

Personalia :

Name:.....

Address: .....

Phone no. .....

SPECIFIC HEALTH SITUATION

11 *Have you had headache in the last month ?*
0 No
1 Yes

If you did not have any headache in the last month please go to the questions concerning other complaints (questions 32 to 56)

12 *How often did you have headache in the last month ?*
0 Less than one day
1 1-7 days
2 8-15 days
3 More than 15 days
4 Every day or almost so
+ Other, please specify .....

13 *What was the usual duration of a headache attack/period?*
1 Less than 4 hours
2 4-72 hours
3 More than 72 hours, but still clearly separate episodes
4 Continuous headache with varying intensity
5 Continuous constant headache
6 Changing pattern; short- and long-lasting attacks
7 Other, please specify .....

14 *What was the usual intensity of the headache?*
1 Mild (can continue any activity)
2 Moderate (cannot continue activity, but can stay out of bed)
3 Severe (must go to bed)
4 Excruciating

15 *What was the location of the headache?*
1 One-sided, always right side
2 One-sided, always left side
3 One-sided, changing side
4 Both sides
5 Sometimes One-sided (always same side), sometimes both sides
6 Others, please specify .....

16 *Where did a pain attack or a worsening of the pain, start?*
1 Neck
2 Forehead
3 Another specific place, please specify .....

17 *Did the pain subsequently spread to other areas of the head?*
0 No
1 Yes, from the neck to the forehead
2 Yes, from the forehead to the neck
3 Yes, other patterns, please specify .....
4 Unknown

18 *What was the character of the headache?*
1 Pressing
2 Pounding (pulsating)
3 Usually pressing, but pounding when maximal
4 Other, please specify .....

19 *Did nausea accompany your headache?*
0 No
1 Yes

20 *Did vomiting accompany your headache?*
0 No
1 Yes

21 *Did swelling around one eye accompany your headache?*
0 No
1 Yes

22 *Did increased sensitivity to sounds accompany your headache?*
0 No
1 Yes

23 *Did increased sensitivity to light accompany your headache?*
0 No
1 Yes

24 *Did blurred vision in one eye accompany your headache?*
0 No
1 Yes

25 *Did you feel aggravation of headache when using stairs or bending forward?*
0 No
1 Yes

26 *Did other symptoms accompany your headache?*
0 No
1 Yes, please specify .....

27 *Did turning your head to one side and keeping this position provoke your headache?*
0 No
1 Yes

28 *Did bending the head backwards provoke your headache?*
0 No
1 Yes

29 *Did external pressure towards the upper neck region provoke your headache?*
0 No
1 Yes

30 *Did coughing, sneezing or bowel movements provoke your headache?*
0 No
1 Yes

31 *Did mental stress provoke your headache?*
0 No
1 Yes

Other complaints in the last month:

32 *Have you had neck pain in the last month ?*
0 No
1 Less than one day per month
2 One to 7 days per month
3 8 - 15 days per month
4 More than 15 days per month
5 Every day or almost every day

33 *Did you have problems with your memory in the last month ?*
0 No
1 Yes, sporadically
2 Yes, regularly

34 *Did you have concentration problems in the last month ?*
0 No
1 Yes, sporadically
2 Yes, regularly but slight
3 Yes, regularly and severe

34 *Did you have ringing or other strange noises in the ear (s) in the last month ?*
0 No
1 Sporadically less than 15 days per month
2 Sporadically more than 15 days per month
3 Every day, but not constantly
4 Every day all the time

35 *If you did have noises in your ear(s), what kind of noises did you have ?*
0 Peep
1 Buzzing
2 Drone
3 Others, please specify .....

36 *Have you been dizzy the last month ?*
0 No
1 Yes

37 *If yes, what type of dizziness did you have ?*
0 Feeling like being in a carrousell
1 Feeling like being on board of a ship
2 Unsteadiness
3 Other type, please specify.....

38 *How often were you dizzy ?*
0 Less than once
1 One time in a week
2 Several times in a week
3 Several times a day
4 Daily
5 Other, please specify.....

39 *What made you dizzy ?*
0 The dizziness appears without obvious reason
1 Physical efforts
2 Change of position (e.g. turning round in the bed, getting up quickly)
3 Psychological stress
4 Other, please specify.....

40 *Did you together with dizziness have nausea ?*
0 Yes
1 No

41 *Did you together with dizziness have vomiting ?*

0 Yes
1 No

For the following questions related to your head trauma with loss of consciousness, please try to remember once more:

42 *Did you have headache after your head trauma with loss of consciousness ?*

0 No
1 Yes

If you did not have any headache after your head trauma then go to question nr. 53

43 *If yes, when did the headache after this head trauma occur for the first time?*

1 Immediately (less than 30 minutes after the trauma)
2 Between 30 minutes and 2 hours after the trauma
3 Between 2 hours and 4 hours after the trauma
4 Between 4 hours and 6 hours after the trauma
5 Between 6 hours and 24 hours after the trauma
6 1- 4 days after the trauma
7 5 - 7 days after the trauma
8 8 - 15 days after the trauma

44 *How long did the headache you got after the trauma last ?*

1 Less than one hour
2 Between 1 and 2 hours
3 Between 2 and 4 hours
4 Between 4 and 6 hours
5 Between 6 and 24 hours
6 1 - 2 days
7 2 - 4 days
8 5 - 7 days
9 8 - 10 days
10 11 - 13 days
11 14 - 15 days
12 16 - 30 days
13 1 - 2 months
14 2 - 3 months
15 I still have the headache that I got after the trauma

45 *If you got a headache after the trauma, what was its character ?*

1 Pressing
2 Pounding (Pulsating)
3 Both pressing and pulsating
4 Stabbing

46 *Where was the headache located most of the time ?*

1 In the whole head
2 In one half of the head
3 In the forehead on both sides
4 In the forehead on one side
5 In the occipital area on both sides
6 In the occipital area on one side
7 Shifting locations

47 *In case you got a headache after the trauma and this headache lasted more than one day, how long was its average duration during 24 hours ?*

1 Less than 4 hours
2 4 - 6 hours
3 6 - 12 hours
4 The whole day

48 *What was the usual intensity of the headache you got after the trauma ?*

1 Mild (can continue any activity)
2 Moderate (cannot continue activity, but can stay out of bed)
3 Severe (must go to bed)
4 Excruciating

49 *Did nausea accompany the headache you got after the head trauma ?*
0 No
1 Yes

50 *Did vomiting accompany the headache you got after the head trauma ?*
0 No
1 Yes

51 *Did increased sensitivity to sounds accompany the headache you got after the head trauma?*
0 No
1 Yes

52 *Did increased sensitivity to light accompany the headache you got after the head trauma ?*
0 No
1 Yes

53 *Did you have dizziness after your head trauma ?*
1 No
2 Yes

54 *If yes, when did the dizziness after the head trauma occur for the first time?*
1 Immediately (less than 30 minutes after the trauma)
2 Between 30 minutes and 2 hours after the trauma
3 Between 2 hours and 4 hours after the trauma
4 Between 4 hours and 6 hours after the trauma
5 Between 6 hours and 24 hours after the trauma
6 1- 4 days after the trauma
7 5 - 7 days after the trauma
8 8 - 15 days after the trauma

55 *In case you got a dizziness after the head trauma, how long did it last ?*
1 Less than one hour
2 Between 1 and 2 hours
3 Between 2 and 4 hours
4 Between 4 and 6 hours
5 Between 6 and 24 hours
6 1 - 2 days
7 2 - 4 days
8 5 - 7 days
9 8 - 10 days
10 11 - 13 days
11 14 - 15 days
12 16 - 30 days
13 1 - 2 months
14 2 - 3 months
15 I still have the dizziness that I got after the trauma

56 *If you got dizziness after the head trauma, what type of dizziness did you have ?*
0 Feeling like being in a carrousell
1 Feeling like being on board of a ship
2 Unsteadiness
3 Other type, please specify.....

After having finished this questionnaire, please go to questionnaire B where you have to indicate on a line the degree of your present symptoms.

First questionnaire for controls in prospective study

Please answer the questions by putting a circle around the appropriate alternative.
Unless otherwise indicated, never encircle more than one possibility!

1-4 Running no.....

5-10 Date today:
dd mm yy

Personalia :

Name:.....

Address: .....

Phone no. .....

11 Sex: 0 Male
1 Female

12-13 Age: ..... years

14-15 Height (cm) .....

16-17 Weight .....

18 *Highest education:*
1 Primary school
2 Secondary school
3 Professional school or special practical education
4 University graduate
5 University, uncompleted
6 Others, please specify.....

19-20 *How many years did you study in total (include schools, University)?* .....

21-26 *Profession* .....

27-28 *Present job:*

29 *Civil status:*
1 Single, living alone
2 Single, living together with a partner
3 Married
4 Widow(er)
5 Divorced
6 Other, please specify .....

GENERAL HEALTH STATUS:

30 *How do you estimate your health status?*
0 I feel healthy
1 I feel unhealthy

Please encircle if you have any of the following diseases/complaints (more than one if necessary):

31 *Diabetes mellitus*
0 No
1 Yes, on medication (please specify:.....)
2 Yes, without medication

32 *Hypertension* (please specify your blood pressure, if you know
..... mm Hg)
0 No
1 Yes, on medication (please specify: .....)
2 Yes, without medication

33 *Rheumatic disease, please specify.....*
0 No
1 Yes, on medication (please specify: .....)
2 Yes, without medication

34 *Heart infarction:*
0 No
1 Yes, once
2 2-3 times
3 More than 3 times

35 *Psychological problems, please specify.....*
0 No
1 Yes, on medication (please specify.....)
2 Yes, without medication

36 *Low back pain in the last month*
0 No
1 Less than 1 day
2 One day to 7 days
3 8 - 15 days
4 More than 15 days
5 Every day

37 *Neck pain in the last month*
0 No
1 One day to 7 days
2 8 - 15 days
3 More than 15 days
4 Every day

38 *Headache in the last month*
0 No
1 One day to 7 days
2 8 - 15 days
3 More than 15 days
4 Every day

39 *Other diseases or complaints*
0 No
1 Yes, please specify .....

40 *Your smoking habits:*
0 Never
1 Smoked, but gave it up
2 Sporadically smoking (less than 1 per day)
3 Regularly 1-5 cigarettes per day
4 More than 5 cigarettes per day

41 *Your alcohol habits* (1 "drink" = 1 glass of wine = 1 small beer = 15 g alcohol):
0 Never
1 Used to, but gave up
2 A few drinks per year
3 One drink per month
4 A few drinks per month
5 1 drink per week

Please encircle any chronic disease that members of your family (parents, siblings, children) suffer from (more than one if necessary):

42 *Psychological problems, please specify.....*
0 No
1 Yes

43 *Neck pain*
0 No
1 Yes

44 *Headache*

0 No
1 Yes

SPECIFIC HEALTH SITUATION

45 *Have you had headache in the last year ?*

0 No
1 Yes

If you did not have any headache in the last year please go to the questions concerning other complaints (questions 68 to 78)

46 *How often did you have headache the last year ?*

0 Less than one day per month
1 1-7 days per month
2 8-15 days per month
3 More than 15 days per month
4 Every day or almost so
5 Other, please specify .....

47 *What was the usual duration of a headache attack/period?*

1 Less than 4 hours
2 4-72 hours
3 More than 72 hours, but still clearly separate episodes
4 Continuous headache with varying intensity
5 Continuous constant headache
6 Changing pattern; short- and long-lasting attacks
7 Other, please specify .....

48 *What was the usual intensity of the headache?*

1 Mild (can continue any activity)
2 Moderate (cannot continue activity, but can stay out of bed)
3 Severe (must go to bed)
4 Excruciating

49 *What was the location of the headache?*

1 One-sided, always right side
2 One-sided, always left side
3 One-sided, changing side
4 Both sides
5 Sometimes One-sided (always same side), sometimes both sides
6 Others, please specify .....

50 *Where did a pain attack or a worsening of the pain, start?*

1 Neck
2 Forehead
3 Another specific place, please specify .....

51 *Did the pain subsequently spread to other areas of the head?*

0 No
1 Yes, from the neck to the forehead
2 Yes, from the forehead to the neck
3 Yes, other patterns, please specify .....
4 Unknown

52 *What was the character of the headache?*

1 Pressing
2 Pounding (pulsating)
3 Usually pressing, but pounding when maximal
4 Other, please specify .....

53 *Did nausea accompany your headache?*

0 No
1 Yes

54 *Did vomiting accompany your headache?*
0 No
1 Yes

55 *Did swelling around one eye accompany your headache?*
0 No
1 Yes

56 *Did increased sensitivity to sounds accompany your headache?*
0 No
1 Yes

57 *Did increased sensitivity to light accompany your headache?*
0 No
1 Yes

58 *Did blurred vision in one eye accompany your headache?*
0 No
1 Yes

59 *Did you feel aggravation of headache when using stairs or bending forward?*
0 No
1 Yes

60 *Did other symptoms accompany your headache?*
0 No
1 Yes, please specify .....

61 *Did turning your head to one side and keeping this position provoke your headache?*
0 No
1 Yes

62 *Did bending the head backwards provoke your headache?*
0 No
1 Yes

63 *Did external pressure towards the upper neck region provoke your headache?*
0 No
1 Yes

64 *Did coughing, sneezing or bowel movements provoke your headache?*
0 No
1 Yes

65 *Did mental stress provoke your headache?*
0 No
1 Yes

66 *At what age did your headache start?*
1 Less than 20 years old, specify if possible ....
2 20-30 years old, specify if possible ....
3 31-40 years old, specify if possible ....
4 More than 41 years old, specify if possible ....
5 Unknown

67 *Has your headache problem changed character since it started?*
0 No
Yes, increased
1 gradually over months/years
2 over days, please specify .....
3 abruptly (in one day), please specify .....
Yes, decreased
4 gradually over months/years
5 over days, please specify.....
6 abruptly (in one day), please specify.....

Other complaints in the last year:

68 *Have you had neck pain in the last year ?*
- 0 No
- 1 Less than one day per month
- 2 One to 7 days per month
- 3 8 - 15 days per month
- 4 More than 15 days per month
- 5 Every day or almost every day

69 *Did you have problems with your memory in the last year ?*
- 0 No
- 1 Yes, sporadically
- 2 Yes, regularly

70 *Did you have concentration problems in the last year ?*
- 0 No
- 1 Yes, sporadically
- 2 Yes, regularly but slight
- 3 Yes, regularly and severe

71 *Did you have ringing or other strange noises in the ear (s) in the last year ?*
- 0 No
- 1 Sporadically less than 15 days per month
- 2 Sporadically more than 15 days per month
- 3 Every day, but not constantly
- 4 Every day all the time

72 *If you did have noises in your ear(s), what kind of noises did you have ?*
- 0 Peep
- 1 Buzzing
- 2 Drone
- 3 Others, please specify .....

73 *Have you been dizzy the last year ?*
- 0 No
- 1 Yes

74 *If yes, what type of dizziness did you have ?*
- 0 Feeling like being in a carrousell
- 1 Feeling like being on board of a ship
- 2 Unsteadiness
- 3 Other type, please specify.....

75 *How often were you dizzy ?*
- 0 Less than once a month
- 1 One time in a week
- 2 Several times in a week
- 3 Several times a day
- 4 Daily
- 5 Other, please specify.....

76 *What made you dizzy ?*
- 0 The dizziness appears without obvious reason
- 1 Physical efforts
- 2 Change of position (e.g. turning round in the bed, getting up quickly)
- 3 Psychological stress
- 4 Other, please specify.....

77 *Did you together with dizziness have nausea ?*
- 0 Yes
- 1 No

78 *Did you together with dizziness have vomiting ?*
- 0 Yes
- 1 No

After having finished this questionnaire, please go to questionnaire B where you have to indicate on a line the degree of your present symptoms.

Questionnaire after 3 months and 1 year for controls in prospective study

Please answer the questions by putting a circle around the appropriate alternative.
Unless otherwise indicated, never encircle more than one possibility!

1-4 Running no.....

5-10 Date today:
dd mm yy

Personalia :

Name:.....

Address: .....

Phone no. .....

SPECIFIC HEALTH SITUATION

11 *Have you had headache in the last month ?*
0 No
1 Yes

If you did not have any headache in the last month please go to the questions concerning other complaints (questions 32 to 41)

12 *How often did you have headache in the last month ?*
0 Less than one day
1 1-7 days
2 8-15 days
3 More than 15 days
4 Every day or almost so
+ Other, please specify .....

13 *What was the usual duration of a headache attack/period?*
1 Less than 4 hours
2 4-72 hours
3 More than 72 hours, but still clearly separate episodes
4 Continuous headache with varying intensity
5 Continuous constant headache
6 Changing pattern; short- and long-lasting attacks
7 Other, please specify .....

14 *What was the usual intensity of the headache?*
1 Mild (can continue any activity)
2 Moderate (cannot continue activity, but can stay out of bed)
3 Severe (must go to bed)
4 Excruciating

15 *What was the location of the headache?*
1 One-sided, always right side
2 One-sided, always left side
3 One-sided, changing side
4 Both sides
5 Sometimes One-sided (always same side), sometimes both sides
6 Others, please specify .....

16 *Where did a pain attack or a worsening of the pain, start?*
1 Neck
2 Forehead
3 Another specific place, please specify .....

17 *Did the pain subsequently spread to other areas of the head?*

0 No
1 Yes, from the neck to the forehead
2 Yes, from the forehead to the neck
3 Yes, other patterns, please specify .....
4 Unknown

18 *What was the character of the headache?*

1 Pressing
2 Pounding (pulsating)
3 Usually pressing, but pounding when maximal
4 Other, please specify .....

19 *Did nausea accompany your headache?*

0 No
1 Yes

20 *Did vomiting accompany your headache?*

0 No
1 Yes

21 *Did swelling around one eye accompany your headache?*

0 No
1 Yes

22 *Did increased sensitivity to sounds accompany your headache?*

0 No
1 Yes

23 *Did increased sensitivity to light accompany your headache?*

0 No
1 Yes

24 *Did blurred vision in one eye accompany your headache?*

0 No
1 Yes

25 *Did you feel aggravation of headache when using stairs or bending forward?*

0 No
1 Yes

26 *Did other symptoms accompany your headache?*

0 No
1 Yes, please specify .....

27 *Did turning your head to one side and keeping this position provoke your headache?*

0 No
1 Yes

28 *Did bending the head backwards provoke your headache?*

0 No
1 Yes

29 *Did external pressure towards the upper neck region provoke your headache?*

0 No
1 Yes

30 *Did coughing, sneezing or bowel movements provoke your headache?*

0 No
1 Yes

31 *Did mental stress provoke your headache?*

0 No
1 Yes

Other complaints in the last month:

32 *Have you had neck pain in the last month ?*
- 0 No
- 1 Less than one day per month
- 2 One to 7 days per month
- 3 8 - 15 days per month
- 4 More than 15 days per month
- 5 Every day or almost every day

33 *Did you have problems with your memory in the last month ?*
- 0 No
- 1 Yes, sporadically
- 2 Yes, regularly

34 *Did you have concentration problems in the last month ?*
- 0 No
- 1 Yes, sporadically
- 2 Yes, regularly but slight
- 3 Yes, regularly and severe

34 *Did you have ringing or other strange noises in the ear (s) in the last month ?*
- 0 No
- 1 Sporadically less than 15 days per month
- 2 Sporadically more than 15 days per month
- 3 Every day, but not constantly
- 4 Every day all the time

35 *If you did have noises in your ear(s), what kind of noises did you have ?*
- 0 Peep
- 1 Buzzing
- 2 Drone
- 3 Others, please specify .....

36 *Have you been dizzy the last month ?*
- 0 No
- 1 Yes

37 *If yes, what type of dizziness did you have ?*
- 0 Feeling like being in a carrousell
- 1 Feeling like being on board of a ship
- 2 Unsteadiness
- 3 Other type, please specify.....

38 *How often were you dizzy ?*
- 0 Less than once
- 1 One time in a week
- 2 Several times in a week
- 3 Several times a day
- 4 Daily
- 5 Other, please specify.....

39 *What made you dizzy ?*
- 0 The dizziness appears without obvious reason
- 1 Physical efforts
- 2 Change of position (e.g. turning round in the bed, getting up quickly)
- 3 Psychological stress
- 4 Other, please specify.....

40 *Did you together with dizziness have nausea ?*
- 0 Yes
- 1 No

41 *Did you together with dizziness have vomiting ?*
- 0 Yes
- 1 No

After having finished this questionnaire, please go to questionnaire B where you have to indicate on a line the degree of your present symptoms.

Rivermead postconcussion symptoms questionnaire

After an injury or accident some people experience symptoms which can cause worry or nuisance. We would like to know if you now suffer any of the symptoms given below. As many of these symptoms occur normally, we would like to compare yourself now with before the accident. For each one please circle the number closest to yous answer.

0 = Nor experienced at all
1 = no more of a problem
2 = a mild problem
3 = a moderate problem
4 = a severe problem

Compared with before the accident do you now (i.e. over the last 24 hours) suffer from:

Headaches	0	1	2	3	4
Felling of dizziness	0	1	2	3	4
Nausea and/or vomiting	0	1	2	3	4
Noise sensitivity; easily upset by loud noise	0	1	2	3	4
Sleep disturbance	0	1	2	3	4
Fatigue; tiring more easily	0	1	2	3	4
Being irritable, easily angered	0	1	2	3	4
Feeling depressed or tearful	0	1	2	3	4
Feeling frustrated or impatient	0	1	2	3	4
Forgetfulness, poor memory	0	1	2	3	4
Poor concentration	0	1	2	3	4
Taking longer to think	0	1	2	3	4
Blurred vision	0	1	2	3	4
Light sensitivity, easily upset by bright light	0	1	2	3	4
Double vision	0	1	2	3	4
Restlessness	0	1	2	3	4
Are you experiencing any other difficulties ? Please specify, and rate as above					
1.	0	1	2	3	4
2.	0	1	2	3	4

Appendix 1

Statistical printouts of the final general linear regression models

Duration of unconsciousness = DURUNCONC
Trauma mechanism = TRMECH
Length of education = STUDYTOT
Sex = SX

Headache (20 days)

Data for the following results were selected according to:
group$="trauma"

Effects coding used for categorical variables in model.

Categorical values encountered during processing are:
SX$ (2 levels)
m, w
TRMECH2$ (2 levels)
assault, other

Dep Var: B1HE14 N: 217 Multiple R: 0.282 Squared multiple R: 0.079

Analysis of Variance

Source	Sum-of-Squares	df	Mean-Square	F-ratio	P
SX$	3209.281	1	3209.281	4.790	0.030
DURUNCONC	3333.386	1	3333.386	4.975	0.027
TRMECH2$	1596.071	1	1596.071	2.382	0.124
STUDYTOT	4311.128	1	4311.128	6.434	0.012
Error	142048.722	212	670.041		

Durbin-Watson D Statistic 1.893
First Order Autocorrelation 0.044

<Bookmark(156)>

Headache (3 months)

Data for the following results were selected according to:
group$="trauma"

Effects coding used for categorical variables in model.

Categorical values encountered during processing are:
SX$ (2 levels)
m, w
TRMECH2$ (2 levels)
assault, other
17 case(s) deleted due to missing data.

Dep Var: B1HE3M N: 200 Multiple R: 0.360 Squared multiple R: 0.130

Analysis of Variance

Source	Sum-of-Squares	df	Mean-Square	F-ratio	P
SX$	6959.180	1	6959.180	11.880	0.001
DURUNCONC	3183.562	1	3183.562	5.435	0.021
TRMECH2$	2623.424	1	2623.424	4.479	0.036
STUDYTOT	5233.460	1	5233.460	8.934	0.003
Error	114226.057	195	585.775		

Durbin-Watson D Statistic 1.809
First Order Autocorrelation 0.093

<Bookmark(157)>

Headache (1 year)

Data for the following results were selected according to:
group$="trauma"

Effects coding used for categorical variables in model.

Categorical values encountered during processing are:
SX$ (2 levels)
m, w
TRMECH2$ (2 levels)
assault, other
25 case(s) deleted due to missing data.

Dep Var: B1HE1Y N: 192 Multiple R: 0.282 Squared multiple R: 0.079

Analysis of Variance

Source	Sum-of-Squares	df	Mean-Square	F-ratio	P
SX$	7077.612	1	7077.612	10.545	0.001
AGE	1450.314	1	1450.314	2.161	0.143
TRMECH2$	1445.918	1	1445.918	2.154	0.144
STUDYTOT	2470.921	1	2470.921	3.681	0.057
Error	125516.071	187	671.209		

Durbin-Watson D Statistic 2.145
First Order Autocorrelation -0.074

<Bookmark(158)>

Memory problems (20 days)

Data for the following results were selected according to:
group$="trauma"

Effects coding used for categorical variables in model.

Categorical values encountered during processing are:
SX$ (2 levels)
m, w
TRMECH2$ (2 levels)

assault, other

Dep Var: B12MEM14 N: 217 Multiple R: 0.147 Squared multiple R: 0.022

Analysis of Variance

Source	Sum-of-Squares	df	Mean-Square	F-ratio	P
SX$	2945.026	1	2945.026	3.212	0.075
STUDYTOT	2027.303	1	2027.303	2.211	0.139
Error	196228.709	214	916.957		

Durbin-Watson D Statistic 2.353
First Order Autocorrelation -0.178

<Bookmark(159)>

Memory problems (3 months)

Data for the following results were selected according to:
group$="trauma"

Effects coding used for categorical variables in model.

Categorical values encountered during processing are:
SX$ (2 levels)
m, w
TRMECH2$ (2 levels)
assault, other
17 case(s) deleted due to missing data.

Dep Var: B12MEM3M N: 200 Multiple R: 0.176 Squared multiple R: 0.031

Analysis of Variance

Source	Sum-of-Squares	df	Mean-Square	F-ratio	P
SX$	4395.422	1	4395.422	4.497	0.035
STUDYTOT	2652.838	1	2652.838	2.714	0.101
Error	192532.022	197	977.320		

Durbin-Watson D Statistic 2.085
First Order Autocorrelation -0.051

<Bookmark(160)>

Memory problems (1 year)

Data for the following results were selected according to:
group$="trauma"
25 case(s) deleted due to missing data.

Dep Var: B12MEM1Y N: 192 Multiple R: 0.248 Squared multiple R: 0.061

Adjusted squared multiple R: 0.047 Standard error of estimate: 30.758

Effect Coefficient Std Error Std Coef Tolerance t P(2 Tail)

CONSTANT 77.402 16.053 0.000 . 4.822 0.000
AGE 0.430 0.168 0.189 0.922 2.566 0.011
WEIGHT -0.434 0.169 -0.189 0.922 -2.574 0.011
STUDYTOT -1.121 0.796 -0.100 0.999 -1.409 0.160

Analysis of Variance
Source Sum-of-Squares df Mean-Square F-ratio P

Regression 11652.443 3 3884.148 4.106 0.008
Residual 177856.802 188 946.047

Durbin-Watson D Statistic 2.430
First Order Autocorrelation -0.217

<Bookmark(161)>

Concentration problems (20 days)

Data for the following results were selected according to:
group$="trauma"

Dep Var: B13CON14 N: 217 Multiple R: 0.174 Squared multiple R: 0.030

Adjusted squared multiple R: 0.026 Standard error of estimate: 27.965

Effect Coefficient Std Error Std Coef Tolerance t P(2 Tail)

CONSTANT 65.752 10.607 0.000 . 6.199 0.000
WEIGHT -0.364 0.140 -0.174 1.000 -2.594 0.010

Analysis of Variance
Source Sum-of-Squares df Mean-Square F-ratio P

Regression 5260.422 1 5260.422 6.726 0.010
Residual 168140.269 215 782.048

Durbin-Watson D Statistic 2.179
First Order Autocorrelation -0.099

<Bookmark(162)>

Concentration problems (3 months)

Data for the following results were selected according to:
group$="trauma"

Effects coding used for categorical variables in model.

Categorical values encountered during processing are:
SX$ (2 levels)
m, w

TRMECH2$ (2 levels)
assault, other
17 case(s) deleted due to missing data.

Dep Var: B13CON3M N: 200 Multiple R: 0.207 Squared multiple R: 0.043

Analysis of Variance

Source	Sum-of-Squares	df	Mean-Square	F-ratio	P
SX$	5044.164	1	5044.164	6.440	0.012
STUDYTOT	2834.040	1	2834.040	3.618	0.059
Error	154295.532	197	783.226		

Durbin-Watson D Statistic 2.105
First Order Autocorrelation -0.060

<Bookmark(163)>

Concentration problems (1 year)

Data for the following results were selected according to:
group$="trauma"

Effects coding used for categorical variables in model.

Categorical values encountered during processing are:
SX$ (2 levels)
m, w
TRMECH2$ (2 levels)
assault, other
25 case(s) deleted due to missing data.

Dep Var: B13CON1Y N: 192 Multiple R: 0.244 Squared multiple R: 0.060

Analysis of Variance

Source	Sum-of-Squares	df	Mean-Square	F-ratio	P
SX$	9814.177	1	9814.177	12.069	0.001
Error	154502.489	190	813.171		

Durbin-Watson D Statistic 1.919
First Order Autocorrelation 0.039

Appendix 2

Univariate regression analysis printouts (including regression coefficients)

Concentration problems versus length of education

Data for the following results were selected according to:
(GROUP$= "trauma")

Dep Var: B13CON14 N: 217 Multiple R: 0.015 Squared multiple R: 0.000

Adjusted squared multiple R: 0.000 Standard error of estimate: 28.396

Effect	Coefficient	Std Error	Std Coef	Tolerance	t	P(2 Tail)
CONSTANT	36.721	9.180	0.000	.	4.000	0.000
STUDYTOT	0.153	0.697	0.015	1.000	0.219	0.827

Analysis of Variance

Source	Sum-of-Squares	df	Mean-Square	F-ratio	P
Regression	38.666	1	38.666	0.048	0.827
Residual	173362.025	215	806.335		

Durbin-Watson D Statistic 2.194
First Order Autocorrelation -0.107

Data for the following results were selected according to:
(GROUP$= "trauma")
17 case(s) deleted due to missing data.

Dep Var: B13CON3M N: 200 Multiple R: 0.107 Squared multiple R: 0.011

Adjusted squared multiple R: 0.006 Standard error of estimate: 28.368

Effect	Coefficient	Std Error	Std Coef	Tolerance	t	P(2 Tail)
CONSTANT	55.219	9.757	0.000	.	5.659	0.000
STUDYTOT	-1.112	0.734	-0.107	1.000	-1.515	0.131

Analysis of Variance

Source	Sum-of-Squares	df	Mean-Square	F-ratio	P
Regression	1847.804	1	1847.804	2.296	0.131
Residual	159339.696	198	804.746		

Durbin-Watson D Statistic 2.148
First Order Autocorrelation -0.082

Data for the following results were selected according to:
(GROUP$= "trauma")
25 case(s) deleted due to missing data.

Dep Var: B13CON1Y N: 192 Multiple R: 0.024 Squared multiple R: 0.001

Adjusted squared multiple R: 0.000 Standard error of estimate: 29.400

Effect	Coefficient	Std Error	Std Coef	Tolerance	t	P(2 Tail)
CONSTANT	45.323	10.070	0.000	.	4.501	0.000
STUDYTOT	-0.250	0.760	-0.024	1.000	-0.329	0.742

Analysis of Variance

Source	Sum-of-Squares	df	Mean-Square	F-ratio	P
Regression	93.616	1	93.616	0.108	0.742
Residual	164223.051	190	864.332		

Durbin-Watson D Statistic 1.984
First Order Autocorrelation 0.006

Memory problems vs length of education

Data for the following results were selected according to:
(GROUP$= "trauma")

Dep Var: B12MEM14 N: 217 Multiple R: 0.083 Squared multiple R: 0.007

Adjusted squared multiple R: 0.002 Standard error of estimate: 30.437

Effect	Coefficient	Std Error	Std Coef	Tolerance	t	P(2 Tail)
CONSTANT	51.281	9.839	0.000	.	5.212	0.000
STUDYTOT	-0.912	0.747	-0.083	1.000	-1.221	0.224

Analysis of Variance

Source	Sum-of-Squares	df	Mean-Square	F-ratio	P
Regression	1380.182	1	1380.182	1.490	0.224
Residual	199173.735	215	926.389		

Durbin-Watson D Statistic 2.357
First Order Autocorrelation -0.180

Data for the following results were selected according to:
(GROUP$= "trauma")
17 case(s) deleted due to missing data.

Dep Var: B12MEM3M N: 200 Multiple R: 0.094 Squared multiple R: 0.009

Adjusted squared multiple R: 0.004 Standard error of estimate: 31.537

Effect Coefficient Std Error Std Coef Tolerance t P(2 Tail)

CONSTANT 60.023 10.847 0.000 . 5.534 0.000
STUDYTOT -1.086 0.816 -0.094 1.000 -1.330 0.185

Analysis of Variance
Source Sum-of-Squares df Mean-Square F-ratio P

Regression 1760.556 1 1760.556 1.770 0.185
Residual 196927.444 198 994.583

Durbin-Watson D Statistic 2.162
First Order Autocorrelation -0.090

Data for the following results were selected according to:
(GROUP$= "trauma")
25 case(s) deleted due to missing data.

Dep Var: B12MEM1Y N: 192 Multiple R: 0.100 Squared multiple R: 0.010

Adjusted squared multiple R: 0.005 Standard error of estimate: 31.425

Effect Coefficient Std Error Std Coef Tolerance t P(2 Tail)

CONSTANT 59.807 10.763 0.000 . 5.557 0.000
STUDYTOT -1.121 0.813 -0.100 1.000 -1.380 0.169

Analysis of Variance
Source Sum-of-Squares df Mean-Square F-ratio P

Regression 1880.857 1 1880.857 1.905 0.169
Residual 187628.387 190 987.518

Durbin-Watson D Statistic 2.503
First Order Autocorrelation -0.253

Headache vs length of education

Data for the following results were selected according to:
(GROUP$= "trauma")

Dep Var: B1HE14 N: 217 Multiple R: 0.165 Squared multiple R: 0.027

Adjusted squared multiple R: 0.023 Standard error of estimate: 26.421

Effect Coefficient Std Error Std Coef Tolerance t P(2 Tail)

CONSTANT 61.699 8.541 0.000 . 7.224 0.000
STUDYTOT -1.593 0.649 -0.165 1.000 -2.455 0.015

Analysis of Variance

Source	Sum-of-Squares	df	Mean-Square	F-ratio	P
Regression	4207.261	1	4207.261	6.027	0.015
Residual	150081.219	215	698.052		

Durbin-Watson D Statistic 1.896
First Order Autocorrelation 0.042

Data for the following results were selected according to:
(GROUP$= "trauma")
17 case(s) deleted due to missing data.

Dep Var: B1HE3M N: 200 Multiple R: 0.192 Squared multiple R: 0.037

Adjusted squared multiple R: 0.032 Standard error of estimate: 25.267

Effect	Coefficient	Std Error	Std Coef	Tolerance	t	P(2 Tail)
CONSTANT	60.900	8.690	0.000	.	7.008	0.000
STUDYTOT	-1.801	0.654	-0.192	1.000	-2.754	0.006

Analysis of Variance

Source	Sum-of-Squares	df	Mean-Square	F-ratio	P
Regression	4843.325	1	4843.325	7.586	0.006
Residual	126406.550	198	638.417		

Durbin-Watson D Statistic 1.820
First Order Autocorrelation 0.088

Data for the following results were selected according to:
(GROUP$= "trauma")
25 case(s) deleted due to missing data.

Dep Var: B1HE1Y N: 192 Multiple R: 0.103 Squared multiple R: 0.011

Adjusted squared multiple R: 0.005 Standard error of estimate: 26.647

Effect	Coefficient	Std Error	Std Coef	Tolerance	t	P(2 Tail)
CONSTANT	50.937	9.127	0.000	.	5.581	0.000
STUDYTOT	-0.981	0.689	-0.103	1.000	-1.424	0.156

Analysis of Variance

Source	Sum-of-Squares	df	Mean-Square	F-ratio	P
Regression	1440.453	1	1440.453	2.029	0.156
Residual	134907.463	190	710.039		

Durbin-Watson D Statistic 2.161
First Order Autocorrelation -0.083

Headache vs duration of unconciousness

Data for the following results were selected according to:
(GROUP$= "trauma")

Dep Var: B1HE14 N: 217 Multiple R: 0.175 Squared multiple R: 0.031

Adjusted squared multiple R: 0.026 Standard error of estimate: 26.373

Effect	Coefficient	Std Error	Std Coef	Tolerance	t	P(2 Tail)
CONSTANT	46.754	2.779	0.000	.	16.821	0.000
DURUNCONC	-1.513	0.579	-0.175	1.000	-2.613	0.010

Analysis of Variance

Source	Sum-of-Squares	df	Mean-Square	F-ratio	P
Regression	4749.644	1	4749.644	6.829	0.010
Residual	149538.836	215	695.529		

Durbin-Watson D Statistic 1.823
First Order Autocorrelation 0.079

Data for the following results were selected according to:
(GROUP$= "trauma")
17 case(s) deleted due to missing data.

Dep Var: B1HE3M N: 200 Multiple R: 0.199 Squared multiple R: 0.040

Adjusted squared multiple R: 0.035 Standard error of estimate: 25.232

Effect	Coefficient	Std Error	Std Coef	Tolerance	t	P(2 Tail)
CONSTANT	43.403	2.737	0.000	.	15.856	0.000
DURUNCONC	-1.654	0.579	-0.199	1.000	-2.856	0.005

Analysis of Variance

Source	Sum-of-Squares	df	Mean-Square	F-ratio	P
Regression	5191.807	1	5191.807	8.155	0.005
Residual	126058.068	198	636.657		

Durbin-Watson D Statistic 1.772
First Order Autocorrelation 0.108

Data for the following results were selected according to:
(GROUP$= "trauma")

25 case(s) deleted due to missing data.

Dep Var: B1HE1Y N: 192 Multiple R: 0.132 Squared multiple R: 0.017

Adjusted squared multiple R: 0.012 Standard error of estimate: 26.554

Effect	Coefficient	Std Error	Std Coef	Tolerance	t	P(2 Tail)
CONSTANT	42.279	2.923	0.000	.	14.465	0.000
DURUNCONC	-1.137	0.620	-0.132	1.000	-1.835	0.068

Analysis of Variance

Source	Sum-of-Squares	df	Mean-Square	F-ratio	P
Regression	2374.678	1	2374.678	3.368	0.068
Residual	133973.239	190	705.122		

Durbin-Watson D Statistic 2.126
First Order Autocorrelation -0.067