

**Personality traits, subjective health complaints, experimental pain
sensitivity, and psychophysiological responding in female
temporomandibular disorder (TMD) patients**

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*PhD thesis
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University of Oslo
2008*

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*Series of dissertations submitted to the
Faculty of Social Sciences, University of Oslo
No. 122*

ISSN 1504-3991

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Cover: Inger Sandved Anfinsen.
Printed in Norway: AiT e-dit AS, Oslo, 2008.

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Acknowledgements

This work was carried out at the Department of Psychology, University of Oslo, and at the Department of Work-Related Musculoskeletal Disorders, National Institute of Occupational Health, Oslo. This project was supported by a grant from the Norwegian Research Council and by a doctoral fellowship from the University of Oslo.

I wish to express my gratitude to my tutors, Professor Stein Knardahl (Department of Psychology and National Institute of Occupational Health) and Professor Olav Vassend (Department of Psychology), and to Berit Schie Krogstad (Department of Clinical Odontology) for introducing me to orofacial pain, designing this study and encouraging me to apply for the doctoral fellowship. Moreover, the technical and statistical assistance and advice of Kjersti Andersen, Cathrine Bjordal Bergheim, Dag Erik Eilertsen, Shahrooz Elka, Dagfinn Matre, Eva Helene Mjelde, Janne Schiøll, and Ole Synnes is gratefully acknowledged. Dagfinn Matre, Cecilie Røe, Ólöf Anna Steingrimsdottir, and Vegard Strøm have provided invaluable expertise in the field of pain during the writing process. Without the encouragement and support of Tor Endestad, Margrethe Seeger Halvorsen, Hanne Haavind, Svein Magnussen, Ivar Reinvang, Janne Schiøll, Ólöf Anna Steingrimsdottir, Karl Halvor Teigen, and Anne-Kari Torgalsbøen, my endeavours would have been much less enjoyable.

I am grateful to my family and friends for their patience and moral support. This thesis is dedicated to my mother, whose daily dinner-table talk of medical topics sparked my own interest in this field, and to the memory of my father, who is finally free from pain.

“The human mind does not involve adequate knowledge of the parts composing the human body”

Benedictus Spinoza (1996:49)

List of original papers

- I. Mohn C, Krogstad BS, Vassend O, Knardahl S. Personality traits and subjective health complaints in female TMD patients and healthy controls.
- II. Mohn C, Vassend O, Knardahl S. Experimental pain sensitivity in women with temporomandibular disorders and pain-free controls: the relationship to orofacial muscular contraction and cardiovascular responses
- III. Mohn C, Vassend O, Knardahl S. Focal and generalized psychophysiological responses to cognitive tasks and experimental pain stimulation in female temporomandibular disorder patients.
- IV. Mohn C, Vassend O, Knardahl S. Cardiovascular modulation of pain perception and affective responses in normotensive, pain-free women.

The papers are referred to in the text by their Roman numerals.

Abbreviations

A	agreeableness
AP	algometric pressure
C	conscientiousness
CFS	chronic fatigue syndrome
CTTH	chronic tension-type headache
CV	cardiovascular
CVR	cardiovascular responses
DNIC	diffuse noxious inhibitory control
E	extraversion
EMG	electromyography
E-PTh	electrocutaneous pain threshold
E-PTo	electrocutaneous pain tolerance
ES	electrocutaneous stimulation
E-STh	electrocutaneous sensory threshold
eVAS	electronic visual analogue scale
FFM	five-factor model
FMS	fibromyalgia syndrome
GI	gastrointestinal complaint index
HR	heart rate
IBS	irritable bowel syndrome
IMC	isometric contraction
LDF	laser-doppler blood flux
MAP	mean arterial pressure

MRI	magnetic resonance imaging
MSI	musculoskeletal complaint index
MVC	maximal voluntary contraction
N	neuroticism
NA	negative affectivity
NTS	nucleus tractus solitarius
O	openness
PAG	periaqueductal grey matter
PP	pressure pain
P-PThm	pressure pain threshold at masseter
P-PTom	pressure pain tolerance at masseter
P-PThs	pressure pain threshold at sternum
P-PTos	pressure pain tolerance at sternum
TMD	temporomandibular disorders
UAII	upper airway infection index
VAS	visual analogue scale

1 Background

1.1 Temporomandibular disorders

Temporomandibular disorders (TMD) comprise a category of chronic complaints of pain and/or mobility dysfunction of the orofacial region. The main symptoms are pain from the periauricular area of the temporomandibular joint (TMJ) and/or in the masticatory structures – sometimes radiating to the temples, head, and neck - clicking sounds from the temporomandibular joint, and restricted movement of the jaw (Dworkin & LeResche, 1992). Psychological characteristics of TMD patients are mainly elevated levels of psychological distress, a relatively low correlation between physiological parameters and severity of pain and suffering, and interference with ability to perform activities of daily life due to pain or fatigue (Dworkin, 1995). Persistent orofacial pain is the main reason for seeking treatment for this disorder.

In population samples, TMD occurs about twice as frequently in women as in men (LeResche, 1997). The range of prevalence of TMD in the adult population has been estimated as 3-15%, and TMD seems to occur most frequently in young adults, i.e., 20-50 years of age (LeResche, 1997). The symptoms (complaints described by the patient) and clinical signs (functional changes detected by the clinician) of TMD seem to fluctuate considerably. For many patients, the symptoms and signs seem to decrease with age, with the exception of osteoarthritis of the TMJ, which is more frequent in the elderly (Carlsson & LeResche, 1995). However, progression to significantly more severe pain or functional level of the masticatory system seems rare (Magnusson et al., 2005). Orofacial pain and clicking sounds of the TMJ are widespread in the general population, while only a minority develop symptoms grave enough to generate help-seeking behaviour (Rantala et al., 2004).

TMD is usually diagnosed according to the Research Diagnostic Criteria (RDC) described by Dworkin & LeResche (1992). Three main subgroups of TMD have been described based on their assumed orofacial structural origin. “Group I - Muscle disorders” is diagnosed if ongoing subjective pain and pain upon palpation is reported, with or without limitations of mouth opening. “Group II - Disc displacement” is diagnosed if the temporomandibular joint disc is displaced from its position between the condyle and the articular eminence, sometimes indicated by clicking sounds during jaw

movement, with or without subjective report of pain. “Group III - Arthralgia, arthritis, or arthrosis” is diagnosed if ongoing pain in the joint upon function or palpation is detected (arthralgia or arthritis), crepitations of the joint (arthritis or arthrosis) are present, or if morphological and/or structural deformities of the condyle and articular eminence are identified during imaging assessment (arthritis or arthrosis). Among those diagnosed with TMD, muscle pain and disc displacement predominate (Dahlström, 1998). Multiple TMD sub-diagnoses are common (LeResche, 1995), but the causal relationship between the sub-diagnoses is undecided.

In addition to clinical examination of the orofacial region, the RDC classifies patients according to pain-related disability and psychological status in order to identify level of function and psychological distress, i.e., symptoms of anxiety, depression, and somatisation, of relevance for planning of and adherence to treatment regimes (Dworkin & LeResche, 1992). Although patients from Group I, relative to the other subgroups, have been found to exhibit higher levels of psychological distress in cross-sectional studies (Huang et al., 2002), it has been reported that the subgroups do not differ with respect to the clinical course of TMD over a 5-year period (Ohrbach & Dworkin, 1998) or with respect to multi-disciplinary treatment (Dworkin et al., 2002).

The etiology of TMD is poorly understood (Sessle et al., 1995). As is the case with other chronic musculoskeletal pain disorders, TMD seems to be best explained from a biopsychosocial perspective (Gatchel & Turk, 1999). According to the theoretical work of Maixner and coworkers (Fillingim et al., 1996; Maixner et al., 1995), TMD is a psychophysiological disorder involving changes in endogenous regulatory pain pathways, resulting in maladaptive emotional, physiological and neuroendocrine responses to physical and psychological stressors. However, no specific models have been presented that aim to describe the relative contribution of and temporal relationship between the factors that may be involved in the etiology and pathogenesis of TMD. Hence, theoretical models of and research findings from studies of other chronic musculoskeletal pain conditions are frequently used to explain the development of TMD (e.g., Vierck, 2006).

Figure 1 describes a schematic model of factors that may be relevant for the development of TMD. The exposure or acute event is suggested to generate chronic TMD if one or several of the other factors listed inside the frame are present. Two-way arrows

indicate possible reciprocal associations. The present thesis discusses some of these variables, i.e., personality traits (Paper I), psychological distress (Paper I), general health complaints (Paper I), pain sensitivity (Paper II and IV), and physiological responding (Paper II-IV).

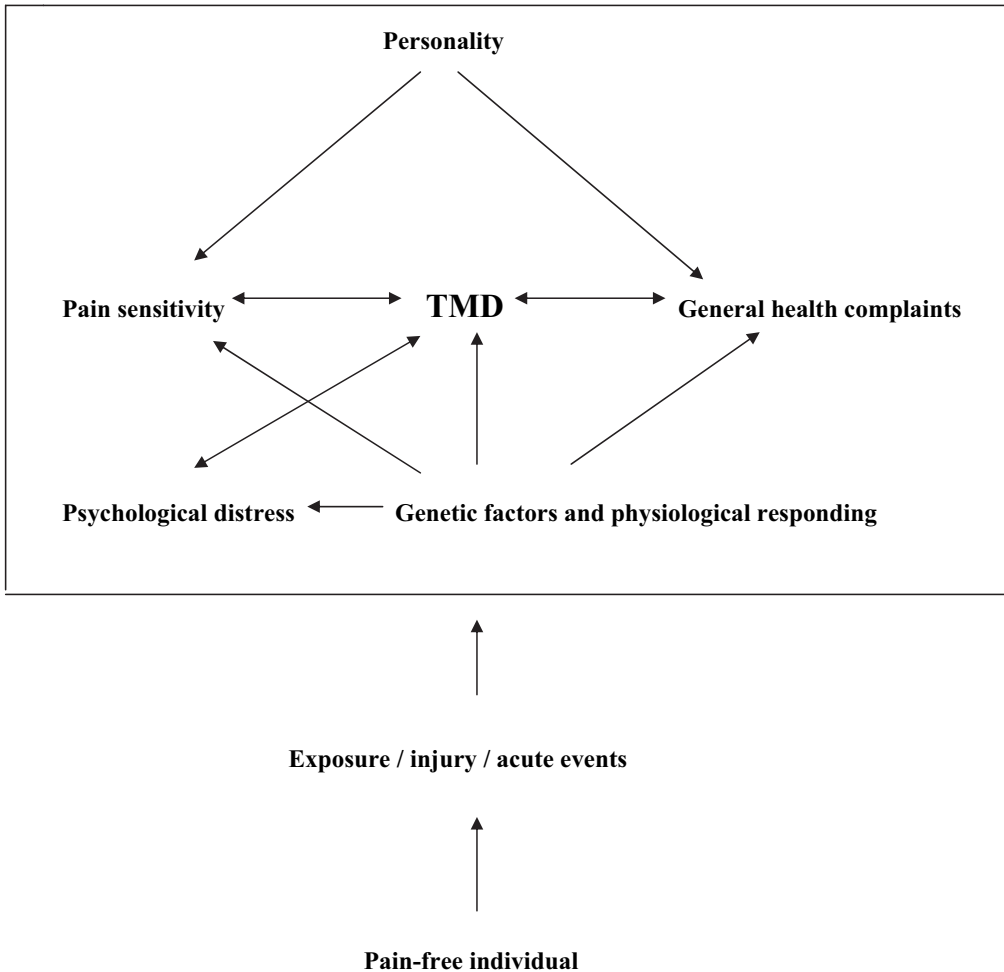


Figure 1. Suggested model of development of TMD in an originally pain-free individual. Adapted from the vulnerability-diathesis-stress model of chronic pain by Dworkin & Banks (1999).

1.2 Nociception and pain

The International Association for the Study of Pain (IASP) defines pain as “an unpleasant sensory and emotional experience associated with actual and potential tissue damage, or described in terms of such damage” (Merskey & Bogduk, 1994).

Nociception is the physiological activity in primary afferent neurons, in the spinal cord, and in supra-spinal structures. Stimulation of nociceptors (receptors responding to mechanical, thermal, or chemical agents that would result in tissue damage if persistent) triggers activation of the myelinated A δ - and unmyelinated C-afferent axons. The afferent nerves terminate in the dorsal horn of the spinal cord, where they synapse with second-order neurons that are either nociceptive specific or wide dynamic range (WDR) neurons that respond to noxious and non-noxious events alike. Nociceptive stimuli from the orofacial region are carried mainly via the maxillary and mandibular branches of the trigeminal nerve (the 5th cranial nerve), and synapses with second-order neurons in the trigeminal subnucleus caudalis in the brainstem. The nociceptive signals ascend up the spinal cord (or the brainstem in the case of orofacial signals) primarily via the spinothalamic tract and mainly transmitted by glutamate, to the thalamus, and then project to the somatosensory cortex.

Pain occurs when the individual interprets this activity as a signal of potential injury or illness, and thus adds an affective component to the sensory activities. While nociception is a sensory event, pain is a psychological experience. Nociception does not inevitably generate pain, and pain may occur in the absence of nociception.

Acute pain is strongly stimulus-dependent and occurs in response to activation of the nociceptors of the skin, muscles, viscera or other anatomical structures. Chronic pain is normally defined as persisting more than 6 months. Chronic pain may be referred to as a disorder of the central nervous system (CNS) structures involved in processing of nociceptive and pain signals. However, the peripheral and central processes involved in the chronification of pain are not well understood.

1.3 Personality traits and chronic pain

Psychological mechanisms, e.g., personality traits, may play a pivotal role in the development and maintenance of pain syndromes characterized by symptoms and functional impairment that are not readily explained by physiological findings (Barsky & Buros, 1999). Personality traits may be defined as "...regularities or broad behavioral consistencies in the conduct of people. As such, traits represent basic categories of individual differences in functioning" (Pervin, 1996). The Five Factor Model (FFM) (Costa & McCrae, 1992) seems to be the most influential current theory of individual differences in personality (Hogan et al., 1997). Support for this model has been found in cross-cultural studies, longitudinal studies of personality development, studies of genetics and heritability, and studies of psychiatric populations (Pervin, 1996). The FFM describes personality along five broad dimensions of relatively stable behaviour patterns: Neuroticism (N), Extraversion (E), Openness to experience (O), Agreeableness or warmth (A), and Conscientiousness (C) (Costa & McCrae, 1992).

Personality traits may be associated with illness and somatic symptoms in several ways. First, some personality traits may predispose individuals to somatic disease. The finding that interpersonal hostility has been found to predict future coronary heart disease through large and frequent activation of the autonomous nervous system is one example (Miller et al., 1996; Smith, 1992). However, in prospective studies, no personality traits have been identified as responsible for the development of chronic pain conditions in the sense that they predict physiological changes that generate chronic pain (Gatchel & Weisberg, 2000).

Second, personality traits may determine the perception and appraisal of pain and bodily sensations and whether these sensations are interpreted as a threat to health and physical function (Costa & McCrae, 1987; Ellington & Wiebe, 1999). Several studies have found a positive relationship between N and the presence of chronic pain (BenDebba et al., 1997; Wade et al., 1992), however, this trait is largely unrelated to biological markers of illness (Costa & McCrae, 1992).

Third, personality traits may determine health behaviour and thereby indirectly affect one's health. Both A, C, and O have been found to be related to diet, exercise, and life-style choices (Booth-Kewley & Vickers, 1994; Ingledew & Bruning, 1999).

Fourth, coping with symptoms and illness and adherence to treatment regimes may be influenced by personality traits. Both N, E, and O seem to be related to coping with chronic pain (Nitch & Boone, 2004). There is a consensus on the importance of individual differences in emotional style, responses to illness, and choice of coping strategies for the outcome of treatment for TMD (e.g., Dworkin et al., 2002). Hence, a personality screening could provide valuable information for the design and implementation of treatment regimes.

The studies summarised above represent valuable attempts at disentangling the personality – pain relationship at the cross-sectional level. However, most studies have concentrated on measuring only one or two personality traits. The term Negative Affectivity (NA; Watson, 1988) is often used interchangeably with N, and NA is not part of any larger theoretical framework explaining individual differences. This is unfortunate, as an exclusive focus on N or NA will not permit conclusions regarding the full coping resources of the individual (Marshall et al., 1994). The FFM aims to describe the comprehensive personality structure of the individual (Costa & McCrae, 1992), and will provide a broader picture of the individual's psychological makeup.

1.4 General health complaints in TMD patients

TMD patients in general seem to exhibit a higher than average prevalence of anxiety and depression compared to healthy controls (Kight et al., 1999; Carlson et al., 1998; Vimpari et al., 1995). Other studies have reported that TMD patients on average exhibit lower psychopathology scores than is common in several other groups of chronic pain patients, but that they are significantly more troubled by psychological distress than pain-free individuals (Krogstad et al., 1998; Dahlström, 1993).

In addition to persistent orofacial pain and dysfunction of the masticatory system, TMD patients tend to report higher levels of pain from anatomical sites other than the orofacial region and higher levels of somatic symptoms like fatigue and dizziness than do healthy controls (Rantala et al., 2003; Vassend et al., 1995). The presence of general

somatic and psychological complaints seems to reduce the likelihood of a favourable treatment outcome for TMD (Krogstad et al., 1996) as well as constituting a predictor for illness severity and disability in untreated TMD (John et al., 2003; Rammelsberg et al., 2003), suggesting that information of general health complaints should be obtained at the onset of treatment, in order to design methods of treatment that better address the needs of these patients.

The direction of causality between psychological distress and TMD is a topic of discussion. Symptoms of psychological disorders, most notably depression, may be a natural consequence of having a chronic pain condition. There is evidence that a reduction of TMD symptoms is followed by reduced levels of emotional distress (Rammelsberg et al., 2003; Turk et al., 1996). On the other hand, depression has been reported to predict the first onset of TMD pain (Sipilä et al., 2001), chest pain and headache (von Korff et al., 1993). Moreover, some affective and nociceptive pathways coincide anatomically, and the neurotransmitters serotonin and norepinephrine are involved in nociception as well as depression and anxiety (Dersh et al., 2002). It has been suggested that at least in some groups of chronic pain patients a trait of susceptibility to both pain and psychological symptoms may exist (von Korff & Simon, 1996), perhaps due to an imbalance of the neurotransmitters involved in both conditions (Dersh et al., 2002). Recently, a prospective study reported that genetic variants of the adrenergic β_2 receptor may influence both psychological characteristics (i.e., anxiety, depression, and somatization), blood pressure level, and the risk of development of TMD in females healthy at baseline (Diatchenko et al., 2006a).

Likewise, the direction of causality between general somatic complaints and TMD is unknown. In particular, similarities between TMD and the fibromyalgia syndrome (FMS), a diagnostic entity sharing some of the symptoms that are quite common in TMD, e.g., widespread pain, fatigue, sleep disturbances, and psychological distress (Wolfe et al., 1990), has been the topic of much debate (Dao et al., 1997; Plesh et al., 1996). These illnesses, along with chronic fatigue syndrome (CFS) and irritable bowel syndrome (IBS), are by some researchers regarded as different manifestations of an underlying, common functional somatic syndrome, a construct describing medically unexplained persistent symptoms from multiple organs, often severely compromising the

individual's daily life (Aaron et al., 2000; Barsky & Borus, 1999). The term "functional" in medical terms denotes a condition for which no physiological cause has been identified, and the etiology of functional somatic syndromes awaits further elucidation. Furthermore, the suggestion that relatively different clusters of symptoms, e.g., TMD versus IBS, are indicators of a common condition, has met with critique (Moss-Morris & Spence, 2006).

One limitation of previous research is the failure to account for the possible influence of personality traits on general symptom report. This is unfortunate, given the numerous and well-known studies of reporting bias related to high levels of N (Gatchel & Weisberg, 2000; Ellington & Wiebe, 1999; Costa & McCrae, 1992).

Another limitation of previous studies is the lack of control for the impact of acute pain sensitivity on general symptom report. One's present pain level is likely to affect the retrospective report of symptoms. High pain levels at present may result in an overestimation of previous or current complaints. As chronic pain patients tend to exhibit increased acute pain sensitivity compared to pain-free controls (Staud et al., 2005; Sarlani & Greenspan, 2003), subjective reports of health variables may be unduly biased in these patient groups.

1.5 Pain sensitivity in TMD patients

1.5.1 The central sensitization model

Elevated acute pain sensitivity, generalized as well as at focal tender areas, is one of the cardinal symptoms of most musculoskeletal pain disorders (e.g., Staud, 2005) including TMD (Sarlani & Greenspan, 2003). According to the theoretical work of Maixner and coworkers (Fillingim et al., 1996; Maixner et al., 1995), the altered pain sensitivity of TMD patients may result from dysfunctional CNS pain regulatory systems. It is still not known whether changes in pain sensitivity are causes or consequences of chronic pain. Recent studies have reported that initially pain-free individuals characterized by high sensitivity to acute pain may be at risk for developing chronic pain problems following surgical procedures, amputation, or other pain-producing events (Edwards, 2005). Moreover, generally healthy individuals with high sensitivity to experimental pain tend to report higher levels of minor daily pain complaints, e.g., headache, back pain, compared

to less sensitive individuals (Edwards, 2005). In individuals presenting with acute symptoms of TMD, high current pain levels as well as high pain levels during the last three months has been predictive of chronic TMD (Epker et al., 1999).

Several current theories of the development of chronic craniofacial pain emphasize the pathogenic role of central sensitization, i.e., increased firing rates or lowered firing thresholds of CNS neurons. Clinical signs of central sensitization are mainly hypersensitivity (i.e., an increased pain response to noxious stimuli) and allodynia (i.e., a pain response to non-noxious stimuli). Physiochemical processes involved in central sensitization have been studied mainly at the dorsal horn of the spinal cord and the brainstem subnucleus caudalis (Woolf & Salter, 2000; Svensson & Graven-Nielsen, 2001; Bendtsen, 2000; Sessle, 2000). However, cortical areas may also be sensitised, i.e., through expansion of the somatosensory receptive fields (Flor, 2003). It is assumed that local events such as trauma, inflammation, or overload, may generate increased afferent traffic to the spinal cord and brainstem and thus sensitize central neurons in biologically, e.g., genetically, vulnerable individuals (Edwards, 2005; Sessle, 2000). In severe cases, it is possible that prolonged peripheral input may establish abnormal central activity that is no longer dependent on peripheral stimuli, and that may exaggerate nociceptive signals from parts of the organism outside of the original painful or injured area, generating a tendency to experience symptoms from multiple organs or widespread pain syndromes like FMS (Vierck, 2006). As pain sensitivity and psychological distress are mediated by some of the same biochemical substances (Dersh et al., 2002; Diatchenko et al., 2006b), alterations in central pain pathways may affect the distress level of the individual. Thus, it is theoretically not inconceivable that the central sensitization model may account for the compromised psychological function in many chronic pain patients, although direct evidence of the influence of many of the physiological and chemical processes assumed to be involved is still lacking. The investigation of this highly complex neuroplastic process is still in its infancy. Given the many spinal and cortical structures assumed to be involved in these changes, these theories seem to be in accordance with suggestions (Fillingim et al., 1996; Maixner et al., 1995) that TMD is related to maladaptive emotional, physiological and neuroendocrine responses to physical and psychological stressors.

Studies of pain sensitivity in TMD have mostly concentrated on stimulation while the participants are resting. However, as most TMD patients report increased pain during orofacial activity like chewing or yawning (Sessle et al., 1995), pain stimulation at close proximity to masticatory load may provide a fuller picture of the patients' everyday difficulties and level of suffering.

A recent study of FMS patients reported no group differences between cases and controls in heat and pressure pain sensitivity at baseline. However, relative to pain-free controls, the FMS group reported lower pain thresholds at several anatomical sites after isometric exercise (Staud et al., 2005). These results were interpreted as evidence of central sensitization and/or dysregulated endogenous pain control mechanisms in FMS (Staud et al., 2005). The similarities between TMD and FMS, e.g., musculoskeletal pain of unknown origin, fatigue, and psychological distress (Plesh et al., 1996), indicate that similar mechanisms of altered pain sensitivity may characterize these patient groups.

Central sensitization due to increased nociceptive afferent traffic may not be the only explanation of chronic pain conditions. The organism is able to attenuate pain through complex endogenous control mechanisms originating in the cortex and brainstem, acting on nociceptive traffic at several sites of the spinal cord and brainstem (Millan, 2002). The periaqueductal grey matter (PAG), a midbrain structure, plays a central role in modulation of nociceptive signals, receiving input from lower levels of the spinal cord as well as higher levels of the CNS such as the hypothalamus, the amygdala, and the prefrontal cortex (Millan, 2002).

1.5.2 The cardiovascular – pain sensitivity model

One endogenous pain regulatory mechanism subjected to increasing scientific interest the last two decades is the analgesic properties of cardiovascular system responses. There is a considerable overlap between CNS regions involved in nociception and control of the cardiovascular system, e.g., the hypothalamus, the PAG, and the n. tractus solitarius (NTS) of the brainstem (Bruehl & Chung, 2004). Accumulated research has demonstrated a relationship between elevated cardiovascular (CV) parameters, e.g., arterial blood pressure, and attenuated pain sensitivity (e.g., Bruehl et al., 1999; France 1999). Several hypotheses regarding mechanisms behind the relationship between the CV

system and pain sensitivity have been suggested. Suggestions of trait-like hypoalgesia being part of a predisposition for hypertension through alterations in the function of the hypothalamic paraventricular nucleus (France, 1999) do not seem to explain this phenomenon in full, as manifest hypertension or genetic risk for hypertension is not necessary for CV-related hypoalgesia to occur (Al'Absi & Petersen, 2003; Al'Absi et al., 2000). Moreover, explanations based on opioid release triggered by baroreceptor stimulation during elevated blood pressure in humans have been questioned (Bruehl et al., 1999; France, 1999). A model in which stimulation of arterial baroreceptors during elevated arterial pressure induce hypoalgesia as well as general CNS sedatory effects, has been supported in animals and humans (Ghione, 1996). Acute pain is assumed to generate elevated arterial pressure through sympathetic activation. Elevated arterial pressure stimulates the sinoartical baroreceptors, which triggers descending pain inhibitory responses. The pain level is consequently reduced, in turn returning the arterial pressure to baseline. The NTS functions as an interface between the sensory and the autonomic systems, and is presumed to play a major role in this process (Bruehl & Chung, 2004).

Another explanation relates to the function of the PAG, which coordinates analgesic and cardiovascular responses during threat and trauma (Bandler & Shipley, 1994). Hypoalgesia may be an integrated part of active coping responses. Pain, being a signal of injury or illness, triggers integrated response patterns that facilitates fight-or-flight behaviour, i.e., through increases in pressor responses coupled with descending inhibitory pain mechanisms (Bandler & Shipley, 1994; Green et al., 2006). The function of this integrated response pattern during ongoing pain is unknown (Green et al., 2006).

Dysregulation of this negative feedback process may be responsible for lack of CV-modulated pain sensitivity in chronic pain patients (Maixner et al., 1997; Bruehl et al., 2002). Both low-back pain (Bruehl et al., 2002) and TMD patients (Bragdon et al., 2002; Maixner et al., 1997) do not seem to demonstrate the pain-attenuating effects of increased CV levels. There is evidence that chronic pain groups are susceptible to hypertension (Bruehl et al., 2005), and that baroreceptor stimulation produces increased experimental pain in chronic low back pain (Brody et al., 1997). The physiological processes underlying this proposed dysregulation have yet to be discovered, although variants of adrenergic β_2 receptors involved in both development of TMD, affective

distress, and blood pressure responding may be genetically transmitted (Diatchenko et al., 2006a).

Moreover, it is not known if all types of experimental pain stimulation are related to CV responding (Poudevigne et al., 2002). Previous studies have employed ischemic and thermal pain (Braddon et al., 2002; Maixner et al., 1997), whereas pressure pain, which is assumed to be more similar to the clinical pain suffered by TMD patients, has not been investigated in relation to CV responding in chronic pain patients.

Recently, it has been suggested that the link between the CV system and pain sensitivity extends to all emotional stimuli, i.e., that increased CV responding is related to a general dampening of emotional responses to environmental stimuli in an attempt to reduce the impact of intense stimuli and facilitate adaptation to chronic, intense emotional stimuli (Pury et al., 2004). These suggestions seem to be compatible with the hypothesis of PAG-coordinated response to stress and challenges described above (Bandler & Shipley, 1994). So far, support for this hypothesis has been demonstrated in one study (Pury et al., 2004), but refuted in another (Nyklicek et al., 2005).

1.6 Focal or generalized psychophysiological responses in TMD patients

According to the diathesis-stress hypothesis of musculoskeletal disorders (Flor et al., 1990), hyperresponsivity of the muscles to various types of stress, i.e., emotional or environmental challenges, may be one of the factors accounting for the development or maintenance of musculoskeletal pain once a diathesis to respond with a specific body site or system has been established. Regarding TMD in particular, symptoms of tenderness and pain of the orofacial muscles in TMD patients have generated studies of electromyographic (EMG) activity at rest or during various cognitively or emotionally challenging tasks. However, the results of EMG studies of the orofacial region of TMD patients are conflicting (e.g., Flor et al., 1992; 1991; Katz et al., 1989; Schroeder et al., 1991). In addition, reduced EMG activity of muscles at painful regions has also been observed and interpreted as an adaptive mechanism to protect an inflamed or injured structure from movement (Lund et al., 1991). Moreover, the narrow focus on EMG as the preferred method for detecting physiological changes of relevance for the development or maintenance of chronic pain conditions ignores the multitude of central, systemic and

local mechanisms that may be involved in this process (Sessle, 2000). Relatedly, if central sensitization plays a role in the development of TMD, one would expect that these patients exhibit hyper-responsiveness to at least some pain stimuli. However, studies of focal and generalized physiological responses to pain stimulation are scarce.

In addition, individual differences in response to the experimental tasks have largely been ignored in previous psychophysiological studies of TMD. The importance of taking individual affective responses to the tasks into consideration was illustrated in a study by Ohrbach et al. (1998), who found that EMG and electrodermal differences between TMD patients and controls to be attributable to affective differences and not the stressful experimental manipulations. This point seems particularly important given the discrepancy between few or uncertain physiological findings and sometimes severe levels of psychological suffering in TMD patients (Dworkin, 1995). Assessments of affective distress during environmental challenges may provide information valuable for psychological treatment of TMD patients presenting with excessive levels of psychological distress.

1.7 Exposure / acute pain events

The stomatognathic system is involved in numerous activities that may contribute to chronic pain in biologically or psychologically vulnerable individuals. The role of occlusal factors is controversial (Sessle et al., 1995). Regarding parafunctions, research interest has mainly concentrated on bruxism: some studies have found a relationship between bruxism and TMD (e.g., Manfredini et al., 2003), while others have not (e.g., Lobezzo & Lavigne, 1997). Dental procedures like third molar extraction may also contribute to development of TMD (Huang & Rue, 2006).

These microtraumatic muscular events may contribute to chronic pain via acute pain that causes alterations in the biochemical characteristics of the orofacial muscles (Svensson & Graven-Nielsen, 2001). Microtrauma may release biochemical agents, e.g., serotonin and substance P, which act upon local nociceptors, increasing the afferent traffic into the CNS and thus contributing to the central sensitisation process (Svensson & Graven-Nielsen, 2001). This process may be enhanced in genetically vulnerable

individuals (Diatchenko et al., 2006a). However, the paucity of research renders this hypothesis somewhat speculative.

1.8 Study objectives

This study aims at elucidating characteristics which differentiate TMD patients and pain-free controls.

The comprehensive personality structure of TMD patients is compared with that of healthy controls in order to generate information relevant for future treatment interventions. Psychological and somatic health complaints in TMD patients are compared with those of healthy controls with statistical control for the impact of personality traits and pain sensitivity.

Focal and generalized pain sensitivity effects of isometric contraction of the jaw in TMD patients and healthy controls are investigated, and the CV-pain relationship is extended to pressure pain stimulation. In addition, the CV-related modulatory effects on pressure pain and emotional responding are studied in a group of healthy women.

Finally, the present thesis compares focal as well as systemic physiological responding to cognitive tasks, orofacial muscular load, and experimental pain stimulation in TMD patients and healthy controls. Measurements of affect are obtained in order to gain a fuller picture of the TMD patients' responses to environmental challenges.

The following topics were examined in the papers:

- Whether there were differences in personality traits and general health complaints between the TMD patients and healthy controls (Paper I)
- Whether there were differences in experimental pain sensitivity after orofacial muscular contraction, and whether the association between pain sensitivity and cardiovascular responding was different in TMD patients and healthy controls (Paper II)
- Whether there were differences in focal and systemic psychophysiological responses to painful and non-painful experimental tasks in TMD patients and healthy controls (Paper III)

- Whether there was evidence of a general emotional dampening process in relation to cardiovascular responding in normotensive, healthy women (Paper IV)

2 Material and methods

2.1 Design

The research questions were studied in a cross-sectional design. In Papers I-III the design is mixed, with both between-group and within-group comparisons. In paper IV, the study has a within-group design.

2.2 Subjects

2.2.1 Papers I-III

Twenty-five female patients with TMD and 25 healthy females matched for age, level of education, smoking, and exercise participated in this study. The TMD patients underwent a clinical examination and were diagnosed according to the RDC-TMD (Dworkin & LeResche, 1992) by the research staff physiotherapist at the Dental Faculty, University of Oslo. Exclusion criteria (self-reported) were other chronic illnesses than TMD (e.g., rheumatic, vascular, or psychiatric disorders), pregnancy, and inability to understand spoken and written Norwegian. Exclusion criteria (self-reported) specifically targeting other orofacial-related illnesses than TMD were rheumatoid arthritis, temporal arthritis, trigeminal neuralgia, parotitis, and sinusitis.

All subjects received written information of the investigation, and all signed an informed consent before the experiment. They were informed that they were free to withdraw from the experiment at any time. The experiment was conducted according to the Helsinki Declaration, and approved by the regional Research Ethics Committee. All subjects received NOK 500 (approximately USD 70-80) for their participation.

See each paper for demographic information of the participants.

See Table 1 for the tenderness to palpation score for the TMD group. Only the most prominent muscles are listed, as some of the craniofacial muscle sites, e.g., the lateral pterygoid and posterior styloid muscles, are very difficult to palpate and may not be valid for the diagnostic process (Dworkin & LeResche, 1992).

Table 1. Tenderness to palpation in selected craniofacial muscles in TMD patients

Muscle site	Tenderness score			
	None	Mild	Moderate	Pronounced
R. temporalis posterior	13 (59.1%)	5 (22.7%)	4 (18.2%)	-----
L. temporalis posterior	15 (68.2%)	4 (18.2%)	2 (9.1%)	1 (4.5%)
R. temporalis anterior	8 (38.1%)	4 (19%)	2 (9.5%)	7 (33.3%)
L. temporalis anterior	11 (52.4%)	4 (19%)	4 (19%)	2 (9.5%)
R. masseter profundus	3 (15%)	6 (30%)	6 (30%)	5 (25%)
L. masseter profundus	5 (25%)	5 (25%)	8 (40%)	2 (10%)
R. masseter superficialis (middle)	1 (4.8%)	5 (23.8%)	7 (33.3%)	8 (38.1%)
L. masseter superficialis (middle)	6 (28.6%)	7 (33.3%)	2 (9.5%)	6 (28.6%)
R. sternocleidomastoideus	6 (28.6%)	1 (4.8%)	6. (28.6%)	8 (38.1%)
L. sternocleidomastoideus	5 (23.8%)	6 (28.6%)	5 (23.8%)	5 (23.8%)

The palpation was performed according to the Research Diagnostic Criteria for TMD (N = 20-25).

2.2.2 Paper IV

Thirty-nine Caucasian women (see Paper IV for demographic characteristics) were recruited among graduate students of medicine and psychology of the University of Oslo via the students' mailing lists. Inclusion criteria were age between 20 and 50 years, and ability to speak and understand spoken and written Norwegian. Exclusion criteria (self reported) were known hypertension, chronic pain, general chronic somatic or mental health problems, pregnancy, and use of regular medication apart from oral contraceptives. The decision to study only females in Paper IV was based on the wish to investigate further some of the results of Paper II, in which the participants were all women.

The study was conducted in accordance with the Helsinki Declaration and approved by the regional Research Ethics Committee. All subjects gave their informed consent to the participation, and were informed that they were able to withdraw from the experiment

at any time. All subjects received a gift-voucher at the price of 250 NOK (approximately USD 35-40) for their participation.

2.3 Psychophysiological experiments

2.3.1 Experimental tasks

Outlines of the experimental procedures are given in Figures 2 and 3. The order of the experimental tasks was not randomized. The rationale for this was to present the least painful tasks at the start of the experiment. There were two electrocutaneous pain stimulation trials associated with the tracking task, and the isometric contraction was expected to generate discomfort or pain in the TMD group. Therefore, these tasks were placed at the end of the experimental session. It may be argued that the order of the experimental conditions should ideally be counter-balanced to avoid systematic carry-over effects in psychophysiological studies. However, analyses of the healthy control group of the present study revealed that the physiological levels of responding were highly similar during the relaxation periods prior to and after the cognitive tasks, indicating negligible carry-over effects (Vassend & Knardahl, 2004; 2005).

2.3.1.1 Papers I-III

The subjects were seated in an upright position in a sound-attenuated and electromagnetically shielded room (2.8m x 2.9m) with a temperature of 22 °C. The female experimenter described the function of the instruments and sensors, without disclosing the hypotheses to be tested. The psychophysiological experiment lasted 2-2.5 hours. All subjects went through the experimental manipulations in the same order. Behind a one-way mirror, a research assistant monitored the experimenter and the subject. A female experimenter was present in the room with the participants throughout the experiment. An outline of the experiment and the data selected for this study are presented in each paper.

After initial instructions, preparation and attachment of electrodes and sensors, and a practice trial of pain stimulation, the experiment consisted of the following manipulations: a habituation task (reading aloud), a simulated job interview, a visuomotoric tracking task, isometric contraction of the jaw, and maximally voluntary

contraction of the trapezius and left biceps muscles. Between the experimental tasks, pain stimulation trials were performed.

2.3.1.2 Paper IV

The psychophysiological experiment took place in a sound attenuated and electromagnetically shielded laboratory with temperature kept constant at 22° C. The subjects were seated in an upright position in a comfortable, upholstered chair.

The first 30-40 min. of the experiment consisted of randomized sequences of pressure and electrocutaneous pain stimulation. All subjects went through three electrocutaneous stimulation trials, three pressure stimulation trials at the right masseter muscle, and three pressure stimulation trials at the sternum (equipment and assessment procedure as described for Papers I-III). Two-minute resting periods between each trial were provided to ascertain that the physiological responses returned to baseline before the next trial.

After the initial series of pain stimulation and a relaxation period, the subjects went through the simulated job interview described in Papers II and III. After the interview, pressure pain stimulation was performed twice at the right masseter muscle.

2.3.2 Pain stimulation

The assessment of pain is complicated by the fact that, in contrast to other sensory and perceptual processes, nociception is not triggered by a unique type of stimulation at a unique anatomical site. Auditory perception, e.g., is triggered by the stimulation of the sensory organ (the ear) with physical energy (sound waves). In contrast, almost every anatomical structure may respond to nociceptive stimulation, and several types of stimulation (e.g., pressure, heat, chemicals) may trigger this process. In addition, the affective component of the pain experience is probably more pronounced than of other types of perception. There exists no golden standard for the assessment of this affective component, which in addition shows considerable individual variability (Price, 1999). These unique features make it difficult to obtain objective measurements of the pain *experience*, although there is some recent evidence that it may be possible (see Nielsen, 2007). However, pain *stimulation* may be readily quantified in a laboratory setting, thus

permitting control over at least one part of the pain perception process. Standardization of stimulation may be relatively less relevant in clinical settings, but is pivotal in studies aiming at determining the mechanisms of pain and their correlation with other biological or psychological variables.

It may be argued that the experience resulting from experimental pain stimulation does not correspond completely to the clinical type of pain that is ongoing and often induced or exacerbated by movement in chronic musculoskeletal pain patients. Assessments of naturally occurring pain during activities of daily life could be described as having stronger ecological validity than experimentally induced pain stimulation. However, there are two reasons why the present study chose a laboratory setting with all participants maintaining the same seated position. First, this procedure was necessary to permit quantification of the pain stimulation. Second, the methods of physiological recordings chosen require the participants to refrain from vigorous movement.

Sensory threshold, pain threshold and tolerance of electrocutaneous stimulation:

Electrocutaneous stimulation (ES, 50 ms pulses, 4 per s) was administered to the dorsal area of the subjects' left hand through two electrodes with a diameter of 5 mm and a center-to-center distance of 20 mm by a Grass S48 Stimulator (Grass Technologies, Rockland, MA, USA) with a Grass stimulation isolation unit (SIU5B) and a Grass constant current unit (CCU1A) attached. All instruments provided electrical isolation of the subjects. The skin of the subjects' left hand was cleansed with alcohol and Ag/AgCl paste applied to the electrodes. The maximum voltage was 150 V. The stimulation was controlled by the experimenter by using an intensity control starting at 0 V.

Electrocutaneous stimulation is widely used, easy to apply, and repeatable (Gracely, 1994). This method induces a sharp, itching type of pain by stimulating superficial skin nociceptors. The subjects were instructed to report immediately when they first noticed a sensation or «itching», and when it became painful, and pressed a hand-held button the moment they evaluated the pain as being so intense that they wanted to interrupt the stimulation.

In addition to a pre-test to familiarize the subjects with the stimulation procedure, one trial of ES was delivered to each subject before and after every experimental condition and during the distraction task, totalling six trials.

Pain threshold and tolerance of pressure algometry: Pressure pain (PP) was induced by a pressure algometer (Somedic, Sollentuna, Sweden), with a 10 mm diameter stimulation probe at the end of a force transducer. The rate of pressure increase is standardized by visual feedback provided by the algometer and was set at 50 kPa/s. This rate of pressure increase was chosen to avoid prolonged pressure to the tissue of the participants and to avoid fatiguing the experimenter. Despite this relatively steep rate of pressure increase, there was a high test-retest reliability between pain stimulation sessions, indicating that the experimenter had no difficulties reading the threshold values: The two first pain stimulation trials (before and after the reading task) were not intended to be affected by the experimental manipulations, and were used to calculate the test-retest reliability (Table 2).

Table 2. Pearson's correlations of the first and second pressure pain stimulation trial.

	TMD (N = 25)	Controls (N = 25)
Pain threshold, masseter	.78 ***	.80 ***
Pain tolerance, masseter	.83 ***	.88 ***
Pain threshold, sternum	.88 ***	.84 ***
Pain tolerance, sternum	.96 ***	.83 ***

*** = $p < .001$ (two-tailed).

Pressure algometry was applied perpendicularly to the belly of the right masseter muscle, approximately 2 cm anterior to and 1 cm above the angle of the jaw. The decision to stimulate the right masseter was based on several studies reporting no statistical site difference in pressure pain thresholds in TMD patients (Isserl e et al., 2002; Svensson et al., 1995; McMillan & Blasberg, 1994; List et al., 1993). Pressure stimulation on the sternum provided a non-muscular reference. The subjects were asked to raise their right index finger when the pressure became painful, and to press a

terminate-test-button when it became so intense that they wanted to interrupt the stimulation.

In addition to a pre-test to familiarize the subjects with the stimulation procedure, one trial of PP was delivered to each subject before and after every experimental condition, totalling five trials. Unpublished pilot studies (Cecilie Røe, National Institute of Occupational Health, personal communication) have demonstrated that there is no risk of increased tenderness influencing experimental pressure pain sensitivity if repeated trials of stimulation of a particular anatomical site are separated by at least 2 min. In the present study, the interval between stimulation trials of the same site was always greater than 2 min.

Pressure algometry induces pain of a different quality than ES does. The type of pain induced is deep/muscular pain, although skin nociceptors are also stimulated (Gracely, 1994). The sensations are aching, cramping and not sharply localized. This similarity to the pain seen in many chronic musculoskeletal pain conditions have led to pressure pain being regarded as a somewhat more «natural» type of pain (Harris & Rollman, 1983).

Masseter muscle pressure stimulation is probably the only non-invasive method currently available for induction of a type of pain that resembles the clinical pain of TMD patients (Fischer, 1998). One of the chief criteria for the TDM diagnosis is palpation tenderness of orofacial muscles. Hence, in this study that partly aimed at explorations of hypothesized mechanisms of TMD development, pressure stimulation of the masseter muscle was deemed appropriate. In order to test the hypothesis that central sensitization is characteristic of many chronic pain patients and may be demonstrated by altered pain sensitivity also in non-muscular regions and through stimulation methods unrelated to muscular pain, pressure stimulation of the sternum and electrical stimulation of the left hand were chosen.

Spontaneous or on-going pain: Before every pain assessment, the subjects reported the intensity of spontaneous pain that was not induced as part of the experimental procedure (e.g., facial pain, headache) using an electronic Visual Analogue Scale.

2.3.3 Psychophysiological recording

The following psychophysiological parameters were recorded continuously during the entire experimental session.

Cardiovascular parameters: Mean arterial pressure (MAP) and heart rate (HR) were continuously monitored by the Penaz method (Finapres, Ohmeda 2300, Englewood, CO, USA).

Skin blood flux (SBF) responses were recorded with a Perimed Multichannel Laser Doppler System (PeriFlux 4001 Master, Perimed, Järfälla, Sweden). Miniature probes (Perimed, Järfälla, Sweden) were attached on the left masseter anterior to the electromyography electrodes (see below) and on the ventral side of the left thumb.

Muscle activity: Surface electromyography (EMG) was recorded from the left m. masseter, the left m. biceps brachii, and bilaterally from the mm. trapezii (Paper III). Only EMG responses from the masseter muscle and the left trapezius are presented, due to the data from the right trapezius being influenced by movements of the right arm and hand during the experimental manipulations.

As the EMG and LDF measurements are superficial and the probes do not exert pressure on the skin, there is probably very little risk of interference between EMG electrodes and LDF probes.

All signals were AD-converted (12 bit A/D card, AT-MIO-16E-10, National Instruments, Austin, Texas, USA) with a sampling frequency of 2000 Hz, stored and reduced by LabView (National Instruments, Austin, TX, USA).

Papers II-IV provide detailed description of types and placements of electrodes and sensors as well as signal amplification.

2.3.4 Affect measurements

2.3.4.1 Paper III

At the start of the experiment, after the job interview, and after the experiment was finished, the subjects filled in the state-version of the Spielberger State-Trait Personality Inventory (STPI, Spielberger, 1979; Håseth & Spielberger, 2000).

After each experimental task, the subjects rated their affective experiences to the task on 23 paper-and-pencil Visual Analogue Scales (VAS), ranging from «not at all» (at 0 mm) to «maximally» (at 100 mm). (See Paper III for details.)

2.3.4.2 Paper IV

Upon entering the laboratory, before the instructions for the job interview were given and at the end of the entire experimental session, the subjects filled in the state-version of the State-Trait Personality Inventory (STPI; Spielberger et al., 1979; Håseth & Spielberger, 2000). After the pain stimulation sequence in the first part of the experiment and after the two pressure pain trials after the job interview, the subjects rated their affective experiences to the pain (Price, 1999). The reports, averaged into four indices, were 16 paper-and-pencil VAS, ranging from «not at all» (at 0 mm) to «maximally» (at 100 mm) (see Paper IV for details).

At the end of the experiment, the subjects rated the simulated job interview in a similar way (see Paper III for details).

Time	Papers	Condition	
0 min		Informed consent, general instructions and preparation	
		Practice of pain testing	
	III	STPI-State	
	I, II	Report of clinical pain	
	I, II, III	Pain testing	
	II, III	Relaxation	
	III	Reading aloud	
	III	Recovery	
	45 min	III	Report of task-related affective experiences
		II	Report of clinical pain
I, II, III		Pain testing	
II, III		Relaxation	
		Preparation for simulated job interview	
II, III		Simulated job interview	
II		Report of clinical pain	
II		Pain testing	
		Recovery	
		Report of task-related affective experiences	
70 min	III	STPI-State	
	III	Relaxation	
	III	Visuo-motoric tracking	
		Electrocutaneous pain testing	
		Visuo-motoric tracking	
	III	Recovery	
	III	Report of task-related affective experiences	
		Report of clinical pain	
	85 min		Pain testing
		III	Relaxation
		Report of clinical pain	
II, III		Isometric contraction of jaw-closing muscles	
II		Report of clinical pain	
100-120 min	II	Pain testing	
	III	Maximally voluntary contraction of trapezius muscles	
	III	STPI-State	

Figure 2. Outline of the experimental procedure and the variables analyzed, papers I-III. Physiological recordings were made continuously. Pain testing: electrocutaneous stimulation of the dorsal left hand and pressure pain stimulation of the right masseter muscle and the sternum. After the experimental session, questionnaires on demography, general health complaints, and personality traits were filled in.

Time	Condition
0 min	Informed consent, general instructions and preparation Practice of pain testing STPI-State Randomized trials of pain testing separated by 2 min relaxation periods Report of pain-related affective experiences
45 min	STPI-State Relaxation Preparation for simulated job interview Simulated job interview Pressure pain testing at masseter Relaxation Pressure pain testing at masseter Report of pain-related affective experiences Report of interview-related affective experiences
70 min	STPI-State

Figure 3. Outline of the experimental procedure, paper IV. Physiological recordings were made continuously. Pain testing: electrocutaneous stimulation of the dorsal left hand and pressure pain stimulation of the right masseter muscle and the sternum. After each pain stimulation trial, reports of sensory and affective experience were made by electronic VAS. After the experimental session, questionnaires on demography, general health complaints, and personality traits were filled in.

2.4 Questionnaires – Paper I

The NEO-PI-R (Costa & McCrae, 1992; Martinsen et al., 2003) was administered to assess personality traits. The NEO-PI-R was developed on basis of the FFM, and is one of the most widely used personality inventories. It is reported to have high reliability and validity, and has been validated both cross-culturally, by self-ratings, and by ratings by peers and spouses (Wiggins, 1995). It has also been validated against other personality inventories, like the California Q-Set and the Eysenck Personality Questionnaire (Hogan et al., 1997).

Each of the five factors of the FFM consists of six sub-scales, or facets (see paper I). The items of the questionnaire are presented as statements, e.g. «I am not a person that worries», or «I like being surrounded by people». Responses are made on a five-point

Likert scale ranging from «Strongly disagree» to «Strongly agree». The full version of the NEO-PI-R, consisting of 240 items, was used in this study.

The Social Desirability Scale (Crowne & Marlow, 1960; Rudmin, 1999) was used to assess self-presentation bias. It consists of 33 items, which are presented as questions, e.g., “I never resent being asked to return a favour”. Responses are made by checking one of two alternatives, “Correct” or “Wrong”.

The Spielberger State-Trait Personality Inventory (STPI, Spielberger, 1979; Håseth & Spielberger, 2000) was used to assess situational affect and stable trait-like affective responses. Both the state and the trait version consist of 40 items each, and measures anxiety, curiosity, anger and depression. Responses are made on a four-point Likert scale ranging from “Not at all” to “Very much”.

The Symptom Checklist 90-R (SCL-90-R) (Derogatis, 1983; Vassend & Skrondal, 2003) was used to assess emotional distress symptoms. It comprises nine sub-scales: somatization, obsessive-compulsive tendencies, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism. In total, the SCL-90-R consists of 90 items. All items are questions, e.g., “During the last 7 days, how often have you been troubled by persistent negative thoughts?”. Responses are made on a five-point Likert scale ranging from “Not at all” to “Very much”.

The Health Complaint Report (HCR) was administered to obtain information on somatic and psychological health complaints. The HCR was designed at the Norwegian National Institute of Occupational Health for use in working populations (Steingrimsdottir et al., 2004). It measures both severity and duration of musculoskeletal pain (12 items), gastrointestinal symptoms (6 items), psychological distress (5 items), allergy (3 items), and common cold (2 items) during the past 14 days. For severity of symptoms, responses are made on a four-point Likert scale ranging from “not troubled at all” to “very troubled”. Indices based on the mean severity scores multiplied with mean duration scores of the musculoskeletal symptoms (MSI), gastrointestinal symptoms (GI), allergic complaints (AI) and upper airway infection complaints (UAI) were computed.

2.5 Data reduction

All signals were AD-converted, recorded, stored and reduced in a computer (Lab View, National Instruments, Austin, TX, USA). The data from the experimental tasks were averaged for one-minute, two-minute, or three-minute periods (see individual papers for specific information). The data recorded during ES were averaged for one-second epochs at the threshold and tolerance levels. The data recorded during the PP were averaged for the entire stimulation period.

See individual papers for information concerning the aggregation of pain stimulation trials and calculation of physiological change scores.

2.6 Statistical analyses

The statistical analyses were performed using SPSS, release 12 (SPSS Inc., Chicago, IL, USA). See Table 3 for an outline of and each paper for details on statistical tests.

In Paper II, there were cases of large standard deviations relative to mean experimental pain values. The experimental pain data presented in that paper were therefore logarithmically transformed to allow the use of parametric statistics.

A 5% significance level was adopted. This increases the risk of Type I errors. However, a too stringent significant level would increase the risk of Type II errors, reducing the chances of identifying relationships worthy of further study. Relatedly, adjustments for multiple tests, e.g., Bonferroni corrections, reduce the risk of Type I errors, but increase the risk of Type II errors. The wish to avoid Type II errors was pronounced in this study, which was partially intended to be hypothesis generating. Therefore, as recommended by Rothman (1990) and Perneger (1998), no adjustments for multiple tests were done.

Significance tests are able to provide information on whether there is a statistically significant relationship between two or more variables. However, they do not describe the strength of these relationships, which may be more informative and more important in clinical practice. Therefore, the present study presents effect sizes of most major statistical associations.

Table 3. Statistical analyses used in Papers I-IV

Research question	Statistical analysis	Paper
Group differences in personality traits	Independent samples t-test	I
Group differences in subjective health complaints	Independent samples t-test, multivariate regression	I
Association between Neuroticism and TMD characteristics	Pearson's correlation	I
Group differences in pain sensitivity	Independent samples t-test	II
Changes in pain sensitivity across the experiment	Repeated-measures ANOVA	II
Associations between CV responding and pain sensitivity	Pearson's correlation, partial correlation	II
Spontaneous, non-experimental pain	Mann-Whitney U-test	II
Group differences in EMG	Mann-Whitney U-test	III
Group differences in LDF, MAP, and HR	Independent samples t-test	III
Changes in EMG, LDF, MAP, and HR across the experiment	Repeated-measures ANOVA	III
Group differences in affective responding	Independent samples t-test	III
Changes in affective responding across the experiment	Repeated-measures ANOVA	III
Changes in MAP and HR across the experiment	Related samples t-test, repeated-measures ANOVA	IV
Changes in pain sensitivity across the experiment	Related samples t-test, repeated-measures ANOVA	IV
Changes in affective responding across the experiment	Repeated-measures ANOVA	IV
Associations between CV responding and pain sensitivity	Pearson's correlation, partial correlation	IV
Associations between CV responding and affect variables	Pearson's correlation	IV

3 Results

3.1 Paper I

Mohn C, Vassend O., Krogstad, BS, Knardahl, S. Personality traits and subjective health complaints in female TMD patients and healthy controls. Submitted.

In Paper I, the following research questions were asked: (1) Do the five personality traits of the FFM and their sub-scales differ in TMD patients and pain-free controls? (2) When controlling for Neuroticism, self-presentation bias, and pain sensitivity, do TMD patients differ from pain-free controls in terms of psychological and non-TMD related somatic complaints?

The TMD patients exhibited a lower level of E and O. In addition, significant differences between the TMD patients and the control group with regard to the facets N-Depression, A-Tendermindedness, and C-Dutifulness were found.

There were higher levels of psychological distress and musculoskeletal pain in the TMD group relative to the control group. Hence, the typical TMD profile of affective distress and extra-craniofacial pain was reproduced. Importantly, these differences were maintained after controlling for N, self-presentation bias, and acute pain sensitivity.

3.2 Paper II

Mohn C, Vassend O, Knardahl S. Experimental pain sensitivity in women with temporomandibular disorders and pain-free controls: the relationship to orofacial muscular contraction and cardiovascular responses. In press, *Clinical Journal of Pain*.

In Paper II, the following research questions were asked: (1) Do TMD patients report lower orofacial pain thresholds at baseline and after isometric contraction of the orofacial region relative to pain-free controls? (2) Do TMD patients report lower extra-craniofacial pain thresholds after isometric contraction of the orofacial region? (3) Are there differential effects of experimentally induced CVR on the sensory detection thresholds, the pain thresholds and the pain tolerance in TMD patients and in pain-free controls?

Relative to the control group, the TMD group exhibited a significantly higher electrocutaneous pain threshold and non-significantly lower pressure pain thresholds at baseline. After isometric contraction of the jaw, the TMD group exhibited increased general pain sensitivity. This did not occur in the control group.

An arousing job interview did not significantly affect the subsequent pain sensitivity in any group. Significant positive correlations between MAP and pain thresholds and tolerance were seen only in the TMD group.

3.3 Paper III

Mohn C, Vassend O, Knardahl S. Focal and generalized psychophysiological responses to cognitive tasks and experimental pain stimulation in female temporomandibular disorder patients. Submitted.

In Paper III, the following research questions were asked: (1) When responding to cognitive challenges and orofacial muscular contraction, do TMD patients exhibit focal orofacial responses or generalized reactivity? (2) Do these psychophysiological responses in TMD patients and pain-free controls parallell subjective reports of affective state? (3) Compared to pain-free controls, do TMD patients respond differently to experimental pain stimulation?

The cognitive tasks elicited significant MAP, HR, and SBF responses, and, overall, these were similar in the two groups. There were significantly lower levels of masseter EMG in the TMD group during relaxation, cognitive tasks, and jaw contraction.

Apart from a significantly lower masseter EMG in the TMD group during ipsilateral masseter pressure pain, there were no group differences in physiological responding during experimental pain stimulation.

Relative to the controls, the TMD patients were more distressed during the experiment, as evidenced by their report of higher levels of state anxiety and depression as well as a more negative experience of the job-interview.

3.4 Paper IV

Mohn C, Vassend O, Knardahl S. Cardiovascular modulation of pain perception and affective responses in normotensive, pain-free women. Submitted.

In Paper IV, the following research questions were asked: (1) Do CV responses induced by a simulated job-interview alter subsequent pain perception? (2) Are there significant associations between CV parameters (resting, task-level and change scores) and pain

perception? (3) Are there significant associations between CV responding and affective responses?

The results from this study do not suggest a strong relationship between CV responding and pressure pain sensitivity in normotensive, pain-free women. There were only few and isolated findings of associations between CV measures, pain sensitivity, and emotional response.

Several methodological aspects strengthen the validity of this finding. Control for menstrual cycle events, weekend-related changes in physiology, and the CV changes during pain stimulation was provided. In addition, cardiovascular and pain stimulation data obtained at three points during the experiment - before, during, and after the arousing intervention - were analysed.

4 Discussion

There were marked group differences in subjective reports of personality traits and psychological and musculoskeletal health complaints. Significant group differences in experimental pain sensitivity largely did not emerge at baseline. However, after isometric contraction of the jaw muscles, experimental pain sensitivity was enhanced in the TMD group. With respect to physiological responding during cognitive tasks, significant group differences were observed only for absolute levels of EMG.

4.1 Methodological considerations and limitations

When interpreting the present data, several limitations must be kept in mind.

This study is limited by the relatively low number of participants, an issue particularly relevant when interpreting the non-significant results of Papers II and III. Moreover, the small TMD sample did not permit division into diagnostic subgroups, a procedure necessary for generating hypotheses of the pathogenesis of TMD and other heterogeneous myofascial pain conditions. Although there was sufficient power to reproduce the typical TMD profile of psychological distress and general musculoskeletal pain in Paper I, this study may have been somewhat underpowered with respect to analyses of pain sensitivity and physiological responding due to possible sub-group variation in the TMD group. However, it must be emphasized that there were no clear,

non-significant trends in altered CV physiological responding in the TMD group (Paper III). This suggests that there really are no differences between TMD patients and controls in terms of MAP, HR, and SBF during cognitive tasks and experimental pain stimulation, or alternatively, that existing differences may be marginal or of little clinical relevance.

The TMD group consisted of clinical and community cases. Population samples of TMD may report lower levels of pain severity, suffering, and functional impairment (Ohrbach & Dworkin, 1998). There were no such differences in the present study, and the pooling of the two samples seems justified. However, the population sample may have been too small (nearly half of the clinical sample) for significant group differences to emerge.

The pain-free status of the participants in the control group was not determined on the basis of a diagnostization process according to the RDC-TMD (Dworkin & LeResche, 1992), but according to self-report of symptoms. Symptoms and signs of TMD, e.g., pain and clicking sounds, are common in the general population, albeit at a level that may not be severe enough to warrant the diagnosis of TMD (Rantala et al., 2004), and it can not be concluded that the current control group consisted of individuals completely free of TMD-related symptoms.

The experimental conditions were presented in the same order for all participants. The participants rested for several minutes between conditions, so carry-over effects should be marginal. However, there is a remote possibility that the increased generalized pain sensitivity of the TMD patients after the jaw contraction was due to the fact that the subsequent pain stimulation was the last in a series of seven trials in addition to the muscular contraction itself. The condition assumed to be most physically challenging were performed at the end of the experiment, so as to avoid inducing excessive fatigue in the participants at an early stage of the experimental procedure. In order to affirm the conclusion that jaw contraction is capable of inducing generalized pain sensitivity in TMD patients, future studies should have participants perform jaw contraction closer to the baseline assessments of pain sensitivity.

The local physiological recording may not have been sufficiently sensitive for the detection of a higher number of group differences in Paper III. Intra-muscular EMG and LDF recordings may provide physiological data of higher sensitivity than superficial

recordings. However, needle electrodes and probes are susceptible to movement artefacts. Surface recordings of EMG and blood flow were chosen as the cognitive tasks, i.e., verbalizing and visuomotoric tracking, were expected to generate movement of the orofacial and shoulder region. In addition, this method is not invasive and therefore less stressful for the participants.

The current results are based on studies of women only. Female TMD sufferers tend to report more psychological distress and physical symptoms compared to male TMD patients (Dao & LeResche, 2002), and women in general have been found to report higher pain sensitivity than men (Berkely, 1997). Thus, the results of Papers I and II may not generalise to the male TMD population. In addition, it was controlled for menstrual cycle events only in Paper IV, thus limiting the generalizability of the results of Paper II with respect to acute pain sensitivity.

MAP and HR were measured by the Peñáz method. Compared to brachial sphygmomanometry, the finger pressure method may underestimate absolute arterial pressure, but provides accurate measurements of pressure changes (Pickering et al., 2005), which was one of the aims of the present study. Moreover, brachial sphygmomanometry may generate moderate pressure pain in the subjects, risking interference with the assessment of the experimental pain sensitivity that was the aim of our study. Nevertheless, it must be acknowledged that the MAP is influenced more by the diastolic than the systolic pressure, and the systolic pressure seems to be better able to predict pain sensitivity (Bragdon et al., 2002; Maixner et al., 1997). That the measurements of MAP were not calibrated with pressure values obtained through sphygmomanometry is a limitation of the present study.

4.2 General discussion

4.2.1 Personality traits and chronic pain

Reduced levels of E and O in addition to non-significantly elevated N in the TMD group were observed. This is a novel finding, as previous research has tended to concentrate on N or NA only.

Based on the relative stability of personality traits in adults, most studies of the personality and health relationship assume that personality characteristics in some way

are involved in the development of somatic illness even in the absence of evidence for a pain-prone personality (Gatchel & Weisberg, 2000). It has recently been demonstrated that many inventories used to assess personality traits e.g., the MMPI, are influenced by state-related affect and fluctuations in chronic pain intensity (Fishbain et al., 2006). However, that study did not investigate the effect of symptom severity on the NEO-PI-R, an inventory assumed to be less contaminated by state affect and current health complaints than the MMPI (Gatchel & Weisberg, 2000), and that has shown relatively strong stability in the face of life events and illness-related changes (Costa & McCrae, 1992). Therefore, although the present cross-sectional study does not enable causal conclusions regarding the personality-pain relationship, it may be argued that E and O may be involved in the development or presentation of TMD symptoms.

A first explanation of such a hypothesized relationship is a direct link between personality and TMD development. Based on previous findings of elevated N in the absence of pathophysiological variables (Costa & McCrae, 1992; Gatchel & Weisberg, 2000) this explanation seems unlikely at first glance. However, recent advances in neuroscience have identified brain regions and biochemical agents relating to different personality traits. In a magnetic resonance imaging (MRI) study, Omura et al. (2005) reported that amygdala grey matter concentration correlated differently with N than with E. Furthermore, compared to those low in N, individuals high in N have been found to exhibit higher levels of salivary cortisol, suggestive of altered hypothalamic-pituitary-adrenal (HPA) axis function (Portella et al., 2005). Abnormalities of the HPA axis have been reported in chronic widespread pain disorder (McBeth et al., 2005). The possibility that certain personality traits and predispositions to develop chronic pain syndromes may share common neurological or physiological background should be explored in prospective studies.

A second explanation may be the effect of personality traits on symptom report. In healthy individuals, N has consistently been related to enhanced levels of health complaints in the absence of illness (Costa & McCrae, 1992; Ellington & Wiebe, 1999). O has been associated with increased symptom report during suffering from common cold, but not in healthy samples (Feldman et al., 1999). A limitation pertaining to this line of research is the absence of studies of the relationship between personality and symptom

report in chronic pain groups. Moreover, there may be significant gender effects on this relationship. In a study of elderly individuals, high levels of A was related to fewer medical problems in women, whereas high levels of C was found in relation to positive health perceptions in men only (Jerram & Coleman, 1999).

The symptom-amplification effects of NA seem to be mediated by attention; high NA is related to a sharpened attention to stimuli emanating from one's own organism (Kolk et al., 2003). It is not known whether other personality traits interact with attentional processes in a similar manner. Relatedly, N-associated vigilance to pain may predispose the individual to catastrophizing, e.g., the tendency to interpret internal and external stimuli in the worst possible manner (Goubert et al., 2004). Hence, NA and N not only seem to direct one's attention inward, but also to exaggerate the negative impact of unpleasant or painful somatic stimuli.

A third possibility is that social and psychological consequences of personality characteristics may create a risk for chronification of acute pain conditions. Low levels of E and O, in particular if combined with high N, may increase the risk of loneliness, isolation, and proneness to maladaptive patterns of thought and affective responding. Perhaps such experiences may be part of the explanation for the observed maladaptive coping strategies in some chronic pain patients (Nitch & Boone, 2004).

The relationship between personality traits and coping strategies seems relevant for cooperation with health care workers and adherence to treatment regimes. Although we are aware of no study tracking treatment effects (and satisfaction with clinicians) in relation to personality traits in chronic illnesses, this topic has long been discussed (Mutén, 1991; Smith & Williams, 1992). It is speculated that low O in combination with low E may offer particular difficulties in terms of the reduced ability to recognize and communicate emotions that may arise from this combination of traits (Phillips & Gatchel, 2000).

4.2.2 General health complaints in TMD

The classical TMD profile of elevated levels of psychological distress and extra-cranial pain complaints was reproduced. Moreover, we have put this finding on a more secure

footing by controlling for the impact of experimental pain sensitivity, N, and self-presentation bias.

As with the personality-pain association, the present cross-sectional study does not permit causal conclusions regarding the pain-general health complaint relationship. Emotional distress has been identified both as a precursor to and a consequence of chronic pain. The first of these possibilities has received extensive theoretical attention for several decades. The comorbidity of psychological distress and pain, in addition to the lack of organic abnormalities in many musculoskeletal pain disorders, has generated suggestions that chronic pain conditions may be masked psychiatric disorders, with patients reporting somatic complaints instead of psychological distress to avoid the social stigma of mental instability. The TMD patients in the present study reported elevated levels of somatic complaints. Previous studies have found somatization processes to be predictive of chronic widespread pain (McBeth et al., 2001) in addition to being predictive of poor treatment outcome in established TMD (Rammelsberg et al., 2003; Ohrbach & Dworkin, 1998).

An elevated level of somatic symptoms does not necessarily imply that a somatization disorder is present. Somatisation processes denote the tendency to communicate emotional and social distress through physical symptoms (Bacon et al., 1994). This tendency is related to, but not equivocal to, the psychiatric diagnosis of somatization disorder, which requires a higher number as well as several years of symptoms (American Psychiatric Association, 1994). It is not inconceivable that somatization may occur secondary to chronic pain. As the pain problem progresses, a response may be an increased focus on bodily processes and symptoms (Gatchel & Weisberg, 2000), even in individuals with high pre-pain levels of somatization or other psychological distress. The ultimate consequence may be a positive feedback-loop where chronic pain and negative affect interact in a circular manner. This raises the possibility that the relationship between psychological distress and chronic pain, regardless of causal direction, may not be linear. In fact, the tendency to overlook possible circular relationships is a point of criticism of diathesis-stress models of the relationship between psychological distress and somatic health (Gatchel & Weisberg, 2000). In order to avoid or reduce the detrimental impact of such a circular relationship, early identification and

treatment of psychological distress is pivotal. Indeed, there is recent evidence that this type of intervention may prevent the transition to chronic pain in individuals with acute TMD (Gatchel et al., 2006).

Recent findings of common genetic sources of both chronic pain and psychological distress challenges the cause-effect way of analysing the pain-distress relationship (Diatchenko et al., 2006a). Moreover, the central sensitisation explanation of chronic pain regards emotional distress as secondary to the pain problem (Svensson & Graven-Nielsen, 2001; Vierck, 2006). The question of which model that best explains the pain-distress association, and the question of whether this association is different in different subgroups of chronic pain patients, awaits further elucidation.

Compared to the pain-free controls, the TMD patients of the present study reported significantly higher levels of headache and pain in the neck, back, and legs. There were, however, considerable inter-individual variations in the TMD group as evidenced by the large standard deviations of the analyses. Possibly, some groups of TMD patients are more troubled by generalised pain than the others.

An issue arising at this point is the relationship between TMD and FMS on the one hand and TMD and chronic tension-type headache (CTTH) on the other. One study found that general musculoskeletal pain predates orofacial pain and concluded that TMD may simply be a characteristic of late-stage FMS (Hedenberg-Magnusson et al., 1999). Despite similarities, there seems to be important differences between these illnesses, as Dao et al. (1997) have found that a sizable minority (21%) of TMD patients had orofacial pain for up to 15 years without general body pain. Moreover, FMS seems to be characterized by more severe pain and higher levels of psychological distress (Dao et al., 1997; Plesh et al., 1996). In addition, the prevalence of TMD does not seem to increase with age the way FMS does (Dao et al., 1997; Plesh et al., 1996). Possibly, TMD and FMS occupy different ends of a continuous spectrum of chronic musculoskeletal pain resulting from similar, as of yet unknown, etiological factors.

However, the possibility that some of our patients would have been diagnosed with FMS can not be ruled out. The presence of (>11 of 18) tender points as detected by palpation by the clinician is required for the diagnosis of FMS (Wolfe et al., 1990), and our patients were not examined with respect to the FMS diagnostic criteria. In addition to

the presence of tender points, however, other FMS diagnosis criteria are widespread chronic pain, psychological distress, sleep problems, and fatigue. We found significant group differences in self-reported headache, neck pain, and pain in the upper and lower back, chest, and legs, as well as psychological distress. These symptoms may be indicative of FMS being present in at least some of our patients.

Likewise, the relationship of TMD to CTTH is difficult to entangle. Based on the significant group differences in self-reported headache, at least some of our patients may have been candidates for a CTTH diagnosis. CTTH (i.e., idiopathic headache more than 15 days pr. month for more than 3 months, International Headache Society; 2004) may be a consequence of facial pain, or orofacial pain may result from tension type headache due to central sensitization (Bendtsen, 2000). Moreover, both facial pain and headache may be symptoms of a common musculoskeletal pain disorder, e.g., FMS (Wolfe et al., 1990). Despite the common finding of comorbidity of TMD and headache (e.g., Ciancaglini & Radaelli, 2001), and the increasing frequency of CTTH in the Western population (Bendtsen & Jensen, 2006), there is surprisingly little research into this relationship.

In the absence of clear biological markers for each diagnostic category, the only way to disentangle the relationship between TMD, FMS, and CTTH – as well as other conditions assumed to be functional somatic syndromes – is to conduct a thorough investigative process where individuals presenting with these symptoms are subject to diagnostization according to the criteria of each of these conditions. Normally, one seeks out specialist care based on the most dominant symptoms and complaints, e.g., someone suffering from persistent, strong orofacial pain may be referred to a dental clinic even if persistent pain, albeit of lower intensity, is present in other parts of the body. The classification of such an individual as a TMD sufferer may be somewhat arbitrary; possibly, an FMS diagnosis could also be correct given a sufficient number of extra-cranial tender points. To date, no such extensive study of the functional somatic syndromes has been undertaken.

4.2.3 Experimental pain sensitivity in TMD

Two of the present findings contrast with most previous research in experimental pain sensitivity in TMD. First, the TMD group exhibited significantly lower electrocutaneous

pain sensitivity and only a non-significant trend of higher pressure pain sensitivity at baseline. Second, the significant correlations between experimental pain sensitivity and CV responding that has been reported in pain-free men, in this study occurred in the female TMD group.

4.2.3.1 Pain sensitivity

The post-contraction reduction in pain thresholds at all anatomical sites tested in the TMD group is suggestive of an enhanced generalized sensitivity due to local muscular load. A similar finding has been reported in FMS (Staud et al., 2005), and taken as evidence that chronic pain conditions are explainable in terms of central sensitization. A further support of this notion comes from the above finding that the TMD group reported elevated levels of general musculoskeletal pain relative to the controls, but that there were no group differences in other somatic complaints. This suggests that TMD patients are not global complainers in search of medical attention, despite the uncertain organic basis for their symptoms, but that a central sensitization process is in operation.

Tonic nociceptive input to the CNS may generate central sensitization (Vierck, 2006), and muscle contractions could be a source of such input (Staud et al., 2005). Several intramuscular processes may be involved in the sensitization of muscle afferents, e.g., release of growth hormones, reduced muscle blood flow, and increases in metabolites (Vierck, 2006). On the other hand, aerobic exercise and strength training have been efficient in reducing clinical pain in FMS patients (e.g., Richards & Scott, 2002). The point at which physical exercise becomes harmful in chronic musculoskeletal pain patients is not established. However, the muscular load of the present study as well as of the study of Staud et al. (2005) was static and strenuous. The type of exercise recommended in rehabilitation studies are typically non-static, of low to moderate intensity, and is based upon activities that most people naturally perform and find enjoyable, i.e., stretching, leisurely walking, dancing, swimming or stretching in warm water (Zijlstra et al., 2005; Richards & Scott, 2002). These activities may not compromise muscle physiology the same way that isometric contractions do, but benefit the organism by improving CV function and increasing muscular blood flow.

The lack of significantly higher pain sensitivity in the TMD group at baseline was surprising. Several explanations may be offered. First, there may be large variations in pain sensitivity within chronic pain populations, as observed by Giesecke et al (2003) in FMS patients. In spite of the general tendency for chronic pain groups to demonstrate higher pain sensitivity than pain-free controls, several studies exist that have not found this association. This point may be particularly relevant in a relatively small sample. Moreover, our study is limited by the fact that we did not assess sensory or affective experiences of the pain stimulation in Papers I-III. Such a procedure would have provided more information on the participants' experience of pain and may have shed light on the unexpected baseline findings.

In a study of chronic low back pain patients and healthy controls, Peters & Schmidt (1992) found a significantly lower electrocutaneous and pressure pain sensitivity in the chronic pain group. Boureau et al. (1991) found that their sample of mixed chronic pain conditions reported the same electrocutaneous pain sensitivity as the healthy control group. The authors suggest two possible explanations for these results. First, the long-term adaptation to pain that these patients experience may reduce their tendency to label experimental pain stimulation as painful (Peters & Schmidt, 1992; Boureau et al., 1991). Second, the presence of chronic pain could generate a neurophysiological inhibition of experimental pain perception through a diffuse noxious inhibitory control (DNIC) mechanism (Peters & Schmidt, 1992; Boureau et al., 1991). However, more recent studies have found that DNIC phenomena generally modulate pain perception in healthy males, and not in healthy females or FMS patients (Staud et al., 2003; Lautenbacher & Rollman, 1997) or facial pain (Sigurdsson & Maixner, 1994). On the other hand, a critique of DNIC studies has been offered by Vierck (2006), who argues that the findings of Staud et al. (2003) and Lautenbacher & Rollman (1997) are confounded by enhanced attentional focus on the clinical pain due to acute pain stimulation. It is not possible to rule out DNIC phenomena in explaining the present data.

A second explanation for our baseline findings may be that different methods of pain stimulation are used. We employed electrocutaneous and pressure pain, in contrast to ischemic and heat pain used in the studies by Bragdon et al. (2002) and Maixner et al. (1997). In a previous study, no group differences have been reported regarding

electrocutaneous pain sensitivity in FMS patients and healthy controls (Lautenbacher & Rollman, 1997). In another study, electrocutaneous sensitivity was significantly lower in TMD patients compared to pain-free controls (Hagberg et al., 1990). Moreover, in the same study, the lowest acute pain thresholds were found in TMD patients with the highest clinical pain ratings (Hagberg, 1990). In our study, the clinical pain ratings obtained at various intervals throughout the experiment were relatively low (see Paper II). In addition, none of our patients were disabled and only 9% on sick leave. These findings suggest that most of those who participated in our time-consuming and presumably stressful study belong to the sub-group of patients with relatively low clinical pain and functional impact. However, a limitation of the present study is that the TMD patients' overall functional status and impact on symptoms on the performance of activities of daily life was not assessed.

However, the lack of significant group difference of pressure pain sensitivity at the masseter muscle was surprising, as measurements were performed at a site that is frequently painful to palpation in TMD (Dworkin & LeResche, 1992). Indeed, Sarlani & Greenspan (2003) note that TMD patients, relative to healthy controls, tend to be more sensitive to pressure pain, but not necessarily to electrically evoked pain. This notion is supported by a study by Svensson et al. (2001), demonstrating increased pressure pain sensitivity, but not heat pain sensitivity, in the masseter muscle of TMD patients compared to pain-free controls. There was, however, a non-significant trend of lower pressure pain sensitivity in our TMD patients.

4.2.3.2 The CVR - pain sensitivity relationship

The present results contrast with previous reports, e.g., by Bragdon et al. (2002) and Maixner et al. (1997). Surprisingly, all significant correlations between MAP and pain sensitivity were seen in the TMD group. This was not due to the influence of state affect, as there were no significant correlations between the STPI-State scales and MAP in the TMD group. One possible explanation for the present finding may be that we employed electrocutaneous and pressure pain stimulation, whereas Bragdon et al. (2002) and Maixner et al. (1997) assessed the responses to ischemic and thermal pain stimulation, suggesting that there may be a differential relationship between cardiovascular responses

and pain sensitivity induced by different stimulation modalities, triggering different classes of nociceptors.

The findings of a clear pattern of significant correlations between CVR and pain sensitivity, are supportive of a model where CVR and hypoalgesia are not causally related, but occur simultaneously due to central nervous changes that have yet to be elucidated (France, 1999). It is not known why this correlational model was supported only in the TMD group in this study. The conflicting results of studies of the relationship between CVR and pain sensitivity, which may at least partly be explained by methodological differences (France, 1999) do not offer the empirical background required for a discussion of causative central nervous processes. Our findings should be replicated before it may be concluded that the superficial type of pain evoked by electrocutaneous stimulation is indeed differently related to CVR in TMD patients compared to healthy controls, or that these results are indicative of an underlying psychophysiological dysfunction in chronic pain patients.

Paper IV describes parts of a study intended to investigate in more detail some of the findings of Paper II. We employed continuous blood pressure recordings, and the test-retest reliability of our pain stimulation trials was high. This permits a large degree of confidence in our results. We found a non-significant trend of associations between Δ MAP and Δ HR and pain sensitivity after the arousing job interview, so until our results are replicated with a larger sample, it is not possible to dismiss the CVR-pain relationship in normotensive, pain-free women altogether. Although the CVR-pain relationship has been assumed to occur mainly in men (Bragdon et al., 2002; Maixner et al., 1997), Bruehl et al. (2002) reported that increases in systolic blood pressure was related to decreased ratings of finger pressure pain intensity in both genders. Bearing in mind the sparse literature on CVR and pressure pain, these results suggest that pressure pain is related to CVR in a different manner than are ischemic and heat pain, perhaps related to activities of different regions of the PAG during deep and superficial pain stimulation (Bandler & Shipley, 1994).

4.2.4 The CVR – emotional dampening relationship

Our results (Paper IV) provide no strong support for the hypothesis that CV responding is correlated both with attenuated pressure pain sensitivity and general emotional dampening (Pury et al., 2004). Several methodological characteristics strengthen these findings: We controlled for menstrual cycle events, weekend-related changes in physiology, and the CV changes during pain stimulation. In addition, we analysed cardiovascular and pain stimulation data obtained at three points during the experiment: before, during, and after the arousing intervention.

However, our sample (N = 39) was smaller than the one of Pury et al. (2004) (N = 57). Some of our non-significant negative correlations between CVR and affective responses to pain stimulation and to the job-interview may have turned out significant given a larger sample. Hence, it may be wrong to dismiss the CVR-emotional dampening hypothesis altogether based on the current data. On the other hand, there were significant positive associations between CVR and general state affect during the experiment, indicating a classical stress-activation response where increases in negative affect occur in parallel with increases in CVR. It would seem prudent to consider the debate of the emotional dampening hypothesis as still undecided.

4.2.5 Psychophysiological responding in TMD

The TMD patients exhibited consistently lower levels of masseter EMG during relaxation periods and cognitive tasks. This finding contradicts previous reports of muscular hyperactivity in chronic musculoskeletal pain (Flor et al., 1991; 1992), but agrees with the pain-adaptation model (Lund et al., 1991), suggesting that reduced levels of EMG occur in response to pain in order to avoid further pain or harm. However, the generalizability of our findings is limited by the fact that we did not control for consumption of analgesics or muscle relaxants in the TMD group on the day of the experiment.

As there were higher levels of negative affect in the TMD group during the experiment, our results present a challenge to the diathesis-stress model of Flor et al. (1991; 1992). An issue arising at this point is the sensitivity of our job interview in generating distress. Was this task sufficiently emotionally challenging to generate

muscular hyper-reactivity in the TMD group if the diathesis-stress model is correct? This is most likely, given that the MAP and HR levels of our participants were significantly elevated during this task. In the studies of Flor et al. (1991; 1992), the emotionally stressful task was personally distressing imagery, whereas our participants actively performed the arousing task through verbalization. Moreover, the increased levels of MAP and HR during the job interview indicate that this task generated significant arousal.

The modest number of significant group differences in physiological responding coupled with significant group differences in self-reported affect is in line with other studies. In matched samples roughly the same sizes as ours, Curran et al. (1996) observed higher levels of anger, anxiety, and sadness in TMD patients relative to controls during stress (mental arithmetic), but no differences in finger pressure pain or EMG levels. Similarly, in a study of 34 TMD patient and 18 controls, Carlson et al. (1993) demonstrated that the TMD group was characterised by higher levels of anxiety and higher systolic blood pressure and HR during stress (mental arithmetic), while subjective reports of muscle tension was not paralleled by EMG changes.

Such findings suggest that the behavioural-physiological adaptation and cognitive-affective response systems are two separate parts of the stress-response systems and are not necessarily highly correlated. However, it may be argued that absence of evidence is not evidence of absence. The fact that several investigators have failed to detect group differences in physiological responding does not necessarily mean that differences do not exist. Instead, the detection methods currently available may not be sufficiently sensitive to demonstrate subtle changes in skin and muscle physiology.

These results, in combination with the significant group differences in subjective health complaints (Paper I), add to several reports of a discrepancy between a marked presence of suffering and perceived ill-health and few physiological signs of disease in TMD patients as well as in other chronic musculoskeletal pain disorders such as FMS and CTTH (Aaron et al., 2000; Barsky & Borus, 1999). The identification of causal factors behind this discrepancy, which should be carried out in parallel with a continued search for biological markers of chronic musculoskeletal disorders, should be assigned priority in future research efforts.

5 Conclusions and practical implications

The TMD patients exhibited a lower level of the personality traits E and O. Higher levels of psychological distress and musculoskeletal pain in the TMD group relative to the control group were observed. Hence, the typical TMD profile of affective distress and extra-craniofacial pain was reproduced. Importantly, these differences in general health complaints were maintained after having statistically controlled for N, reporting bias, and acute pain sensitivity.

It is recommended that TMD patients undergo a personality screening in order to identify traits that are relevant for adjustment to chronic pain and cooperation with health care workers. Moreover, the possibility that personality traits affect symptom report differently in chronic pain groups and healthy samples needs to be elucidated.

Regardless of causal direction between affective tone and chronic pain, the present data fit well with the consistent findings of TMD patients being characterized by psychological distress as well as chronic pain, and that psychological function should be targeted during treatment in parallel with the pain problem.

The findings of increased levels of self-reported general musculoskeletal pain in TMD patients, but no group differences in gastrointestinal, allergy, or upper airway infection symptoms, indicate that TMD patients are not global complainers. Possibly, a central sensitization process has taken place, although it must be acknowledged that in our study, there were few group differences in experimental pain sensitivity. This is important, as the lack of identifiable organic causes for their pain sometimes results in TMD patients being told that their pain “is all in the head”. The rate of development of central sensitization processes as well as risk factors should be studied in sub-chronic samples or ideally prospectively with individuals healthy at baseline.

Relative to the control group, the TMD group exhibited a significantly higher electrocutaneous pain threshold and non-significantly lower pressure pain thresholds at baseline. After isometric contraction of the jaw, the TMD group exhibited increased general pain sensitivity, while this did not occur in the control group. This finding may be interpreted in terms of a central sensitization process.

The arousing job interview did not significantly affect the subsequent pain perception in any group. Significant positive correlations between MAP and pain

thresholds and tolerance were seen in the TMD group. These data indicate that the CVR – pain sensitivity relationship may be dependent on method of pain stimulation. Moreover, to the best of the author’s knowledge, this study is the first to demonstrate that also women with TMD may experience the correlational relationship between CV responding and pain previously thought to occur mainly in pain-free men. The study of pain attenuation in the face of increased CV responding in chronic pain groups is, however, still in its infancy.

The cognitive tasks elicited significant MAP, HR, and SBF responses, and, overall, these were similar in the two groups, providing no support for the notion that TMD is related to a general psychophysiological dysfunction. There were significantly lower levels in masseter EMG in the TMD group during relaxation and the cognitive tasks, suggestive of a pain adaptation process in the region affected by clinical pain.

Relative to the controls, the TMD patients were more distressed during the experiment, as evidenced by their report of higher levels of state anxiety and depression as well as a more negative experience of the job-interview. These findings, in addition to the marked group differences in general health complaints, point in the direction of subjective reports of orofacial symptoms and general health being more reliable indicators of a TMD diagnosis than would assessments of general psychophysiological responding during stressful tasks.

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