Pain and disability in the jaw and neck regions after whiplash trauma:

A short- and long-term perspective

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This project was carried out within the Swedish National Clinical Research School program in Odontology, founded by the Swedish Research Council.
Men ought to know that from the brain, and from the brain only, arise our pleasures, joys, laughter and jests, as well as our sorrows, pain, griefs and tears.

Through it, in particular, we think, see, hear and distinguish the ugly from the beautiful, the bad from the good, the pleasant from the unpleasant.

Attributed to Hippocrates, Fifth Century, B.C.
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Abstract

Background
Whiplash trauma, a hyperextension-flexion trauma to the neck that is often related to a car accident, affects tens of thousands in Sweden every year. A significant proportion will develop long-term symptoms including neck pain and dysfunction – this is embraced as Whiplash associated disorders (WAD). Some individuals also develop pain and dysfunction in the orofacial region that is denoted as Temporomandibular disorder (TMD). TMD is common in the population with a prevalence of about 10% but the relation to whiplash trauma is still unclear. The limited number of prospective studies on TMD after whiplash trauma show diverging results, but it has been suggested that TMD develops over time and not in close proximity to the trauma. Prospective studies are needed to determine the course of jaw pain and disability after whiplash trauma. The general aim of this thesis was to evaluate the presence and course of pain and disability in the jaw and neck regions at the acute and chronic stages after whiplash trauma.

Methods
This prospective cohort study included at baseline 176 cases with a recent whiplash trauma, and 116 age and gender matched controls without a history of neck trauma that were recruited from the general population. The cases had visited the emergency department at Umeå university hospital, Sweden, with neck pain within 72 hours following a car accident and had been diagnosed with neck distortion by a physician. The cases were examined within one month after the trauma (December 2010 to January 2016) and at a 2-year follow-up (December 2012 to January 2018). All participants completed questionnaires regarding pain and disability in the jaw and neck regions, physical symptoms (pain and non-pain items), and depression. At baseline, 80 of the cases and 80 of the controls also completed a 5-minute chewing capacity test. At the 2-year follow-up, 119 cases (68%) and 104 controls (90%) were re-examined with the same questionnaires.
Results
Compared to controls, within one month after a whiplash trauma cases reported significantly more pain in the jaw and neck regions with a positive correlation between the intensity of pain in these regions (Paper I). In the acute stage after trauma, cases, compared to controls, showed a reduced chewing capacity, and this was related to the severity of neck disability (Paper II). For cases, jaw and neck pain correlated positively to each other, to non-specific physical symptoms, and to depression at both the acute (Paper III) and chronic stages (Paper IV). About one third (34%) of cases reported frequent orofacial pain at baseline, and for a majority of these, the pain persisted at the 2-year follow-up (Paper IV).

Conclusions
The presence of orofacial pain early after a whiplash trauma indicates involvement of central sensitization and spread of pain between the jaw and neck regions. The positive correlations between pain in the jaw and neck regions, and to psychosocial factors, underline the integration of these regions and the importance of a biopsychosocial perspective. The impaired jaw function shortly after a neck trauma further underlines the close sensorimotor relationship between the trigeminal and cervical regions. The finding that orofacial pain is common shortly after whiplash trauma, and often persists into the chronic stage, indicates that assessment in the acute stage should include both the neck and jaw regions. From this, it follows that multidisciplinary teams that entail both medical professions and dentists specialised in orofacial pain can be beneficial in the early assessment after whiplash trauma.
# Abbreviations

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<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>CI</td>
<td>Confidence interval</td>
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<tr>
<td>CNS</td>
<td>Central nervous system</td>
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<td>DC/TMD</td>
<td>Diagnostic Criteria for Temporomandibular Disorders</td>
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<td>ENT</td>
<td>Ear Nose and Throat</td>
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<td>IASP</td>
<td>International Association for the Study of Pain</td>
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<td>ICD-10</td>
<td>International Statistical Classification of Diseases and Related Health Problems 10th Revision</td>
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<td>IQR</td>
<td>Interquartile range</td>
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<td>NDI</td>
<td>Neck disability index</td>
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<td>NRS</td>
<td>Numeric rating scale</td>
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<td>QTF</td>
<td>Québec task force</td>
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<td>RDC/TMD</td>
<td>Research Diagnostic Criteria for Temporomandibular Disorders</td>
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<td>SCL-90-R</td>
<td>The Symptom Checklist -90 Revised</td>
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<tr>
<td>Strada</td>
<td>Swedish Traffic Accident Data Acquisition</td>
</tr>
<tr>
<td>STROBE</td>
<td>STrengthening the Reporting of OBservational studies in Epidemiology</td>
</tr>
<tr>
<td>TMD</td>
<td>Temporomandibular Disorders</td>
</tr>
<tr>
<td>TMJ</td>
<td>Temporomandibular joint</td>
</tr>
<tr>
<td>WAD</td>
<td>Whiplash-Associated Disorders</td>
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<td>3Q/TMD</td>
<td>Three screening questions (Q1, Q2 and Q3) on jaw pain and dysfunction</td>
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Det generella syftet med denna avhandling var att utvärdera förekomst och förlopp av smärta och funktionsstörning i käk- och nackregionerna i de akuta och kroniska stadierna efter whiplashtrauma.


Efter 2 år undersöktes 119 av fallen (68%) och 104 av kontrollerna (90%) med samma frågeformulär.

Inom en månad efter whiplaschtraumat rapporterade fallen mer smärta i käk-ansikts- och nackregionerna än kontrollerna. Det fanns ett samband mellan smärtintensiteten i dessa regioner (studie I). Jämfört med kontrollerna uppvisade fallen också i det akuta skedet efter trauma en sämre tuggkapacitet, som var relaterad till svårighetsgraden av nackbesvår (studie II). För fallen var käk- och nacksmärta relaterade till varandra samt till övriga fysiska symptom och depression, både i det akuta (studie III) och kroniska (studie IV) skedet. Ungefär en tredjedel av fallen rapporterade frekvent käk-ansiktssmärta i det
akuta skedet och för majoriteten av dessa kvarstod smärten efter 2 år (studie IV).

Original papers


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Introduction

Jaw function

A dinner can be a moment of pleasure, a moment in life to remember, not only for the taste and nutrition, but also for the sensory experience in a social gathering. But for some individuals, this moment can be memorable in the wrong way when pain is present, when eating and chewing provoke pain and discomfort. The primary function of the human jaw system in eating and mastication includes activities such as mouth opening, biting, and chewing. Our teeth are important for these activities but also other parts of the jaw system such as jaw muscles and joint, and in fact, also the neck. This thesis addresses questions regarding pain and impairment in the jaw and neck regions following a whiplash trauma.

The neck and its function

The neck, with the cervical spine, is composed of seven vertebrae that support the weight of the head. Nerves pass through the cervical spine inside these vertebrae and are thereby protected from mechanical damage (Sobotta et al. 1990). The movement of the head and neck is performed by the neck muscles that adjust the position of the head. The bulk of knowledge on neck function is related to the visual and vestibular systems, and most neurophysiological studies have dealt with the coordination of head and eye movements in gaze-shifting behaviour (Berthoz et al. 1992). The neck, together with the visual and the vestibular systems, is also involved in postural control and related movements (Peterson 2004). Furthermore, the neck is also involved in movements of the jaw.

Thus, in jaw movements, both the jaw and neck regions are functionally involved. The lower jaw, or mandible, is a single bone that together with the temporal bones on both sides of the skull, compose the temporomandibular joint (TMJ). Via muscles, the lower jaw is further connected to the head, the hyoid bone, the upper ribs, the clavicula and the vertebrae in the neck. The innervation needed for natural jaw function, including eating, is based on six out of the twelve cranial nerves together with some of the spinal nerves. The cranial nerves have their origin in the brain stem, a small but complex region of the central nervous system (CNS). The brain stem contains the ascending tract that brings information to the brain cortex about conditions in the environment, body position and movement. These inputs allow the cortex and brain stem to send coordinated information about activation to the muscles (Kandel et al. 2000). During jaw function, this intricate neuromuscular system activates the
Introduction

Jaw as well as neck muscles resulting in coordinated movements in three joint systems – the temporomandibular, atlanto-occipital, and cervical spine joints (Eriksson et al. 2000; Häggman-Henrikson et al. 2006; Zafar et al. 2000b; 2002). This integrated jaw-neck motor function is suggested to be innate (Zafar et al. 2000b) and can be seen already in the foetus during yawning (Sepulveda and Mangiamarchi 1995). Taken together, the jaw and neck region is an extremely complex part of the musculoskeletal system that requires balance between the jaw and head/neck systems for optimal jaw function (Okeson 2013b) (Fig. 1).

Figure 1. A schematic illustration of the close relationship between jaw and neck muscles that provide the movement and position of the head and jaw. From Okeson JP: Management of temporomandibular disorders and occlusion, 7th ed. P 25, Mosby, and imprint of Elsevier Inc. Reprinted with kind permission from Professor Okeson and Elsevier.

Assessment of jaw function

The function and capacity of the jaw motor system can be assessed in several different dimensions, e.g. movement, bite force, precision, endurance and chewing efficiency. To assess the motor function of the jaw and neck, movements can be recorded with cameras and markers attached to the facial skin of the head and jaw (Eriksson et al. 1998; Häggman-Henrikson et al. 1998; Zafar et al. 2000a) The endurance can be tested with different load tests such as static clenching (Christensen et al. 1982; Svensson et al. 2001) or dynamic...
chewing tests (Dao et al. 1994; Farella et al. 2001; Gavish et al. 2002; Häggman-Henrikson et al. 2004; Kalezic et al. 2010; Karibe et al. 2003; Koutris et al. 2009). During an endurance task, fatigue and pain will develop sooner or later (Noakes 2012). The sensation of fatigue is a psychophysical quantity with changes both locally and centrally, in the muscles and brain, respectively thus indicating a protective role and a signal to change a behaviour (Ament and Verkerke 2009). Fatigue results in reduced speed, power and performance (Noakes 2012). Disturbed sensorimotor function or reduced capacity in the jaw-neck system can manifest as impaired movements (Eriksson et al. 2004; Häggman-Henrikson et al. 2002; Zafar et al. 2006) and reduced endurance (Häggman-Henrikson et al. 2004; Kalezic et al. 2010; Svensson et al. 2001). Over the last decades, the importance of patient reported outcomes have been stressed and their use increased both in clinical and research settings (John 2018). Therefore, patient reported outcomes such as grading of pain, functional limitations and disability, as well as psychosocial factors have been incorporated in diagnostic systems for TMD (Dworkin and LeResche 1992; Schiffman et al. 2014).

**Acute and chronic pain**

The Task force on taxonomy of the International Association for the Study of Pain (IASP) defines pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage” (Merskey and Bogduk 1994). According to IASP terminology, pain can be divided into different categories, *nociceptive pain* is the warning signal for a potentially damaging threat to the body; this is a basic and vital physiologic response for our survival. Noxious stimuli, such as chemical or mechanical, activate nociceptors in the tissues. *Neuropathic pain* describes pain caused by a lesion or disease of the nervous system (Treede 2018). *Nociplastic pain* has been proposed (Kosek et al. 2016) as a third mechanistic descriptor for clinical classification of chronic pain that arises from altered nociception despite no clear evidence of actual or threatened tissue damage. The term has recently been accepted by IASP (Treede 2018). The duration of pain is also used to classify the pain as acute or chronic (Treede et al. 2015). Acute pain is a warning signal for a disease or threat for our survival. Normally the pain will cease in a few weeks when damaged tissue has healed. Chronic pain is defined as pain that persists or occurs for longer than three months, and it can be further subcategorized (Treede et al. 2015). Chronic pain is not only prolonged acute pain with the function to protect the body, but there are also changes described on different levels in the nervous system (DeLeo and Winkelstein 2002). These changes involve several mechanisms that contribute to periferal and central sensitization (Nijs et al. 2011). Furthermore, chronic pain is associated with a range of psychosocial symptoms (Linton and Shaw 2011).
Pain and the Biopsychosocial model

Every individual’s experience of pain is sculptured by interacting internal and external factors (Fillingim 2017). Pain is always subjective with many dimensions (Merskey and Bogduk 1994), and because it is unpleasant, it also involves emotions. To broaden the perspective from the biomedical model with biological measures as a norm accounting for health or disease, the biopsychosocial model was introduced in 1977 with three domains (Engel 1977). The bio part includes physical mechanisms, for example, genetic and biomedical markers. The psychosocial part includes psychological factors such as anxiety and depression and also social factors, for example, the home and work environment (Engel 1977). This conceptual model was initially proposed in the field of psychiatry, but a decade later it was also brought into the sphere of musculoskeletal disorders (Waddell 1987). The model has relevance for both acute and chronic pain, but has been used most widely in chronic pain disorders (Gatchel et al. 2007). The relative contribution of the bio and psychosocial parts in the model is not static, and the relevance varies between individuals and also during the course of a disorder. The model has been discussed regarding its limitations as being too broad and without guidelines or recommendations. Even so, the model is proposed to be highly commendable for embedment in both research and patient care (Jull 2017) including management of TMD (Suvinen et al. 2005). In patient care, the model has supported the growth of interdisciplinary rehabilitation programs (Jull 2017).

Nomenclature for symptoms related to the jaw system

In common with other parts of the musculoskeletal system, the jaw system can be affected with pain and dysfunction. Over time the nomenclature for this condition has varied, which reflects different concepts of pathogenesis, and difficulties in pinpointing the source of the symptoms (Okeson 2013a). Some examples are Costen’s syndrome, TMJ dysfunction syndrome, Myofascial pain dysfunction syndrome, Facial arthromyalgia, Occlusomandibular disturbances, and Craniomandibular disorders. Today, the most commonly used term is temporomandibular disorders (TMD). Due to the complexity of the integrated jaw-neck region described earlier, Cervico-cranio-mandibular-dysfunction disorders was suggested as a description for musculoskeletal disorders comprising both the head–neck and jaw regions (Eriksson and Zafar 2005; Häggman-Henrikson and Eriksson 2004). In this thesis, together with the term “jaw pain and disability”, the term ”Temporomandibular disorders” (TMD) is used since it is the internationally most established term and also it relates to diagnostic systems (Dworkin and LeResche 1992; Schiffman et al. 2014). Regardless of nomenclature, symptoms from the jaw system constitute a
significant health problem and were described early, i.e. in the Old and New Testaments (Psalms 112:10, Matthew 13:1-48).

**Temporomandibular disorders (TMD)**

TMD is the embracing term for pain and impaired function involving the jaw muscles, the temporomandibular joint (TMJ) and associated structures (Dworkin and LeResche 1992; Okeson and de Kanter 1996). Pain symptoms may develop in the temples, face, jaw, or jaw joint, and can manifest as pain on movement, reduced mouth opening or clicking/catching in the TMJ. TMD is the most common cause for chronic pain in the orofacial region (Maixner et al. 2011; Schiffman et al. 2014) and is one of the diseases and clinical conditions associated with chronic pain (Treede et al. 2015). Chronic pain, especially when present in the orofacial region, has a great impact on the quality of life for the individual (Dahlström and Carlsson 2010) and it incurs large costs for our society (Gatchel et al. 2006).

**Epidemiology of TMD**

Epidemiology is a study method in health research on the natural occurrence of disease in different populations as well as its natural course if left untreated. One main purpose with epidemiological studies is to gain knowledge as to why some individuals develop a specific medical condition or disease while others do not. The occurrence of a disease can be described by its prevalence – the number of individuals divided by the size of the population at a given time. Incidence, another term in epidemiology, describes the occurrence or onset of new cases with a disease over a specified time period (Rothman 2012). Studies on the prevalence of diseases can therefore provide information about how common different health conditions are and the associated burden on the individuals and society (Drangsholt 1999). Knowledge about the natural course of a disease is therefore a key for our understanding of pathophysiological mechanisms as well as for identification of risk factors.

One of the first epidemiological studies on pain and dysfunction of the masticatory system was published in 1972 (Helkimo et al. 1972). Early (Helkimo 1976) as well as later studies (Lövgren et al. 2016a) indicate that TMD is a common heterogeneous pain condition that occurs more frequently in women. Both TMD pain and dysfunction have a fluctuating pattern over time (Könönen and Nyström 1993; Lövgren et al. 2017; Marklund and Wänman 2010; Wänman and Agerberg 1987) and vary over the life span (Lövgren et al. 2016a). The prevalence of severe TMD-related symptoms is fairly low in young children (Köhler et al. 2009; Lövgren et al. 2016a), but increases during adolescence, particularly in girls (List et al. 1999; Lövgren et al. 2016a; Nilsson et al. 2007).
In the age group 10 to 15 years, 5 to 9% have severe symptoms (Köhler et al. 2009). From the age of 12, females report twice as much TMD pain as males. In adult populations, about 10% report jaw pain and dysfunction and this is more frequent in females especially in the 20-50 year olds (LeResche 1997; Lövgren et al. 2016a; Macfarlane et al. 2002). After its peak in middle age, the occurrence of TMD symptoms gradually decreases in older age groups (Lövgren et al. 2016a). The annual incidence for first-onset TMD pain in an adult population is about 4% in both men and women (Slade et al. 2013). The similar incidence of TMD in women and men, in combination with the higher prevalence in women, indicate that women do not recover to the same extent as men.

**Risk factors and aetiology for TMD**

General health influences the development of TMD. The frequency of psychological factors is a strong predictor for the incidence of TMD (Fillingim et al. 2013). Furthermore, the presence of painful and non-painful physical symptoms such as low back pain, irritable bowel syndrome and poor sleep quality predict first-onset TMD (Sanders et al. 2013). In accordance with this, TMD is no longer considered as solely a local disorder but rather a condition with multifactorial aetiology (Suvinen et al. 2005). Putative strong risk factors are health conditions such as abdominal pain, depression, ringing in the ears, and “nonspecific orofacial” symptoms for example as jaw stiffness and fatigue together with self-reported multiple parafunctions such as clenching and grinding (Slade et al. 2016). Whiplash trauma may be one of the risk factors for the onset of TMD (De Boever and Keersmaekers 1996; Häggman-Henrikson et al. 2013b).

**Pain in the jaw and neck regions**

Co-morbidity of pain between the jaw and neck regions is common (Ciancaglini et al. 1999; Visscher et al. 2001). Thus, individuals with TMD have more pain in the neck compared to the general population and vice versa (De Laat et al. 1998; Visscher et al. 2001). A mutual relationship has been demonstrated between pain in the trigeminal and spinal regions (Marklund et al. 2010). Furthermore, increased frequency and severity of spinal pain increased the odds for developing symptoms in the jaw-face region and vice versa, thus demonstrating a reciprocal dose-response relationship between pain in the spinal and trigeminal regions (Wiesinger et al. 2009). Anatomically, the spinal and trigeminal nerves have a close relation in the brainstem (Sessle et al. 1986). Taken together, the findings further underline the close relationship between the jaw and neck regions.
Introduction

Neck pain in the population

Neck pain is common (Hoy et al. 2014) with most individuals experiencing neck pain at some point in their life (Haldeman et al. 2010). More than 50% of individuals that have experienced an episode of neck pain also report chronic neck pain after 1 to 5 years (Carroll et al. 2008a).

Neck pain is one of the leading global causes of disability and overall burden in most western countries (Hoy et al. 2014; Vos et al. 2012). Most neck pain is classified as non-specific, but is specific when related to a whiplash trauma. In an adult population-based study, continuous neck pain lasting for more than 6 months was reported by about 20%, and of those one in three had a history of neck trauma (Guez et al. 2002). Individuals with neck pain related to a neck trauma were more frequently on sick leave and their perceived health was worse compared to individuals with neck pain but no history of trauma (Guez et al. 2003).

Whiplash, terminology and history

A traumatic neck injury is not a modern occurrence. It was already described as ‘sprain in the cervical vertebrae’ in ‘The Edwin Smith Surgical Papyrus’ (Papyrus 1930) from the pre-Greek age of mankind (17th century B.C) that was proposed to be one of the most important scientific documents in history. In the 19th century, symptoms occurring after railway accidents were seen as “spinal concussion” also named ‘railway spine’ or ‘Erichsen disease’ (Keller and Chappell 1996). The term whiplash was launched by Crowe in 1928 at a symposium when he mentioned the term “whiplash” to refer, not to the injury but to the mechanism (Crowe 1964). From the 1950s, the term has been more widely used in scientific papers and today is common in both research and clinical work. However, the physical neck trauma is not just a whiplash motion, but it has a complex mechanism where abnormal motions yield strain on various tissues that may lead to the injury (Kaneoka et al. 1999). Today, the most common cause for a whiplash trauma is related to car accidents that may lead to so-called whiplash injury (Holm et al. 2009). Whiplash is defined by the Quebec Task Force (QTF) as “an acceleration-deceleration mechanism of energy transfer to the neck. It may result from rear-end or side-impact motor vehicle collisions, but can also occur during diving or other mishaps” (Spitzer et al. 1995). The source of the injury is seldom uncovered (Sterner and Gerdle 2004), but even without a specific lesion, evidence supports a lesion-based model (Curatolo et al. 2011). Patients with chronic symptoms after whiplash trauma, present with a variety of symptoms, most common are neck pain, neck stiffness and headache (Häggman-Henrikson et al. 2014; Sterner and Gerdle 2004). Patients may also report dizziness, vertigo, pain in other parts of the body, and
cognitive symptoms such as fatigue, concentration problems and poor memory (Styrke et al. 2017). In addition, pain from the jaw-face region has reported to be part of the spectrum of chronic symptoms (Häggman-Henrikson et al. 2011).

**Incidence and symptoms of whiplash trauma**

The incidence of whiplash trauma in Sweden, Western Europe and North America is about 2-3 per 1000 (Holm et al. 2009; Sterner et al. 2003; Styrke et al. 2012). That means that in Sweden, every year tens of thousands are affected by a whiplash trauma (Styrke 2012). The variety of symptoms that may occur after a whiplash trauma are embraced as Whiplash Associated Disorders (WAD) to describe the injury-related symptoms, and to distinguish them from the mechanism of injury (Spitzer et al. 1995) (Table 1).

Thus, individuals with a whiplash trauma are a heterogeneous group that presents with a variety of symptoms already in the acute stage (Jull et al. 2011) and with varying recovery. The main recovery occurs within the first three months (Sterling et al. 2010). Most individuals are expected to recover after a whiplash trauma, but at one year post injury up to 50% will have some degree of ongoing symptoms (Carroll et al. 2008b; Kamper et al. 2008; Sterling et al. 2010; Sterner and Gerdle 2004; Sterner et al. 2003). High neck pain intensity and neck disability in the acute stage after the trauma are strong prognostic factors for poor recovery, predicting remaining symptoms, predominately neck pain (Walton et al. 2013).

<table>
<thead>
<tr>
<th>Grade</th>
<th>Symptoms and signs</th>
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<tr>
<td>WAD O</td>
<td>No complaints about the neck; no physical sign(s).</td>
</tr>
<tr>
<td>WAD I</td>
<td>Neck complaint of pain, stiffness or tenderness only, no physical sign(s).</td>
</tr>
<tr>
<td>WAD II</td>
<td>Neck complaint and musculoskeletal sign(s) including decreased range of movement and point tenderness.</td>
</tr>
<tr>
<td>WAD III</td>
<td>Neck complaint and neurological sign(s) including decreased or absent deep tendon reflexes, muscle weakness, and sensory deficits.</td>
</tr>
<tr>
<td>WAD IV</td>
<td>Neck complaint and fracture or dislocation.</td>
</tr>
</tbody>
</table>

Table 1. Classification of Whiplash associated Disorders (WAD) according to the Quebec Task Force (QTF) criteria (Spitzer et al. 1995)
TMD - WAD

In patients with chronic WAD, both the prevalence and incidence of TMD pain are higher compared to healthy controls (Häggman-Henrikson et al. 2013b). In patients with TMD, one in four report a history of head-neck trauma as a factor for the onset (De Boever and Keersmaekers 1996; Häggman-Henrikson et al. 2013b). Patients with TMD in combination with WAD often present with more severe jaw pain and disability compared to patients without a neck trauma (Goldberg et al. 1996). Furthermore, patients with posttraumatic TMD seem to have a poorer prognosis for recovery, and they seek and demand more treatment (Kolbinson et al. 1997). Also in chronic WAD patients, signs of impaired sensorimotor function have been reported with sensory disturbances in the trigeminal area (Häggman-Henrikson et al. 2013a; Knibestol et al. 1990; Sterner et al. 2001), disturbed coordination and smaller amplitudes of jaw and head-neck movements in jaw opening-closing tasks, (Eriksson et al. 2004; Häggman-Henrikson et al. 2002) as well as reduced endurance during chewing (Häggman-Henrikson et al. 2004; Kalezic et al. 2010). Furthermore, patients with chronic WAD report jaw pain and discomfort in daily jaw activities such as eating and chewing (Grönlund et al. 2008). All of these mentioned functional impairments in patients with a whiplash trauma underline the close sensorimotor connection between the jaw and neck regions.
Rationale for this thesis

TMD is common in the population (Lövgren et al. 2016a) and a whiplash trauma can be an initiating factor (Häggman-Henrikson et al. 2013b) but the relation to a whiplash trauma is still unclear. Patients with jaw pain and dysfunction related to a whiplash trauma may seek help in both dental and general medical health care. From medical primary or secondary care, these patients may be referred to specialists in neurology, ENT-specialists, or dentists specialized in orofacial pain. General dental practitioners in primary dental care are also expected to frequently meet patients with TMD of varying severity in their daily practice where whiplash trauma may be an important contributing factor. Most studies on pain and dysfunction in the jaw-face region after whiplash trauma are cross-sectional and have been conducted within chronic WAD patient populations. Cross-sectional studies report a prevalence of TMD pain up to 50% in populations with chronic WAD (Häggman-Henrikson et al. 2013b). The limited number of prospective studies on TMD after whiplash trauma show diverging results and the results from these studies are also difficult to compare due to heterogeneity in data collection, study populations, and outcome measures (Fernandez et al. 2009; Häggman-Henrikson et al. 2013b). Pain and disability in the jaw region have mostly been suggested to develop over time rather than being a part of the acute stage after whiplash trauma (Häggman-Henrikson et al. 2014). Taken together, there is a shortage of studies evaluating pain and disability in the jaw region and jaw motor function in the acute stage after whiplash trauma, as well as prospective studies describing the course of pain and disability in the jaw region during the transition from acute to chronic WAD.

Improved knowledge on the relationship between whiplash trauma and development of jaw pain and dysfunction can contribute to a scientific base for both for dental and medical professionals in assessment and management of individuals exposed to a whiplash trauma. Prospective studies are therefore needed in order to gain more knowledge on the link between TMD and whiplash trauma both in a short- and long-term perspective.
Objective

The overall aim for this thesis was to evaluate the presence and course of pain and disability in the jaw and neck regions in relation to whiplash trauma in a short and long-term perspective.

The goal was to better understand how a neck trauma may affect the interaction between the jaw and the neck regions as well as the possible involvement of psychosocial factors. The results can thus provide a scientific basis for assessment and improved management of individuals after a whiplash trauma.

Specific aims

Paper I  To analyse the prevalence of jaw pain and disability, as well as the relationship between pain and disability in the jaw and neck regions shortly after a whiplash trauma.

*The null hypothesis* was that no relationship exists between jaw and neck pain and disability shortly after a whiplash trauma.

Paper II  To assess the functional capacity of the jaw system during a dynamic chewing test shortly after a whiplash trauma.

*The null hypothesis* was expressed as no difference between cases and controls with respect to elicited symptoms during the chewing task.

Paper III  To analyse jaw and neck pain and disability in relation to physical symptoms and depression and jaw pain related disability shortly after a whiplash trauma.

*The null hypothesis* was expressed as no differences between cases and controls with regard to severity of physical symptoms, depression, and disability.

Paper IV  To evaluate the course of jaw pain and disability following a whiplash trauma both shortly after a whiplash trauma and at a 2-year follow-up.
Materials and Methods

Study population

The thesis is based on a prospective cohort study comprising 176 cases with a recent whiplash trauma and 116 age and gender matched controls at baseline. The cases had visited the emergency department at Umeå university hospital, Umeå, Sweden with neck pain within 72 hours following a car accident. The neck pain was diagnosed with neck distortion (ICD-10-S13.4) by a physician. The hospital had a well-defined catchment area of about a 60 km radius around Umeå with almost 150,000 inhabitants in 2013. The cases were consecutively invited to the study via the Hospital’s Injury Data base and the Strada (Swedish Traffic Accident Data Acquisition) (Fig. 1).

Figure 2. Flowchart over the study population at baseline and at follow-up examination.
From December 2010 to January 2016, the cases were examined within one month after the trauma, and at a 2-year follow-up from December 2012 to January 2018. The age and gender matched control group was recruited from the general population by local advertising. All participants completed questionnaires that included questions on jaw and neck pain and disability, non-specific physical symptoms and depression. At baseline, 80 of the cases and 80 of the controls also completed a 5-minute chewing capacity test. At the 2-year follow-up, 119 cases (68%) and 104 controls (90%) were re-examined with questionnaires. All participants were contacted by a dental nurse who scheduled the appointments and administrated the questionnaires. The examiner was blinded to whether participants were cases or controls.

Inclusion criteria for both cases and controls:

- Age 18–70 years
- Living in the Umeå municipality
- Able to understand oral and written Swedish language.

Exclusion criteria for cases was a WAD grade IV (fracture) (Spitzer et al. 1995), and for controls any history of neck trauma.

Study sample

In total, 292 individuals, 176 cases and 116 controls, participated in the project (Table 2). At the time of the follow-up, four individuals were excluded from the case group due to incorrect code number (n=1), participation twice due to repeated whiplash traumas (n=2), and could not be matched to baseline data due to change of name (n=1). One control was incorrectly categorised as a case at baseline, but was correctly included in the control group at the follow-up. In the control group, two individuals had participated twice in the baseline examination, and their second follow-up examination was therefore excluded (Fig. 2).
Table 2. Overview of the four studies in the thesis.

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<tr>
<th></th>
<th>Paper I Pain</th>
<th>Paper II Function</th>
<th>Paper III Axis II</th>
<th>Paper IV Prospective</th>
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<tr>
<td><strong>Aim</strong></td>
<td>Analyse prevalence of jaw pain and disability, and the relationship between pain and disability in the jaw and neck regions shortly after whiplash trauma</td>
<td>Evaluate the functional capacity of the jaw system during a dynamic chewing test shortly after whiplash trauma</td>
<td>Analyse jaw and neck pain and disability in relation to non-specific physical symptoms and depression shortly after whiplash trauma</td>
<td>Evaluate the course of jaw pain and disability following a whiplash trauma both shortly after a whiplash trauma and at a 2-year follow-up</td>
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<tr>
<td><strong>Design</strong></td>
<td>Cross-sectional case-control</td>
<td>Cross-sectional case-control</td>
<td>Cross-sectional case-control</td>
<td>Prospective 2-year cohort</td>
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<tr>
<td><strong>Sample</strong></td>
<td>Baseline: Cases 1* (n=70) (40♀, 30♂, 35.5 yrs**)</td>
<td>Baseline: Cases (n=80) (47♀, 33♂, 34.1 yrs)</td>
<td>Baseline: Cases (n=181) (106♀, 75♂, 35.2 yrs)</td>
<td>Baseline: Cases (n=176) (104♀, 72♂, 35.2 yrs) Controls (n=116) (68♀, 48♂, 32.8 yrs)</td>
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<td></td>
<td>Cases 2* (n=70) (42♀, 28♂, 33.8 yrs)</td>
<td>Controls (n=80) (47♀, 33♂, 35.0 yrs)</td>
<td>Controls (n=117) (67♀, 50♂, 33.9 yrs)</td>
<td>2-year follow-up: Cases (n=119) (73♀, 46♂, 34.9 yrs) Controls (n=104) (59♀, 45♂, 34.9 yrs)</td>
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<td>Controls (n=70) (42♀, 28♂, 33.8 yrs)</td>
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<td><strong>Variables</strong></td>
<td>- 3Q/TMD</td>
<td>- 3Q/TMD, NDI, JDC</td>
<td>- NRS, current pain, Physical symptoms, Depression, JDC, DS</td>
<td>- 3Q/TMD, NDI, JDC, Physical symptoms, Non-pain Physical, Depression</td>
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<td>- NRS, current pain</td>
<td>- Chewing test</td>
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<td>- JDC</td>
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<td>- Kruskal-Wallis</td>
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<td><strong>Statistical analysis</strong></td>
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*Cases 1 and controls were assessed with questionnaires and a chewing test. Cases 2 were assessed with questionnaires only.

**Mean age

Materials and Methods

Data collection

Questionnaires

Neck Disability Index
The Neck Disability Index (NDI) includes ten items, each scored individually on a 6-point Likert scale from 0 (no disability) to 5 (complete disability), and the total score (0-50) describes the degree of disability (Vernon and Mior 1991). The sum-score of 0-50 can be converted to a 0-100 percentage scale by multiplying the total score with 2 (Ackelman and Lindgren 2002). The NDI scores are classified as 0-8% = no disability, 10-28% = mild, 30-48% = moderate, 50-68% = severe, and 70-100% = complete disability. Several studies have reviewed these categories to determine a dichotomous cut-off for "disabled" vs "not disabled" or "recovered" vs "not recovered" following a neck trauma. Proposed cut-offs, range from 20 to 40%, with the average of 30% (Vernon 2008).

Numeric Rating Scale
The numeric rating scale (NRS) is a unidimensional single-item eleven point scale graded from 0 (no pain) to 10 (worst pain imaginable) for rating pain intensity (Hawker et al. 2011). In this thesis NRS was used for rating of pain in the face/mouth region and neck region (denoted Jaw pain and Neck pain, respectively).

3Q/TMD
The 3Q/TMD includes three screening questions on jaw pain and dysfunction with Yes/No responses (Lövgren et al. 2016a)
  - Question 1 (Q1): Do you have pain in your temple, face, jaw, or jaw joint once a week or more?
  - Question 2 (Q2): Do you have pain once a week or more when you open your mouth or chew?
  - Question 3 (Q3): Does your jaw lock or become stuck once a week or more?

RDC/TMD, Axis II
Psychosocial factors and disability related to jaw pain were assessed according to Axis II of the Research Diagnostic Criteria for TMD (RDC/TMD) (Dworkin and LeResche 1992; List and Dworkin 1996). The Axis II questionnaire includes assessment of jaw pain intensity, jaw disability and pain-related disability, together with non-specific physical symptoms and depression:
  - Jaw disability checklist (JDC); includes twelve items with a dichotomous scale (yes/no) for evaluating the jaw function (0 to 12 points). This non-
Materials and Methods

validated checklist was constructed from items used by investigators on the RDC/TMD project team.

- Disability score (DS) relates to jaw pain with three questions on how jaw pain affects the ability to carry out daily, social and work activities in the past 6 months. The mean value of the three questions, each rated 0-10, is multiplied with 10 to provide the disability score (0-100).

The non-specific physical and depression subscales were adapted from the Revised Symptoms-Checklist-90 (SCL-90-R) (Derogatis 1986) and modified for RDC/TMD (Dworkin and LeResche 1992).

- The non-specific physical symptom scale comprises 12 items that include physical pain symptoms, such as low back pain, heart or chest pain and non-pain items, such as dizziness, nausea or upset stomach.
  - Non-pain physical symptoms is a subgroup of non-specific physical symptoms with seven items that include only non-painful physical symptoms.

- Depression Scale; includes 20 items. It is a screening measure for the existence of depressive symptomatology only, and not a diagnostic instrument for depression (Dworkin et al. 2002b).

For non-specific physical symptoms and depression, the severity of each item is rated from 0 ‘not at all’ to 4 ‘very much’. The mean score provides the severity of the different subscales and subgroups, and is classified as ‘normal’, ‘moderate’ and ‘severe’ in accordance with normative values (Dworkin and LeResche 1992).

Assessment of chewing function

The dynamic load chewing test is a standardised 5-minute dynamic chewing task as described in previous studies (Häggman-Henrikson et al. 2004; Kalezic et al. 2010). Participants performed self-paced unilateral chewing of three pieces (1.45 g x 3) of chewing gum (V6®, MONDELEZ, Sweden) on their preferred chewing side. During the test, participants were seated in an upright position in a chair with foot support and a backrest up to chest level but without head/neck support. Participants were instructed to report any elicited symptoms experienced during the chewing test by pointing at the descriptive keywords "fatigue", "stiffness", "weakness", "exhaustion", "ache", and "pain" on a clipboard; this was used to avoid any interference from talking. The reported symptoms, locations and the onset times were noted. In the analyses, the words "fatigue", "stiffness", "weakness" and “exhaustion" were pooled as "fatigue", and “pain" and "ache" were pooled as "pain". The chewing test was administered by an examiner that was blinded to the group allocation of the participant.
**Ethical considerations**

All participants received written and oral information and signed a written informed consent prior to their enrolment. Participants were free to omit items in questionnaires, discontinue the chewing test or withdraw from the study at any time without providing an explanation. The registry steering group for the Hospital’s injury register data for research at the county council in Västerbotten provided permission for use of data. The study was approved by the Regional Ethical Review Board in Umeå, Sweden (Dnr 2010-156-31M) and was conducted in accordance with the World Medical Association’s declaration of Helsinki and the STROBE guidelines for observational studies.

**Data analysis**

**Paper I**

The study was based on the baseline data for consecutive cases from January 2011 to January 2015 and age and gender matched controls (n=70). To evaluate possible selection bias, they were assessed in two groups – cases 1 (n=70) who attended both a clinical examination and completed the questionnaires, and cases 2 (n=70) who declined to attend a clinical examination but agreed to fill in the questionnaires if posted to them.

The two case groups (cases 1 and cases 2) were compared to the control group, and to each other, for NDI, current pain intensity in the jaw and neck regions NRS, 3Q/TMD, and JDC.

For the regression analysis, the items were dichotomized as follows:

- Neck disability, NDI ≤8% or >8%
- Current pain intensity ratings (11-point NRS): <3 or ≥3
- Answers to the screening questions, 3Q/TMD: yes (1) or no (0)
- Jaw function, JDC 0 or >0

**Paper II**

The study was based on the baseline data for 80 consecutive cases who attended a clinical examination and completed the questionnaires from December 2010 to January 2015, and 80 randomly selected age and gender matched controls.

Participants carried out a 5-minute chewing capacity test. The case group was compared to the control group for elicited fatigue and pain and location of symptoms during the chewing test, together with NDI and JDC from the completed questionnaires.
**Materials and Methods**

**Paper III**

The study was based on the total cohort of 181 cases (including 88 cases 1 and 93 cases 2) and 117 controls.

Participants rated their current pain intensity (NRS) in the jaw and neck regions, and completed the Non-specific physical symptoms and the Depression subscales of the SCL-90R. Non-specific physical symptoms were further analysed with and without inclusion of the pain-related items.

**Paper IV**

The study was based on consecutively collected cases (n=176) and controls (n=116) at the baseline examination from December 2010 to January 2018, and cases (n=119) and controls (n=104) at the 2-year follow-up. The case group was compared to the control group at baseline and year 2, respectively. Furthermore, a comparison between baseline and the 2-year follow-up was carried out for cases and controls for all variables.

Participants rated NDI, current pain in the jaw and neck regions (NRS), three questions on jaw pain and dysfunction (3Q/TMD), non-specific physical symptoms, depression, Jaw disability and pain related disability both at baseline and at the 2-year follow-up. A dropout analysis was carried out by comparing the baseline data for the dropouts with data for the participants who attended both the baseline and the follow-up examinations.

**Statistics**

The analyses were carried out using GraphPad Prism version 6, 7.0b and 7.0d for Mac (GraphPad Software, La Jolla California USA, [www.graphpad.com](http://www.graphpad.com)) and IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.

**Paper I**

Demographic descriptive data were presented as mean and median values. For comparisons between the three groups (cases 1, cases 2 and controls), Kruskal-Wallis and Mann-Whitney U-test were used for NDI, NRS and JDC, and Fisher’s exact test for 3Q/TMD. The association between intensity of jaw and neck pain (NRS) was calculated with Pearson’s correlation. Odds ratios (OR) and 95% confidence intervals (CI) were assessed in univariate binary logistic regression analyses with cases and controls defined as dependent variables and NDI, NRS, 3Q/TMD and JDC used as covariates (Table 2). A P-value < 0.05 was considered statistically significant.
**Materials and Methods**

**Paper II**

The differences between cases and controls for elicited fatigue and pain were evaluated with Fisher’s exact test, and the difference in onset time of elicited symptoms with Log-rank (Mantel-Cox) test. Mann-Whitney U-test was used for age and gender differences, and for the NDI and JDC. A $P$-value < 0.05 was considered statistically significant.

**Paper III**

Descriptive statistics were presented as means (age) and medians (other variables). Differences between cases and controls were evaluated with Fisher’s exact test for gender differences and pain-related disability score. Differences between cases and controls for age, NRS, NDI, non-specific physical symptoms and depression were analysed with Mann-Whitney U test. Spearman’s correlation was used to evaluate the association between jaw and neck pain intensity and pain-related disability, non-specific-physical symptoms and depression. A $P$-value < 0.05 was considered statistically significant.

**Paper IV**

Descriptive data were presented as mean (age) and median (gender) values. Differences between the case and control groups were analysed with Fisher’s exact test for gender. Differences between cases and controls at baseline and at the 2-year follow-up for age, NDI, NRS, JDC, DS, non-specific physical symptoms with pain items included and excluded, and depression were analysed with Mann Whitney U-test, and for 3Q/TMD with Fisher’s exact test, both with Bonferroni correction. Correlation between intensity of jaw pain and neck pain (NRS) at baseline and at the 2-year follow-up was analysed with Spearman’s correlation. Pairwise comparison between baseline and the 2-year follow-up for cases and controls, respectively, was analysed with Wilcoxon paired test for age, McNemar’s test for 3Q/TMD, and with both Wilcoxon and Paired sample t-test for all other variables.

In the drop-out analysis, each baseline group was compared with the corresponding drop-out group. Differences between these groups were tested with Fisher’s’ exact test for gender and 3Q/TMD, and with Mann Whitney U-test for age, NDI, NRS, non-specific physical symptoms and depression. A $P$-value < 0.05 was considered statistically significant.
Results

Jaw pain and disability in the acute stage after whiplash trauma (Paper I)

This study evaluated jaw pain and disability in relation to neck pain and disability in cases with a recent whiplash trauma. Cases 1 (n=70) completed questionnaires and a clinical examination, whereas Cases 2 (n=70) declined to attend the clinical examination but agreed to complete postal questionnaires. Both case groups were compared to a control group (n=70) without a history of neck trauma (Table 2). Compared to controls, the median NDI score was significantly higher for both case groups (\( P = 0.0001 \) for both). There was no significant difference in NDI between Cases 1 and Cases 2 (\( P = 0.053 \)).

Compared to controls, both Cases 1 and Cases 2 reported higher jaw pain intensity (\( P < 0.0001 \) and \( P = 0.003 \), respectively) (Fig. 3). Cases 1 reported higher jaw pain intensity compared to Cases 2 (\( P = 0.026 \)). For neck pain intensity, cases reported higher neck pain intensity (\( P < 0.0001 \)) compared to controls, with no difference between the two case groups (\( P = 0.480 \)).

![Figure 3](image.png)

**Figure 3.** Jaw pain (Median, 10-90 percentiles) rated on the Numeric rating scale (NRS) for Cases 1 and Cases 2, with a recent whiplash trauma, compared to Controls (n = 70 in each group).
For the three screening questions, i.e. 3Q/TMD, both case groups reported significantly more jaw pain (Q1) ($P < 0.0001$ and $P = 0.001$, respectively) compared with controls, with no difference between the two case groups. Cases 1, but not Cases 2, reported more jaw pain on movement (Q2) compared to controls ($P < 0.0001$ and $P = 0.097$, respectively). Cases 1 reported more jaw pain on movement (Q2) compared with Cases 2 ($P = 0.012$). For frequent jaw locking (Q3), there was no difference between case groups and controls, or between the two case groups.

There was a moderate positive correlation between jaw and neck pain for Cases 1 (Fig. 4) and Cases 2 ($P < 0.0001$ for both), but there was no correlation in the Control group.

The univariate regression analysis showed significantly higher odds ratios for both case groups compared to controls for all tested variables, except for pain on jaw movements (Q2) for Cases 2, and jaw dysfunction (Q3) for both Cases 1 and 2.

**Figure 4.** Scatterplot between jaw and neck pain rated on the Numeric rating scale (NRS), for cases with a recent whiplash trauma ($n = 70$) who attended the clinical examination (Cases 1). Correlation calculated with Spearman’s correlation. (Dots may overlap, i.e. dots can represent more than one individual).
Impaired chewing function in the acute stage after whiplash trauma (Paper II)

This study evaluated jaw function in cases with a recent whiplash trauma (n=80) compared to controls (n=80) (Table 2). The median NDI score was higher for cases compared to controls ($P < 0.0001$). There was no gender difference for NDI among cases ($P = 0.21$), whereas women had a higher NDI score compared to men in the control group ($P = 0.01$).

One case subject discontinued the chewing task, but all other cases and controls completed the 5-minute test. Elicited symptoms during the chewing test were reported by 47 cases (59%) and 25 controls (31%), with significantly more cases than controls reporting fatigue ($P = 0.006$) and pain ($P = 0.003$). The time for onset of fatigue and pain was significantly shorter for the cases reporting symptoms compared to controls ($P = 0.001$ for both).

Furthermore, for the cases who reported fatigue or pain during the chewing test, 30 reported symptoms located in the trigeminal region only, 12 in both the trigeminal and spinal regions, and three reported symptoms in the spinal regions only. For the controls reporting elicited fatigue or pain, 21 individuals reported symptoms in the trigeminal area only, and two individuals reported in both trigeminal and spinal regions (Fig. 5)

The subgroup of cases reporting fatigue and/or pain during the chewing test (n = 47) had significantly higher NDI score ($P = 0.01$) compared with the subgroup of cases not reporting symptoms. For the controls reporting elicited symptoms, there was no difference in NDI compared to controls without symptoms during the test ($P = 0.61$).
Results

Figure 5. Locations of elicited fatigue and pain for the 47 cases and 25 controls who reported symptoms during a 5-minute chewing test. The number of participants with elicited symptoms is in green circles for trigeminal areas and red for spinal areas. Participants could report symptoms in more than one location. Bar diagrams illustrate elicited symptoms (fatigue/pain) in percent for cases (n=80) and controls (n=80).
Psychosocial factors and pain in the jaw and neck regions (Paper III)

This study compared 181 cases with 117 controls (Table 2) regarding non-specific physical symptoms, depression and disability related to pain in the jaw and neck regions. Jaw pain intensity higher than NRS 4 was reported by 10.5% of the individuals in the case group, but in none of the controls. Compared to the control group, cases reported significantly higher neck disability score ($P < 0.0001$) and higher pain intensity in the jaw and neck regions ($P < 0.001$ for both).

Compared to controls, cases reported more physical symptoms and non-pain physical symptoms. Cases also reported a higher degree of depression compared to controls (Fig. 6). In relation to normative values, more than half of the cases had moderate or severe scores for all psychosocial variables, whereas the majority of individuals in the control group were classified within the normal ranges.

**Non-specific Physical symptoms and Depression**

![Boxplots of physical (pain items included), non-pain physical (pain items excluded) and depression scores rated on the SCL-90-R scale (0-4) for cases (n = 181; hatched boxes) and controls (n = 117; clear boxes). Normative cut-offs for normal, moderate and severe categories are indicated with grey and red dashed lines (Dworkin and LeResche 1992).](image)

*Figure 6.* Boxplots (median, IQR) of physical (pain items included), non-pain physical (pain items excluded) and depression scores rated on the SCL-90-R scale (0-4) for cases (n = 181; hatched boxes) and controls (n = 117; clear boxes). Normative cut-offs for normal, moderate and severe categories are indicated with grey and red dashed lines (Dworkin and LeResche 1992).
Figure 7. Scatterplot between jaw pain rated on the Numerical rating scale (NRS) and A) Physical symptoms, B) Non-Pain Physical symptoms, and C) Depression rated on the SCL-90-R scale for cases (n=181). Correlations were calculated with Spearman’s correlation. (Dots may overlap, i.e. dots can represent more than one individual).
For cases, there was a moderate positive correlation between physical symptoms and jaw pain and neck pain ($r = 0.54$ and $0.61$ respectively, $P < 0.0001$ for both). Also for non-pain physical symptoms, the correlation to jaw pain and neck pain was moderate ($r = 0.54$ and $0.58$ respectively, $P < 0.0001$ for both). For depression, the correlation to both jaw pain (Fig. 7) and neck pain was low ($r=0.34$ and $0.39$ respectively, $P < 0.0001$ for both). For the control group, there were no correlations between the abovementioned variables and jaw or neck pain.

Course of orofacial pain and jaw disability after whiplash trauma (Paper IV)

At baseline, this study included 176 cases examined within one month after a whiplash trauma, and 116 controls. At the 2-year follow-up, 119 cases (68%) and 104 controls (90%) were re-examined. At the baseline and the 2-year examinations, there were no significant differences between cases and controls for age ($P = 0.36$ and $P = 0.09$, respectively) or gender ($P = 1.00$ and $P = 0.50$ respectively). In the dropout analyses, baseline data for participants who returned for the follow-up examination were compared with participants who did not return. For both cases and controls, compared with the corresponding dropout groups, there were no significant differences regarding any of the studied variables – age, gender, neck disability, intensity of neck pain, 3Q/TMD, physical symptoms, non-pain physical symptoms and depression ($P > 0.05$ for all).

Compared to controls, cases reported more neck disability and jaw pain, both at baseline and at the 2-year follow-up (Table 3). Compared to baseline, cases reported less neck disability and neck pain at the follow-up ($P = 0.007$ and $0.001$, respectively), whereas controls reported more neck disability and neck pain over time, i.e. at follow-up ($P = 0.003$ and $0.041$, respectively). For jaw pain intensity, there were no changes over time, i.e. at the follow-up compared to baseline, for cases or controls ($P = 0.295$ and $P =0.147$, respectively) (Table 4).

For the three screening questions, 3Q/TMD, cases reported significantly more jaw pain (Q1) and jaw pain on function (Q2) compared to controls, both at baseline and at follow-up. There was no significant difference between cases and controls for jaw dysfunction (Q3) at baseline or at the follow-up (Table 3). Compared to baseline, there was no significant change for frequent jaw pain (Q1), jaw pain on function (Q2), or jaw dysfunction (Q3) over time, i.e. at follow-up, for cases or controls ($P >0.05$ for all) (Fig. 8). About one-third of the cases
reported frequent jaw pain (Q1), both at baseline and at follow-up. The majority of cases with frequent jaw pain (Q1) at baseline also reported frequent jaw pain at the 2-year follow-up (Fig. 9).

Table 3. Variables for cases with a whiplash trauma and controls, at baseline and at the 2-year follow-up.

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<td>Cases</td>
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<td>(n=176)</td>
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<td>NDI (0-100%)</td>
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<tr>
<td>median (min-max)</td>
<td>12 (0-74)</td>
<td>2 (0-30)</td>
</tr>
<tr>
<td>Neck Pain NRS (0-10)</td>
<td></td>
<td></td>
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<tr>
<td>median (min-max)</td>
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<td>0 (0-6)</td>
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<tr>
<td>Jaw Pain NRS (0-10)</td>
<td></td>
<td></td>
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<tr>
<td>median (min-max)</td>
<td>0 (0-8)</td>
<td>0 (0-3)</td>
</tr>
<tr>
<td>JDC (0-12)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>median (min-max)</td>
<td>0 (0-8)</td>
<td>0 (0-2)</td>
</tr>
<tr>
<td>DS (0-100)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>median (min-max)</td>
<td>0 (0-90)</td>
<td>0 (0-33)</td>
</tr>
<tr>
<td>Q1 (positive) n (%)</td>
<td>59 (33.5)</td>
<td>7 (6.0)</td>
</tr>
<tr>
<td>Q2 (positive) n (%)</td>
<td>34 (19.3)</td>
<td>5 (4.3)</td>
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<tr>
<td>Q3 (positive) n (%)</td>
<td>26 (14.8)</td>
<td>9 (7.8)</td>
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<tr>
<td>Physical (0-4)</td>
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<td></td>
</tr>
<tr>
<td>median (min-max)</td>
<td>0.7 (0-3.2)</td>
<td><strong>0.2 (0-2.3)</strong></td>
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<tr>
<td>Non-pain (0-4)</td>
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<tr>
<td>median (min-max)</td>
<td>0.4 (0-3.1)</td>
<td><strong>0.1 (0-1.9)</strong></td>
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<tr>
<td>Depression (0-4)</td>
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<tr>
<td>median (min-max)</td>
<td>0.6 (0-3.2)</td>
<td><strong>0.3 (0-2.4)</strong></td>
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</table>

NDI, Neck disability index (0-100%). Neck and jaw pain: NRS, Numerical Rating Scale. JDC, Jaw disability checklist. DS, jaw pain related disability. Q1-Q3: Three screening questions on jaw pain and dysfunction (3Q/TMD). Non-specific physical symptoms with pain and non-pain items. Bold numbers indicate significant difference between cases and controls after Bonferroni correction tested with Fisher’s exact test (3Q/TMD) and Mann Whitney U-test (all other variables).
Table 4. Changes between baseline and the 2-year follow-up for cases and controls.

<table>
<thead>
<tr>
<th></th>
<th>CASES Baseline vs Year 2</th>
<th>CONTROLS Baseline vs Year 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median</td>
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<tr>
<td>Change</td>
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<td></td>
</tr>
<tr>
<td>Change P-value**</td>
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<tr>
<td>NDI</td>
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<tr>
<td>Neck pain</td>
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<tr>
<td>Jaw pain</td>
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<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>JDC</td>
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<td>1</td>
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<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DS</td>
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<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-pain</td>
<td>0</td>
<td>1</td>
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<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>0</td>
<td>1</td>
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</table>

NDI, Neck disability index (0-100%). Neck and jaw pain: NRS, Numerical Rating Scale (0-10). JDC, Jaw disability checklist (0-12). DS, jaw pain related disability (0-100). Non-specific physical symptoms with pain and non-pain items, and Depression (0-4). Bold numbers indicate significant difference between baseline and 2-year follow-up after Bonferroni correction tested with *Wilcoxon paired test and **Paired T-test.

Cases reported more physical symptoms, both with and without pain items included, both at baseline and at the 2-year follow up, compared to controls (P = 0.002 for all) (Table 4). Compared to baseline, cases and controls reported no difference in physical symptoms at follow-up, both with pain items included and excluded. Compared to controls, cases reported higher degree of depression at baseline, but no difference between the groups was found at the 2-year follow-up. For both cases and controls there was no significant difference in depression over time, i.e. between baseline and follow-up (Table 4).
Results

Figure 8. Affirmative answers to the three screening questions (3Q/TMD), on frequent jaw pain (Q1), jaw pain on function (Q2) and jaw dysfunction (Q3) for cases (n = 119; hatched) and controls (n = 104; clear) at baseline and at the 2-year follow-up.

Figure 9. Course of frequent jaw pain (Q1) from baseline to the 2-year follow-up for cases (n = 119) and controls (n = 104).
For cases, there was a moderate positive correlation between jaw and neck pain intensity both at baseline and at the 2-year follow-up (Fig. 10). Both at baseline and follow-up, cases also showed moderate positive correlations between jaw pain and physical symptoms, non-pain physical symptoms ($r = 0.43 - 0.54$, $P < 0.0001$ for all) and a low positive correlation to depression ($r = 0.34 - 0.38$, $P < 0.0001$ for all). Cases also showed a moderate positive correlation, both at baseline and at the follow-up, between neck pain and physical symptoms, non-pain physical symptoms ($r = 0.59 - 0.74$, $P < 0.0001$ for all) and depression ($r = 0.60$, $P < 0.0001$ for all).

**Figure 10.** Scatterplot between jaw and neck pain rated on the Numeric rating scale (NRS) for Cases at baseline ($n = 176$) and at the 2-year follow-up ($n = 119$). Correlations were calculated with Spearman’s correlation. (Dots may overlap, i.e. dots can represent more than one individual).
Discussion

Main finding

The main findings in this thesis were that cases with a recent whiplash trauma, compared to controls, reported more pain and disability in the jaw and neck regions and higher degree of non-specific physical symptoms, both at baseline and at the 2-year follow-up. At baseline, cases also reported more fatigue and pain during a dynamic chewing test. Furthermore, both at baseline and at the follow-up, there was a positive correlation between intensity of jaw pain and neck pain, and non-specific physical symptoms and depression (but to lesser degree).

A strength of this thesis was that most of the utilized questionnaires were validated and adopted to allow comparison with other studies. Also adding strength was the use of a matched control group and that the examiner who administrated the chewing test was blinded to the answers in the questionnaires and to whether the participants were cases or controls.

Study population

The control group was recruited by local advertising from the general population and was age and gender matched to the case group. The group was similar to the general population with regards to the main outcome, jaw pain and disability (Lövgren et al. 2016a), and also with regard to neck disability (Vernon 2008). All cases were from a well-defined population from the only Emergency department in a well-defined catchment area about 60 km in diameter around the city of Umeå. It was previously reported that the Hospital’s Injury data base, from which the cases were recruited, has a high coverage of more than 90% of admitted injuries (Styrke et al. 2012). Our study had a similar proportion of women (58%) as the reported proportion of women with a whiplash trauma following a car accident (52%) at this emergency department (Styrke et al. 2012).

The baseline assessment of cases was carried out within one month after the whiplash trauma. The main reason for this time span was logistics related to clinic organisation and patient handling. For practical reasons, the follow-up assessment was carried out after 2 years, but this also allowed recovery for the cases since this is a long enough period after which no further improvements are expected (Sterling et al. 2010; The Whiplash commission 2005).
recovery after whiplash trauma is presumed to occur within the first three months after injury, followed by a plateau after 6 months, and after that minor if any improvements are expected (Sterling et al. 2010). Assessments after 6 and 12 months would also have been desirable, but due to the study design and time limits this was not feasible. There was no information in the injury register about the WAD grade (Spitzer et al. 1995) after the whiplash trauma, apart from the fact that WAD grade IV (fracture) was an exclusion criteria. We did not have access to patient records and no information on previous neck trauma or pre-accident health factors such as neck pain, pain in other parts of the body, or smoking. Between baseline and the 2-year follow-up, the cases might have received some interventions, but we had no access to information regarding this. It is reasonable to assume however, that any treatment received by cases would not affect our main findings of differences between cases and controls.

The cases were invited for a clinical examination that included questionnaires. One group (Cases 1) attended both the clinical examination and completed questionnaires. The other group (Cases 2) were individuals who declined to attend the clinical examination but agreed to complete postal questionnaires. Due to the possibility that individuals with more pain would be more prone to attend a clinical examination, the two case groups were compared to evaluate a possible selection bias. Cases 1 who attended the clinical examination had significantly more affirmative answers to the screening question (3Q/TMD) on frequent pain on jaw movement (Q2) and they also reported higher pain intensity in the jaw region. However, there were no other significant differences between the two case groups. Thus, higher intensity of jaw pain and frequent jaw pain on movement were related to being more willing to attend a clinical examination. However, Cases 2 who did not attend the clinical examination still reported significantly more frequent jaw pain and higher jaw pain intensity compared to controls, thus suggesting that the main findings in our study are reliable.

The drop-out rate between the baseline and 2-year follow-up was 32% for cases and 10% for controls, but the drop-out analyses did not show any significant differences at baseline between the drop-outs and the follow-up groups with regard to age, gender or outcome variables. Based on this we conclude that the risk for attrition bias was probably low. It is possible that individuals are more willing to participate in a follow-up, or indeed participate at all, if they have symptoms from the jaw-face region. However, the majority of cases admitted to the Emergency department with neck pain did not report frequent jaw pain at the baseline examination, and the control group reported a prevalence of frequent jaw pain and disability comparable to the normal population (Lövgren et al. 2016a).
All participants were also examined clinically according to the RDC/TMD by the examiner who was blinded both at the baseline and follow-up assessments. It would have been beneficial to also include data from clinical examinations in this thesis. This was not possible for practical reasons. All through the data collection period until completion of the follow up examinations, the clinical data were not analysed to ensure that the clinical examiner remained naive to any possible differences between the groups. These clinical data will be subsequently analysed to form the subject for future studies.

### Jaw pain and disability in the acute stage after whiplash trauma (Paper I)

The main findings in Paper I were that already shortly after a whiplash trauma individuals reported a higher prevalence of frequent jaw pain, higher pain intensity in both the jaw and neck regions, and more neck disability compared to controls without a history of neck trauma. In addition, there was a correlation between pain intensity in the jaw and neck regions.

The control group in the study generally reported no or mild neck disability that was comparable to studies in the general population (Bunketorp et al. 2005; Croft et al. 2016; Kato et al. 2012) indicating that our control group was representative. As expected, individuals with a recent whiplash trauma reported a higher intensity of neck pain compared to the control group. The intensity of neck pain for the cases was lower in our study compared to some other studies on acute whiplash populations (Stålnacke 2009). This may be due to the fact that our cases were recently exposed to a whiplash trauma, while many other studies are based on chronic WAD patients (Vernon 2008; Vernon and Mior 1991). Thus, some cases in our study, in common with other study populations exposed to a recent whiplash trauma may develop chronic WAD, while many cases are expected to recover completely (Sterner and Gerdle 2004).

In general, studies on chronic WAD populations have reported a higher prevalence of jaw pain than studies on acute WAD, thereby leading to the suggestion that orofacial pain following whiplash mainly develops over time (Häggman-Henrikson et al. 2014). However, there are some studies reporting jaw pain and disability already in the early stage after neck trauma (Carroll et al. 2007; Kronn 1993; Sale and Isberg 2007). These results are in line with our findings. Thus, already within one month after whiplash trauma, cases had a higher prevalence of affirmative answers to frequent jaw pain and jaw pain on
movement (3Q/TMD) compared to controls. There was no difference, however, between cases and controls with regard to the third 3Q/TMD screening question on frequent jaw dysfunction such as locking and catching of the TMJ. This indicates that symptoms of TMJ dysfunction are not a part of the acute stage after whiplash trauma. This is indirectly supported by prospective studies on individuals with a whiplash trauma where no differences between cases and controls were found regarding internal TMJ derangement both at a 1-year and at a 15-year follow up (Sale et al. 2014; Sale and Isberg 2007).

Compared to the general population, patients with TMD more often report neck pain, and vice-versa, patients with neck pain more often report TMD (De Laat et al. 1998; Visscher et al. 2001). Moreover, pain in one of these regions was shown to increase the risk of developing pain in the other region (Marklund et al. 2010). The correlation we found between jaw and neck pain intensity could be due to an overlap of pain, spread of pain or referred pain, between the jaw and the neck regions. A neurobiological basis for such mechanisms between the trigeminal and cervical regions has been proposed with support by both clinical (Wiesinger et al. 2009) and experimental (Hellström et al. 2000; Schmidt-Hansen et al. 2006; Svensson et al. 2004) studies.

**Impaired chewing function in the acute stage after whiplash trauma (Paper II)**

The main findings in Paper II were that individuals with a recent whiplash trauma reported more fatigue and pain during chewing compared to controls. Furthermore, severity of neck disability was associated with elicited symptoms during chewing. In addition, for cases the symptoms during chewing developed not only in the trigeminal area but also in the cervical/spinal regions.

Healthy subjects will generally complete a chewing test with chewing gum with no (Dao et al. 1994) or few (Farella et al. 2001; Häggman-Henrikson et al. 2004) elicited symptoms. For TMD patients however, a chewing test can often increase fatigue and pain (Dao et al. 1994; Gavish et al. 2002; Häggman-Henrikson et al. 2004; Karibe et al. 2003), and this is also the case in healthy subjects after experimentally induced masseter muscle pain (Koutris et al. 2009). In chronic WAD patients, a large proportion of subjects terminated the test before the time limit, thus indicating a significantly reduced endurance compared to both healthy subjects (Häggman-Henrikson et al. 2004; Kalezic et al. 2010) and TMD patients (Häggman-Henrikson et al. 2004). In addition to reporting more fatigue and pain during the test, WAD patients also had increased heart rate and
Discussion

blood pressure, thus indicating an increased autonomic response (Kalezic et al. 2010).

In the present study, the assessment was carried out in the acute stage after a whiplash trauma and the WAD group showed reduced endurance with more elicited fatigue and pain compared to the control group. More than half of the cases reported fatigue or pain during the chewing test compared to less than one-third of controls, and one case subject terminated the test before the time limit. This reduced endurance is in line with earlier studies in chronic WAD patient with longstanding jaw-neck disability (Häggman-Henrikson et al. 2004; Kalezic et al. 2010). In those studies, in addition to reporting fatigue and pain, more than half of the chronic WAD patients terminated the test before the time limit (Häggman-Henrikson et al. 2004; Kalezic et al. 2010). The probable reason for the difference is that the cases in the present study were in the acute stage after a whiplash trauma, thereby also including some individuals with mild symptoms or being in the recovery phase, as opposed to the studies in chronic WAD populations.

Some controls also reported symptoms during the chewing test which was expected. The control group reflects a normal population, except that a previous neck trauma was an exclusion criteria, meaning that the control group will likely also include individuals with TMD (Lövgren et al. 2016a) who are more prone to develop fatigue or pain during a chewing test (Dao et al. 1994; Farella et al. 2001; Gavish et al. 2002; Häggman-Henrikson et al. 2004; Koutris et al. 2009).

The reduced endurance in cases shortly after a whiplash trauma may be a result of pain, but may also be due to disturbed function (Zafar et al. 2006) and coordination between the jaw and head-neck as seen in chronic WAD patients (Eriksson et al. 2007; Häggman-Henrikson et al. 2002). In addition to reduced endurance during chewing, this can also manifest as eating difficulties (Grönqvist et al. 2008).

Elicited symptoms during the test were mainly located in the trigeminal area, but also in regions outside of this area, e.g. head, neck, throat, shoulder and lower back. This indicates a relation to mechanisms involved in central sensitization and widespread pain (Häggman-Henrikson et al. 2013b; Visscher et al. 2005). Taken together, shortly after a neck trauma, cases seem to have an increased vulnerability to a dynamic load task during natural jaw motor function, and for some individuals a tendency for chewing to provoke also widespread and remote symptoms.

The elicited symptoms during the chewing test were related to the severity of neck disability, suggesting an association between neck disability and jaw
impairment after neck trauma. An association between neck disability score and reduced chewing capacity has also been reported in patients with headache attributed to TMD (La Touche et al. 2015).

**Psychosocial factors and pain in the jaw and neck regions (Paper III)**

The main finding in Paper III was that individuals reported more psychosocial symptoms in the acute stage after whiplash trauma compared to controls. Furthermore, for cases there was a correlation between psychosocial symptoms and pain in both the jaw and neck regions.

It has been suggested that both acute and chronic pain conditions, for example, onset of acute and chronic TMD, are affected by psychological risk factors (Fillingim et al. 2013). In acute as well as in chronic conditions, psychosocial factors such as depression, anxiety, catastrophizing and fear of movement together with coping strategies are factors that may maintain and preserve pain and dysfunction. Psychosocial impairment can also have a negative effect on oral health in general (Visscher et al. 2018). Thus, in dental patients, psychosocial aspects related to pain contributed to more than 25% of their perceived oral health. In the limited number of studies on patients with acute orofacial pain and psychological comorbidity, it is reported that psychosocial factors may be valuable in predicting pain severity and chronicity (Garofalo et al. 1998; Law et al. 2015). Due to this, assessment of psychosocial factors has been promoted both for dental education and in general dental practice (Häggman-Henrikson et al. 2018; Visscher et al. 2018).

For the degree of physical symptoms and depression, the controls were within the ‘normal’ normative ranges for a general population, whereas half of the cases were within the ‘moderate to severe’ range. The higher degree of psychosocial symptoms for the case group is comparable to reports in the acute stage after whiplash trauma (Campbell et al. 2018). Increased scores for somatic symptoms and depression have been reported within one month after whiplash injury (Sterling et al. 2004), which is the same time span as in our study.

In both general pain conditions and in chronic TMD, higher prevalence of physical symptoms and depression has been reported (Forssell et al. 2017; Manfredini et al. 2003; Manfredini et al. 2010; Su et al. 2017). For patients with TMD, both scores within the normal range (Dworkin et al. 2002a) and increased levels (Doepel et al. 2017) have been reported. On balance though, the importance of psychosocial factors has been underlined based on findings of
Discussion

psychosocial impairment of somatic symptoms and depression in patients with TMD (Manfredini et al. 2010).

Based on our results, psychosocial factors are indicated to exist already within one month after a whiplash trauma and were correlated to the intensity of pain in the jaw and neck regions. However, we do not know if these symptoms existed before the neck trauma, or are a consequence of the trauma. It is possible that pre-existing neck pain could affect the degree of depression and somatic symptoms as well as post-traumatic intensity of neck pain. The reported correlations between psychosocial factors and pain in the jaw as well as neck regions are nevertheless essential since these factors can contribute to the development of chronic TMD (Fillingim et al. 2013; Suvinen et al. 2005).

Course of orofacial pain and jaw disability after whiplash trauma (Paper IV)

The main finding in Paper IV was that frequent pain in the jaw region for most cases persisted two years after a whiplash trauma. Pain intensity in the jaw region was correlated to the pain intensity in the neck region both at baseline and at follow-up. Furthermore, both jaw and neck pain intensity were correlated to non-specific physical symptoms, and depression although to a lesser degree.

The cases reported more neck pain and disability compared to controls both within one month after the neck trauma and at the 2-year follow-up. Over this time span there was, however, an improvement in neck pain intensity for cases. This can be expected as most individuals are assumed to recover from an acute whiplash injury (Sterling et al. 2010; Sterner and Gerdle 2004) even though some neck pain and disability can persist (Kivioja et al. 2008). The case group in our study generally reported a mild degree of neck pain and disability compared to other WAD patient populations (Stålnacke 2009). This is probably due to the fact that the cases in our study were individuals who visited an emergency department after a whiplash trauma, while many other studies are based on chronic WAD patients (Vernon 2008; Vernon and Mior 1991). In accordance with previous studies, a proportion of cases in our study maintained long-term whiplash associated symptoms (Carroll et al. 2008b; Kamper et al. 2008; Kivioja et al. 2008; Sterling et al. 2010; Sterner and Gerdle 2004; Sterner et al. 2003) although some cases recovered completely from their neck pain.

The majority of studies on TMD in relation to whiplash have been cross-sectional in chronic whiplash populations. In most prospective studies on whiplash in general, orofacial pain is not included as an outcome. The few
prospective studies that include symptoms from the jaw system are difficult to compare (Carroll et al. 2007; Kronn 1993; Sale and Isberg 2007; Severinsson et al. 2010) due to differences in study populations, outcome measures and heterogeneity in data collection (Fernandez et al. 2009; Häggman-Henrikson et al. 2013b). Commonly TMD has been reported to develop over time rather than being a part of the acute stage of a WAD (Häggman-Henrikson et al. 2013b). Carroll et al reported that only 10% did not recover from jaw pain after one year. However, the drop-out rate in their study was 55%, which may have affected their results (Carroll et al. 2007).

In our study, frequent pain in the orofacial region was reported by one in three within one month after the trauma, and for about 70% of these individuals this pain persisted after 2 years. Compared to controls, cases reported more affirmative answer to the two screening questions on frequent jaw pain and frequent pain on movement (3Q/TMD) both at baseline and follow-up. Both of these questions have been shown to relate to a TMD pain diagnosis (Lövgren et al. 2016b). However, for frequent joint locking/catching, there was no difference between cases and controls at baseline or the 2-year follow-up. This result indicates that clinical symptoms related to internal TMJ derangement are not a common part of acute or chronic WAD. This is supported by a study where the TMJ was assessed after whiplash trauma with magnetic resonance imaging, and compared to controls, there were no more signs of internal derangement at inception or at follow-up (Sale et al. 2014; Sale and Isberg 2007).

Non-specific physical symptoms include both pain symptoms in different parts of the body and non-pain symptoms such as dizziness or nausea. Compared to controls, cases reported more pain and non-pain physical symptoms, both shortly after the whiplash trauma and at the 2-year follow-up. This is in line with studies reporting that individuals after a whiplash injury, have more physical symptoms compared to controls (Styrke et al. 2017). At baseline, cases reported higher degree of depression compared to controls, but there was no difference at the follow-up. This may reflect a ‘normal’ response to a physical trauma at baseline, and the recovery with reduced neck pain at the 2-year follow up may be related to reduced depression scores (Phillips et al. 2010). In chronic WAD patients, a higher prevalence of psychosocial distress has been reported (Visscher et al. 2005). Our finding of a positive correlation between psychosocial symptoms and intensity of pain, in both jaw and neck regions may be important since psychosocial factors can be involved in the development of central sensitisation (Nijs et al. 2011), in chronic pain and disability after whiplash trauma (Campbell et al. 2018).
Methodological considerations

Diagnostic systems for TMD
The Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) was introduced to allow standardization and replication of research for the most common forms of muscle and joint related TMD (Dworkin and LeResche 1992). Since the introduction in 1992, the RDC/TMD has been widely used in clinical research settings around the world, and was translated to a Swedish version that was published in 1996 (List and Dworkin 1996). The RDC/TMD is a dual axis system that combines diagnosis of physical symptoms (Axis I) with the assessment of psychosocial factors (Axis II) to classify the global severity and the impact of pain. In 2014 an updated version, the Diagnostic Criteria (DC/TMD), was published, with the dual axis system retained (Schiffman et al. 2014). This updated version is considered appropriate for use in both research and clinical settings and was founded on a large set of research data to improve the reliability and validity and with updated instruments. The baseline data collection for the present thesis was started before the DC/TMD was introduced, and we therefore retained the RDC/TMD also for the follow-up assessments.

Assessment of Neck Disability
The Neck Disability index (NDI) is the most established and widely used instrument for the self-reporting of neck disability, on how neck pain affects the ability to manage activities of daily life (ADL) such as personal care, lifting, working and sleeping. The NDI was originally developed due to the need to evaluate patients with soft tissue neck injuries, primarily after whiplash trauma, and was constructed and validated by Vernon (Vernon and Mior 1991). The index is based on the Oswestry Low Back Pain Index – an instrument developed to assess lumbar pain, from which items that were considered suitable also for neck pain were selected and adapted. In addition, items in ADL areas were added where neck pain was considered to have a significant impact. These additional items, 'headaches', 'concentration', 'reading', and 'work', were based on informal patient surveys together with the consensus by a small consulting team (Vernon 2008; Vernon and Mior 1991).

The translated Swedish version of the scale has been validated and modified in order to increase specificity by clarifying that nine of the ten items refer to pain specifically located to the neck, whereas the remaining item concerns headache (Ackelman and Lindgren 2002). Some of the items may be difficult to interpret for the participants when completing the questionnaire. For example, the item asking for the ability to drive a car is not appropriate for all individuals. In the Swedish version, Ackelman modified and added a possibility to include the additional response option "do not have a driving license/do not drive"
(Ackelman and Lindgren 2002). This should not be considered as a missing reply and the total score is calculated with this item excluded. However, since most studies in the research field have not used the Swedish version, we chose to include all items to enable comparison with a wider range of studies.

Whiplash trauma can give rise to a range of different symptoms, and as mentioned before, neck pain and stiffness are among the most common (Sterner and Gerdle 2004). Ackelman investigated whether there were important domains missing in the NDI (Ackelman and Lindgren 2002). Individuals with a whiplash trauma reported that there were a number of consequences from neck trauma, apart from neck pain, that had an effect on ADL. For example, dizziness (one of the most common consequences of a neck trauma) can cause severe constraints in everyday life and is absent in NDI. On balance however, the NDI is a relatively short, paper-pencil instrument, that is easy to apply and is the most strongly validated instrument for assessing self-rated neck disability in patients with neck pain (Vernon 2008) in both acute and chronic populations (MacDermid et al. 2009). Furthermore, the NDI is strongly correlated to a number of similar indices and is also related to both physical and mental aspects of general health (MacDermid et al. 2009).

Assessment of pain intensity
Pain intensity is often assessed in the clinic and in research, and its measurement is complex since pain is a subjective experience (Merskey and Bogduk 1994). To grade the severity of pain, different scales can be used (Hawker et al. 2011; Hjermstad et al. 2011) and the Numeric rating scale (NRS) has become one of the most common. This instrument has a simple scoring and is easy to administrate and complete both verbally and in writing. There are variations of the NRS, but the 11-graded version (Farrar et al. 2001), as used in this thesis, is the most common (Hawker et al. 2011). Pain intensity is considered to be one of the most clinically relevant dimensions of pain experience regardless of type of injury or disease (Hjermstad et al. 2011) and is a highly recommended measure (Turk et al. 2006).

Axis II of the RDC/TMD includes items on pain intensity in the face, jaw, temple, in front of the ear or in the ear in the past month, rated on the NRS. Pain intensity is rated for pain at present, pain at worst and pain on average in the past six months. These pain scores can be combined into an average score of these three ratings, denoted Characteristic Pain Intensity (CPI), which is considered to be a better representation of a chronic pain situation (Von Korff et al. 1992). In the present thesis, individuals were examined within one month of a whiplash trauma. Therefore, we only used pain at present, and not CPI at the baseline assessment, in order to capture an individual’s pain in the month since
the whiplash trauma. The time period of six months was later reduced to one month in the DC/TMD, which could have been suitable also for our study.

**Screening questions for TMD**
The three screening questions, 3Q/TMD, were constructed to identify patients with a possible TMD diagnosis. The first two screening questions, frequent (once a week or more) jaw pain (Q1) and jaw pain on movement (Q2), were introduced in Östergötland, Sweden in 2000 (Nilsson et al. 2006). These two pain related questions have been validated and found to accurately identify the majority of both adolescents (Nilsson et al. 2006) and adults (Lövgren et al. 2016b) with a probable TMD pain diagnosis (myalgia/arthralgia). The third question (Q3) was constructed to also capture dysfunction and was based on a consensus discussion among experienced specialists in orofacial pain/TMD. Compared to the first two pain related screening questions (frequent jaw pain (Q1) and frequent pain on movement (Q2)), the third question on frequent locking (Q3) was found to have a lower validity in relation to a TMD diagnosis according to DC/TMD (Lövgren et al. 2016b).

**Assessment of psychosocial factors**
The biopsychosocial model and the importance of the psychosocial factors are well established in pain assessment and management. For patients suffering from acute pain in the jaw-face region, psychosocial factors may be useful in the prediction of pain severity and development of chronicity (Garofalo et al. 1998; Law et al. 2015). The importance of psychosocial factors was shown in a recent study were they contributed to the experience of oral health in more than 25% of dental patients (Zucoloto et al. 2017). For the assessment of psychosocial factors, RDC/TMD Axis II includes the adapted scales Physical symptoms (somatisation) and Depression, from the revised version of the Symptom Checklist (SCL-90-R). The physical symptom scale incorporates items both with and without pain. The Depression scale is modified by additional Vegetative symptoms items. Although these psychosocial scales have been replaced in the DC/TMD, these instruments have revealed good to excellent reliability, validity, and clinical utility (Dworkin et al. 2002b), and normative values from the population are available for comparison (Dworkin and LeResche 1992).

**Assessment of chewing function**
Jaw function comprises several essential behaviours such as mouth opening, biting and chewing. To assess jaw motor function, different types of motor outputs can be tested, e.g. bite force, amplitude and precision of movements, chewing efficiency and endurance. The capacity and endurance can be evaluated by static tests such as tooth clenching (Christensen et al. 1982) or dynamic tests such as chewing (Dao et al. 1994; Farella et al. 2001; Gavish et al. 2002; Häggman-Henrikson et al. 2004; Kalezic et al. 2010; Karibe et al. 2003; Koutris
et al. 2009). Symptoms such as fatigue and pain may be provoked during such capacity tests, with reduced endurance being one indicator of impaired jaw function (Dao et al. 1994; Farella et al. 2001; Gavish et al. 2002; Häggman-Henrikson et al. 2004; Kalezic et al. 2010; Karibe et al. 2003; Koutris et al. 2009).

General discussion

Risk factors for WAD

Different risk factors for development of chronic WAD after whiplash trauma have been proposed. High initial neck pain, greater than 5.5 out of 10 (on NRS or Visual Analog Scale) and neck disability scores greater than 28% (NDI), are suggested as strong prognostic factors for persistent symptoms. Not as strong, but risk factors to some degree, were for example restricted cervical range of motion, disturbed sleep since the accident, history of headache or neck pain, severity of WAD (grade 2 or 3), female sex and psychosocial factors such as catastrophizing, (Walton et al. 2013). Furthermore, poor expectations of recovery, posttraumatic stress symptoms and passive coping are other psychosocial factors that has emerged as prognostic factors for the development of chronic neck pain and disability after a whiplash trauma (Campbell et al. 2018). Higher age, severity of collision, pre-accident history of headache, and rear-end collision showed no significant predictive value (Walton et al. 2013). We show that jaw and neck pain correlated positively to each other, to non-specific physical symptoms and depression at both acute and chronic stages. This indicate that intensity of neck and jaw pain as well as psychosocial factors may be possible risk factors also for the development of chronic TMD after whiplash trauma.

Jaw pain after whiplash trauma

It has been proposed that jaw pain in the acute stage after whiplash trauma is a rare occurrence (Kasch et al. 2002). This conclusion was based on the results from a study on young adults with a mild degree of WAD, Grade I-II, making comparisons with wider groups of WAD patients difficult. Another study, however, suggested that jaw pain can be present already in the acute stage after trauma (Sale and Isberg 2007). This is in contrast with suggestions that TMD after whiplash trauma is a condition that develops over time along with the development of chronic WAD (Severinsson et al. 2010). Different study design, study populations and outcome measures may contribute to these diverging results, together with the general lack of prospective studies. Most studies on
TMD after whiplash trauma have been carried out on populations with chronic WAD. In a systematic review, the prevalence of TMD after a whiplash trauma varied from 2.4% to 52% (Häggman-Henrikson et al. 2013b). The lowest prevalence of 2.4%, in a Lithuanian study (Ferrari et al. 1999b) is even lower than in the general population (Lövgren et al. 2016a). Many aspects of the Lithuanian study have been criticized. For example, the questionnaires were sent out on average 27 months after the whiplash trauma, thereby inducing a risk of recall bias, (Sale et al. 2010). Furthermore, the majority of participants were young males (Ferrari et al. 1999a), which introduces the risk of selection bias. A considerably higher prevalence of reduced and/or painful jaw movement after whiplash trauma (17.4%) was reported in a study based on claimants’ forms from an insurance data base (Carroll et al. 2007). Generally, uncertainties and differences with regard to the criteria for TMD (Carroll et al. 2007; Kronn 1993; Sale and Isberg 2007), lack of control groups (Heise et al. 1992; Magnusson 1994), different outcomes (Carroll et al. 2007; Heise et al. 1992; Klobas et al. 2004; Magnusson 1994; Sale and Isberg 2007), or outcomes that can be deemed as unreliable (Ferrari et al. 1999b) makes it difficult to compare different studies.

Functional relationship between the jaw and neck regions

During normal jaw function, joints and muscles in both the jaw and neck regions are activated to execute integrated jaw-neck movements (Eriksson et al. 2000; Häggman-Henrikson 2004; Häggman-Henrikson and Eriksson 2004; Zafar 2000; Zafar et al. 2000b), these muscles are innervated by trigeminal and cervical nerves that are closely connected in the brainstem (Sessle et al. 1986). This extremely complex part of the musculoskeletal system must be in balance for a proper function (Okeson 2013b). The close functional relationship between the jaw and neck regions exists not only in health (Eriksson et al. 2000; Häggman-Henrikson 2004; Häggman-Henrikson and Eriksson 2004; Zafar 2000; Zafar et al. 2000b) but also in disease (Eriksson et al. 2007; Häggman-Henrikson et al. 2006). Thus, a disturbed jaw motor function was earlier demonstrated in patients with chronic WAD with regard to coordination and amplitude of jaw and head-neck movements together with reduced endurance during chewing. Our present finding of reduced endurance during chewing also in the acute stage after whiplash trauma underlines the important functional integration between the jaw and neck sensorimotor system. Furthermore, we found a correlation between jaw disability, assessed by the Jaw Disability Checklist, and the intensity of neck pain (Paper IV). An association between disability in the jaw and neck regions was previously reported for patients with TMD (Olivo et al. 2010; Silveira et al. 2015), but to our knowledge, ours is the first study reporting such a relationship in the acute stage after whiplash trauma.
“Mandibular whiplash”

Patients with TMD related to a chronic whiplash trauma report more jaw pain and dysfunction compared to patients without a history of neck trauma. Also, patients with posttraumatic TMD report more headache, dizziness, stress and sleep problems. This indicates that jaw pain and dysfunction related to a whiplash trauma may have a different pathophysiology (Häggman-Henrikson et al. 2014).

Factors related to the course and development of TMD after whiplash trauma have been debated. An early theory was that the acceleration-deceleration of the head-neck induced in the trauma situation also overstretched or compressed the Temporomandibular joint and thereby caused a local TMJ injury, “mandibular whiplash” (Weinberg and Lapointe 1987). This concept has however been refuted in favour of a neurobiological basis (Howard et al. 1998). The neurobiological explanation is supported both in experimental (Hellström et al. 2000; Schmidt-Hansen et al. 2006; Svensson et al. 2004) and clinical (Wiesinger et al. 2009) studies demonstrating an overlap, spread and referral of muscle pain between the cervical and trigeminal regions. Furthermore, pain in the jaw or neck regions can increase the risk of developing pain in the other region (Marklund et al. 2010). Compared to the general population, patients with neck pain report more TMD, and vice-versa, patients with TMD report more neck pain (De Laat et al. 1998; Visscher et al. 2001).

Spread of pain between jaw and neck regions

The spread of pain between the jaw and neck regions may be explained by the intricate relationship between the trigeminal and cervical motor systems together with pain mechanisms. The regions have a functional connection since jaw movements are the result of activation of jaw as well as neck muscles thereby leading to simultaneous movements in the temporomandibular, atlanto-occipital, and cervical spine joints (Eriksson et al. 2000). By experimental restriction of head–neck mobility in healthy individuals, jaw function can be impaired (Häggman-Henrikson et al. 2006). During chewing it is suggested that the head-neck behaviour is modulated as a response to changes in jaw sensorimotor input such as size and texture of bolus (Häggman-Henrikson and Eriksson 2004) and increased load, increased demand and recruitment of neck muscles (Häggman-Henrikson et al. 2013c). Anatomically in the brainstem, the jaw and neck regions have a close relationship with the trigeminal and spinal nerves being closely connected in the brainstem (Sessle et al. 1986). Pain is suggested to be one reason for a changed somatosensorimotor function (Svensson et al. 1996; Svensson and Graven-Nielsen 2001), and after experimental pain in the jaw-neck regions, an altered strategy for jaw–neck motor control has been demonstrated (Wiesinger et al. 2013). This changed
strategy is seen in chronic WAD patients as deranged integrated jaw and neck behaviour (Häggman-Henrikson et al. 2002).

Pain is probably one explanatory factor for the impaired jaw function for individuals with a recent whiplash trauma. Trigeminal nociceptive input to the brain stem is reported to reduce amplitude and speed of mandibular movements (Lund 1991; Stohler 1999; Svensson and Graven-Nielsen 2001). The fusimotor muscle spindles are proposed to play an important role in the development and spread of painful musculoskeletal conditions (Johansson 2003; Johansson et al. 1999). Such mechanisms are found also in the jaw muscles (Ro and Capra 2001) (Ro and Capra 2001), and muscle spindles in the masseter muscles are of a particularly complex composition (Eriksson and Thornell 1987; Österlund et al. 2013). Between the trigeminal and spinal regions, a reflex connection between chemosensitive muscle afferents and the fusimotor system has been demonstrated (Hellström et al. 2000). In addition, an intersegmental nociceptive connection is supported between the trigeminal and spinal region (Hu et al. 1993; Svensson et al. 2004; Yu et al. 1995). Taken together, our results are in accordance with the neurobiological basis for the sensorimotor connection between the jaw and neck regions.

Chronic pain in the jaw-face region is considered to most often originate from muscles (Lövgren et al. 2016b), and even when pain is located to the TMJ area it may not always represent a sign of joint engagement but may instead be referred pain from the masseter muscle (Fricton et al. 1985; Travell and Simons 1983) or be a part of a sensitisation process. In our study, there was no difference between cases and controls for frequent TMJ locking/catching, either at baseline or at the 2-year follow-up. This finding is in line with a prospective 15-year follow-up study where magnetic resonance imaging of the jaw joint did not show more signs of structural damage to the TMJ following a whiplash trauma compared to a control group at inception or at follow-up (Sale et al. 2014; Sale and Isberg 2007). Taken together, this reinforces the notion that TMD pain following whiplash trauma is largely unrelated to internal derangements in the TMJ. Furthermore, the correlation between jaw and neck pain found in the present study suggests that TMD pain following whiplash trauma is probably related to the spread of pain, as a part of a regional pain condition (Eriksson et al. 2000; Häggman-Henrikson et al. 2006; Zafar et al. 2000b; 2002).
Clinical implications and future directions

Patients with a whiplash trauma constitute a heterogeneous group with a wide range of symptoms that are not always easy to understand for the dental or medical professions. In general dental practice, attention to previous whiplash trauma is important to include as part of the clinical assessment to broaden the understanding of the individual patient. Self-reported measures of pain and disability, for both the jaw and neck regions together with psychosocial factors are easy to administer and can provide a more comprehensive “picture” of the patient. Axis II from the DC/TMD is recommended for capturing the psychosocial part in the assessment of patients with orofacial pain, as a guide for prognosis and treatment planning (Schiffman et al. 2014). The DC/TMD covers the most common TMD diagnosis, and therefore the expanded DC/TMD was introduced to include less common but clinically important disorders (Peck et al. 2014). A future step in the development of DC/TMD would be to include TMD related to cervical pain and whiplash trauma in the expanded DC/TMD classification.

Our studies are in agreement with previous reports of symptoms from the jaw region early after whiplash trauma (Carroll et al. 2007; Kronn 1993; Sale et al. 2014; Sale and Isberg 2007). In addition, our results indicate that not only is jaw pain common in the early stage after whiplash trauma, but is also correlated to neck pain and is not a transient pain condition. Consequently, since the majority of individuals with jaw pain in the acute stage still had frequent jaw pain after 2 years, “wait and see” is not a good strategy. Instead, these patients should be identified and assessed at the acute stage, i.e. within 3 months after a whiplash trauma. Care providers can utilize the screening questions 3Q/TMD (Lövgren et al. 2016b; Nilsson et al. 2006) as a tool to identify patients who need further assessment and in some cases referral to a specialist in orofacial pain/TMD.

Taken together, for a significant proportion of individuals, jaw pain and dysfunction may be present already in the acute stage after a whiplash trauma, and eating may provoke pain and discomfort not only in the trigeminal region but also in spinal areas. To our knowledge our study is the first to report elicited extra-trigeminal symptoms in an acute whiplash population during natural jaw function.

Finally, further research is needed on risk factors for the development of jaw-face pain following a whiplash trauma. Being able to identify individuals at risk for developing chronic orofacial pain shortly after a whiplash trauma is essential for clinical management and for reducing individual suffering as well as societal costs.
Summary of results

The presence and course of pain and disability in the jaw and neck regions, after a whiplash trauma, was analysed in a short- and long-term perspective, as well as in relation to psychosocial factors.

Within one month after a whiplash trauma, cases:

- reported more neck pain and pain in the orofacial region compared to controls without a neck trauma.
- had a positive correlation between the intensity of pain in the jaw and neck regions.
- showed a reduced chewing capacity compared to controls, which was correlated to the severity of neck disability.
- had higher scores for non-specific physical symptoms and depression compared to controls without neck trauma.
- showed a positive correlation between pain in jaw and neck regions, and between pain in these respective region and non-specific physical symptoms and depression.

Two years after a whiplash trauma, cases:

- showed a positive correlation between pain intensity in the jaw and neck regions and between pain in these respective regions and psychosocial factors.
- reported frequent orofacial pain that for a majority had persisted from the acute stage.
Conclusions

- The presence of orofacial pain after a recent whiplash trauma indicates an early involvement with central sensitization and spread of pain between the jaw and neck regions.

- The positive correlation between pain in the jaw and neck regions underlines the sensorimotor coupling between these regions.

- The impaired jaw function shortly after a whiplash trauma, together with the finding of elicited symptoms outside the trigeminal area during the chewing test, underline the close functional integration between the trigeminal and cervical regions.

- The finding of higher scores for physical symptoms and depression, and their correlation to jaw and neck pain in both the acute and chronic stages after whiplash trauma, underlines the importance of a biopsychosocial perspective in assessment and management of patients with pain conditions after whiplash trauma.

- The finding that orofacial pain is common shortly after whiplash trauma, and often persists into the chronic stage indicates that assessment in the acute stage should preferably include both the neck and jaw regions. From this follows that multidisciplinary teams that entail both medical professions and dentists specialised in orofacial pain may be beneficial in the early assessment after whiplash trauma.
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