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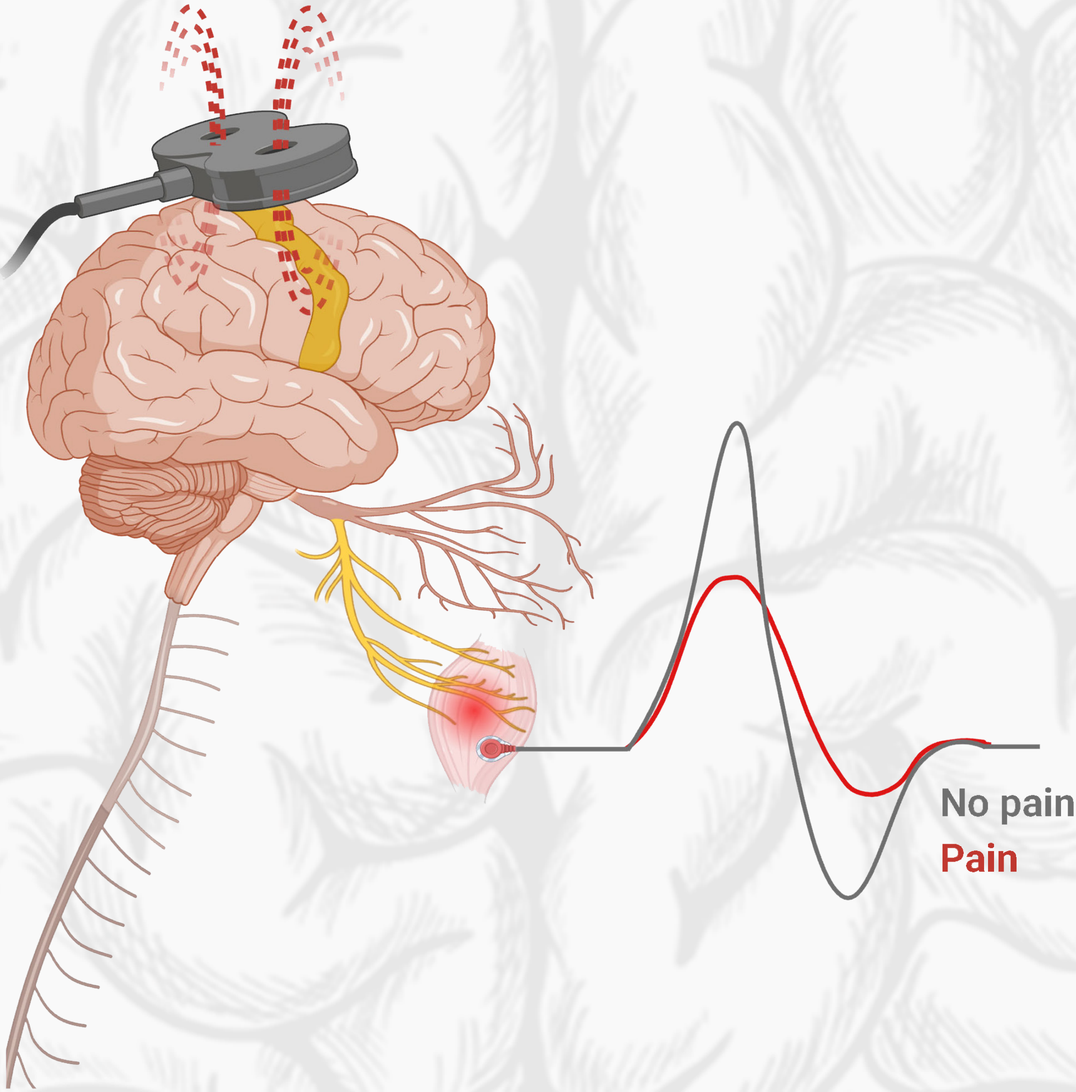

Pain, Function, and Parafunction of the Jaw System in Relation to Neuroplasticity

Nikola Stanisic

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Pain, Function, and Parafunction of the Jaw System in Relation to Neuroplasticity

Thesis for Double Doctoral Degree (double Ph.D)

By Nikola Stanisic

The thesis will be defended in public at the Faculty of Odontology, Malmö university

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Malmö university
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LIST OF STUDIES

This thesis is based on the following studies, referred to in the text by their Roman numerals:

I. **Stanisic N**, Häggman-Henrikson B, Kothari M, Costa YM, Avivi-Arber L, Svensson P. Pain's Adverse Impact on Training-Induced Performance and Neuroplasticity: A Systematic Review. Brain Imaging Behav. 2022;16(5):2281–2306.

II. **Stanisic N**, Baram S, Nykänen L, List T, Bracci A, Svensson P, Manfredini D, Häggman-Henrikson B. Exploring the relationship between muscle activity, jaw behaviour and pain. Sci Rep. 2025;15(1):35029.

III. **Stanisic N**, Kothari M, Häggman-Henrikson B, Svensson P, Castrillon E. Relationship between training-induced neuroplasticity and jaw sensorimotor function. (In manuscript).

THESIS AT A GLANCE

	Study I Systematic review	**Study II** Cross-sectional observational	**Study III** Case-control intervention
Aims	To investigate the impact of pain (acute or chronic) on training-induced motor performance and neuroplasticity assessed by transcranial magnetic stimulation (TMS).	To investigate the relationship between self-reported awake bruxism using EMA and jaw muscle activity registered by sEMG, and differences between individuals with and without temporomandibular disorder (TMD) pain.	To investigate whether a jaw exercise programme can induce changes in masseter corticomotor excitability, assessed with TMS, and in jaw sensorimotor performance, and whether these responses are influenced by TMD pain and overload-related jaw behaviour.
Methods	Followed: • PRISMA guidelines • PROSPERO protocol. Studies of short-term motor training performed with pain vs pain-free controls. Functional and TMS outcomes extracted and synthesised after a risk of bias assessment.	• 48 participants w/o TMD pain • 22 participants w TMD pain. EMA 3 days (≥12 prompts/day) Simultaneous masseter sEMG Day 1. Functional activities (eating/talking) excluded. Overload defined as >20% of maximum voluntary contraction.	• 19 pain-free controls • 10 TMD pain cases. 7-day training programme: • jaw stretching • thickness recognition. Outcomes: jaw opening replication and recognition tasks, TMS stimulus–response curves with masseter (and FDI control) MEPs.
Results	17 studies: 7 acute, 10 chronic pain. 258 individuals with pain, 248 controls. Only one study in the cranial motor system. Pain impaired training-induced corticomotor plasticity in most acute pain studies and half of chronic pain studies. Functional outcomes showed less consistent patterns.	EMA awake bruxism correlated with: • duration sEMG overload • overload intensity (AUC). Participants with TMD pain had: • longer overload duration • more awake bruxism • more stress • different overload profile with longer duration of low-intense activity.	Training improved jaw sensorimotor performance: • replication improved more in controls • recognition improved more in TMD pain cases. Masseter MEP amplitudes increased after training. Higher bruxism scores were linked to smaller MEP changes and higher aMT.
Conclusions	Both acute and chronic pain may perturb training-induced corticomotor neuroplasticity, although the evidence is more consistent in acute pain.	Combining EMA and sEMG provides a valid assessment of awake bruxism-related muscle overload and identifies distinct overload patterns in TMD pain.	Short-term jaw training may induce both sensorimotor and corticomotor adaptation, but responses may differ in TMD pain and with parafunctional behaviour.

aMT, Active Motor Threshold; AUC, Area Under Curve; EMA, Ecological Momentary Assessment; FDI, First Dorsal Interosseous; MEP, Motor Evoked Potential; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; PROSPERO, International Prospective Register of Systematic Reviews; sEMG, Surface Electromyography; TMD, Temporomandibular Disorder; TMS, Transcranial Magnetic Stimulation.

ABBREVIATIONS

aMT	Active Motor Threshold
AUC	Area Under Curve
CNS	Central Nervous System
CPG	Central Pattern Generator
CRH	Corticotropin-Releasing Hormone
DC/TMD	Diagnostic Criteria for Temporomandibular Disorders
EMA	Ecological Momentary Assessment
EMG	Electromyography
EMI	Ecological Momentary Intervention
FDI	First Dorsal Interosseous
JFLS-8	Jaw Functional Limitation Scale-8
MAD	Mandibular Advancement Device
MEP	Motor Evoked Potential
MSO	Maximum Stimulator Output
MVC	Maximum Voluntary Contraction
NGF	Nerve Growth Factor
NOS	Newcastle–Ottawa Scale
NRS	Numeric Rating Scale
OBC-21	Oral Behavior Checklist–21
PAG	Periaqueductal Gray
PICO	Population; Intervention; Comparison; Outcome
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROSPERO	International Prospective Register of Systematic Reviews
PSS-10	Perceived Stress Scale–10
RCT	Randomised Controlled Trial
RMS	Root Mean Square
RVM	Rostral Ventromedial Medulla
S1	Primary Somatosensory Cortex
sEMG	Surface Electromyography
TMD	Temporomandibular Disorders
TMS	Transcranial Magnetic Stimulation
3Q/TMD	Three-Question Screening for Temporomandibular Disorders

ABSTRACT

Pain and parafunctional behaviour may influence how the jaw motor system functions and adapts. The jaw system provides a relevant model for studying these interactions because of its high sensorimotor demands and its susceptibility to temporomandibular disorders (TMD) and bruxism. This thesis investigated how pain and parafunction influence training-induced neuroplasticity and sensorimotor performance in the jaw system, with a focus on corticomotor excitability assessed via transcranial magnetic stimulation.

Three studies were conducted. Study I was a systematic review of 17 studies examining the effects of acute and chronic pain on training-induced corticomotor plasticity and functional outcomes. Study II was a cross-sectional observational study of 70 adults with and without TMD pain, combining ecological momentary assessment of awake bruxism with simultaneous masseter surface electromyography (sEMG) to assess jaw muscle overload in daily life. Study III was a case-control intervention study with 29 participants examining the effects of a seven-day jaw exercise programme on jaw sensorimotor performance and masseter corticomotor excitability.

Study I showed that both acute and chronic pain may perturb training-induced corticomotor neuroplasticity, with more consistent effects in acute pain. Study II showed that self-reported awake bruxism correlated with sEMG-assessed muscle overload, and that individuals with TMD pain exhibited more awake bruxism, higher stress levels, and longer periods of low-intensity muscle overload. Study III showed that short-term jaw training improved sensorimotor performance in both the pain-free and TMD pain groups, although the pattern differed between groups. Higher bruxism scores were associated with higher active motor threshold and smaller training-related increases in motor evoked potential amplitude.

Taken together the results suggest that pain and parafunctional behaviour can influence the loading, capacity, and adaptive potential of the jaw motor system. These findings support a model in which TMD pain and bruxism interact to shape corticomotor neuroplasticity and jaw sensorimotor adaptation.

POPULÄRVETENSKAPLIG SAMMANFATTNING

Ungefär 20 % av befolkningen lever med långvarig smärta från mun, käkar eller ansikte, s.k. orofacial smärta. Denna typ av smärta är särskilt vanlig hos kvinnor och unga vuxna. Orofacial smärta påverkar både käkfunktion, välbefinnande och livskvalitet. Den vanligaste orsaken till långvarig orofacial smärta är temporomandibulär dysfunktion, TMD, som omfattar smärta och funktionsstörningar i käkmuskler och käkleder. Besvären kan yttra sig både som värk, trötthet och ömhet i käkmuskler och svårigheter att gapa, tugga och äta.

En möjlig bidragande faktor till TMD är överbelastning av käksystemet, till exempel tandpressning eller tandgnissling, s.k. bruxism. Eftersom detta ofta sker omedvetet kan det vara svårt att upptäcka och bedöma, både för individen och behandlaren.

Träning är en viktig del av behandling och rehabilitering vid långvarig smärta för att förbättra funktion, minska smärta och stärka förmågan att hantera belastning. Trots det vet man fortfarande förhållandevis lite om hur smärta och överbelastning påverkar neuromuskulär anpassning till träning. Detta gäller även i käksystemet.

Syftet med denna avhandling var därför att undersöka hur TMD-smärta och överbelastning påverkar käkfunktion och käkmuskulatur, hur käksystemet svarar på träning, samt hur hjärnan och nervsystemet anpassas till denna träning, s.k. neuroplasticitet.

Avhandlingen bygger på tre delstudier. Den första studien var en systematisk översikt av tidigare forskning om hur smärta påverkar träningsinducerad neuroplasticitet. Den visade att smärta kan påverka neuroplastisk respons i hjärnans motoriska system vid träning och att detta var tydligast vid akut smärta. Studien visade också att det vetenskapliga underlaget huvudsakligen bygger på studier av ryggmärgsinnerverade muskelsystem, medan käksystemet är mindre studerat.

Den andra studien undersökte sambandet mellan självrapporterad vaken-bruxism och registrerad käkmuskelaktivitet hos personer med och utan TMD-smärta. Den visade att självrapporterad vaken-bruxism hade ett tydligt samband med registrerad käkmuskelaktivitet och var vanligare hos personer med TMD-smärta.

Den tredje studien undersökte om ett käkträningsprogram kunde påverka käkfunktion och hjärnans motoriska system, och om träningseffekten påverkades av TMD-smärta och bruxism. Här visade det sig att träning förbättrade funktionen i båda grupperna, men att förbättringen påverkades av smärta. Bruxism var också kopplat till en större tröghet i hjärnans motoriska svar på träning. Resultaten visar att träningseffekter kan påverkas av smärtstatus och förekomst av bruxism, samt att de neuroplastiska förändringarna var relaterade till förbättrad funktion.

Sammantaget visar avhandlingen att smärta, överbelastning och bruxism hänger nära samman. Resultaten tyder också på att käksystemet är träningsbart, men att smärta och bruxism kan påverka hur käksystemet och hjärnan svarar på träning.

Denna kunskap kan bidra till bättre förståelse av TMD-smärta och till mer individanpassad bedömning och behandling, där hänsyn tas både till smärta och till hur käken (över)belastas i vardagen.

INTRODUCTION

Pain – Friend and Foe

Pain is a double-edged sword. On the one hand, it can keep us alive; on the other hand, it has the potential to destroy our lives. At its most useful, pain is a temporary warning signal: sharp, immediate, and essential. It tells us to stop, to pull away, to protect ourselves [76; 99]. From an evolutionary perspective, pain has been crucial for survival, helping us distinguish harmful from harmless stimuli [118].

This protective function is rooted in a highly sophisticated physiological system. At its core is nociception; the process by which the nervous system detects and transmits signals about potential or actual tissue damage [81; 121]. Specialised receptors, nociceptors, located in skin, muscles, joints, and viscera, act as sentinels. When they detect harmful stimuli, whether mechanical (such as a cut), thermal (heat or cold), or chemical (such as capsaicin), they generate electrical signals that travel along either A-delta fibres, transmitting fast, sharp pain, or C-fibres transmitting slow, dull, aching pain [30; 51].

These nociceptive signals travel differently depending on whether they originate from spinally or cranially innervated regions (Figure 1). Spinally mediated nociceptive signals, from, for example, the back or limbs, enter the central nervous system through the spinal cord, travelling via ascending pathways including the spinothalamic tract [23; 120]. In contrast, cranially innervated nociception from the face and jaw, is transmitted through the trigeminal system and brainstem nuclei, bypassing the spinal cord. These pathways are routed through the trigeminal sensory nucleus complex and then projected to higher brain centres, thereby differing anatomically from the spinal pathways [61; 93]. Whether and how these anatomical distinctions may translate into differences in pain processing, modulation, and clinical outcomes remains unexplored.

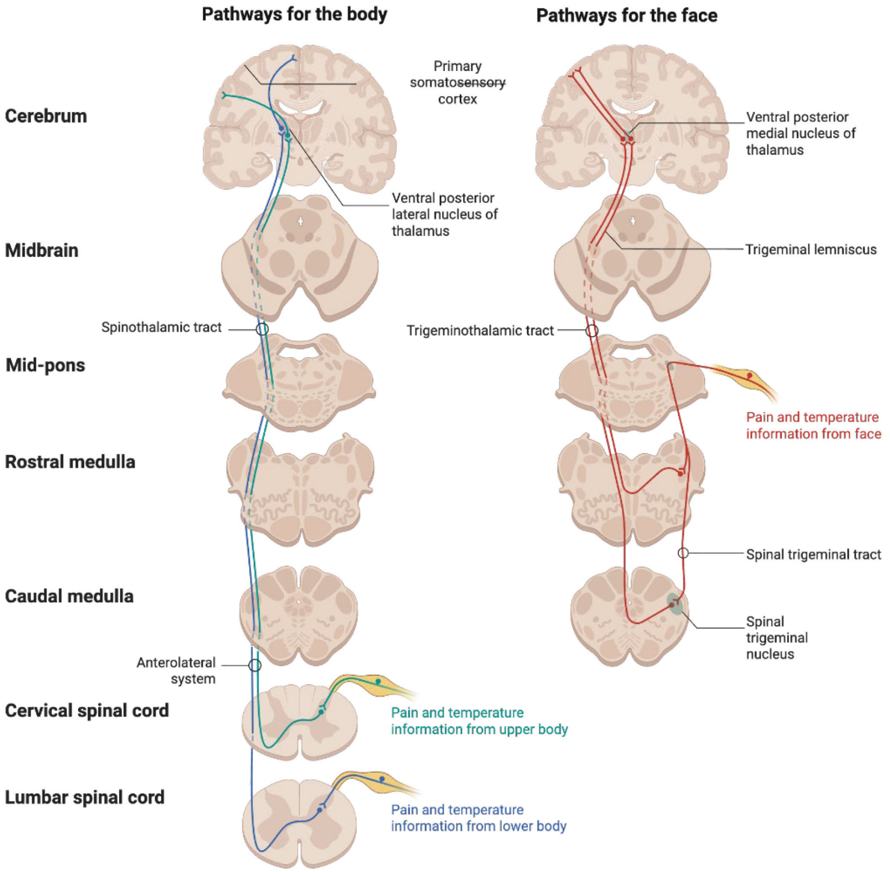

Figure 1. Discriminative pain pathways illustrating the ascending transmission of nociceptive and temperature information from the body and face to the brain.

Regardless of whether nociceptive signals travel cranially or spinally, they ultimately converge in higher-order structures such as the thalamus and the primary somatosensory cortex (S1), where the intensity and origin of signals are mapped. Within the primary somatosensory cortex, the facial and oral structures occupy a prominent portion of the sensory map, consistent with the dense trigeminal input and the high sensorimotor demands of the jaw system (Figure 2). However, this sensory map only illustrates one aspect of the pain experience. Cortical regions, including the anterior cingulate cortex, insula, amygdala, and prefrontal cortex, influence how this input is interpreted, adding emotional, cognitive, and contextual aspects. This applies to both acute and chronic pain, albeit with differences in clinical significance. Acute pain is typically short-lasting and protective, closely linked to actual or threatened tissue damage, whereas chronic pain, commonly defined as pain lasting for more than three months after healing, may outlast its protective purpose and become a condition in its own right [21]. This dynamic interplay forms the central basis of the biopsychosocial model of pain, in which pain is viewed not as only a direct result of somatosensory input, but as a broader experience shaped by biological, psychological, and social factors [21; 116].

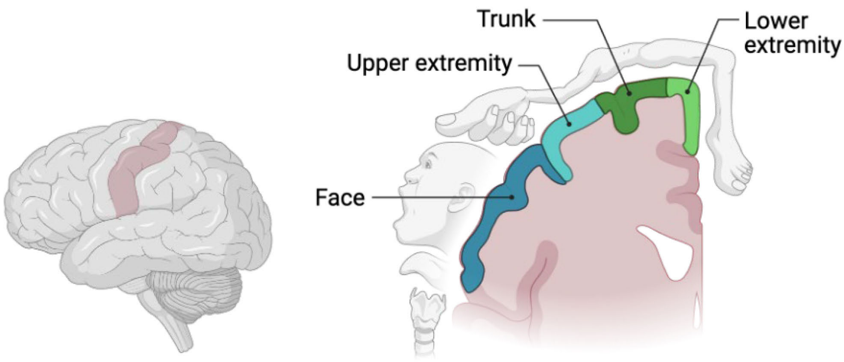

Figure 2. Sensory homunculus used to depict a “topical” version of the body in the brain.

Nociceptive signals can also be modulated by descending pathways from the brain (Figure 3). These descending pathways can increase (facilitate) or decrease (inhibit) sensitivity to pain via mediation by neurotransmitters such as serotonin, noradrenaline, and endogenous opioids. Overall, through these modulatory systems, similar nociceptive input may result in different pain responses depending on the overall context [6; 78].

For example, imagine waking up in the morning of a big competition with knee pain. On a regular day and under normal circumstances, this pain might be manageable or even barely noticed. But given the significance of the occasion, your anxiety and heightened attention may amplify your perception of pain significantly. In such situations, pain is interpreted in the brain not only as physical discomfort but also as a threat, thereby magnifying the overall pain experience.

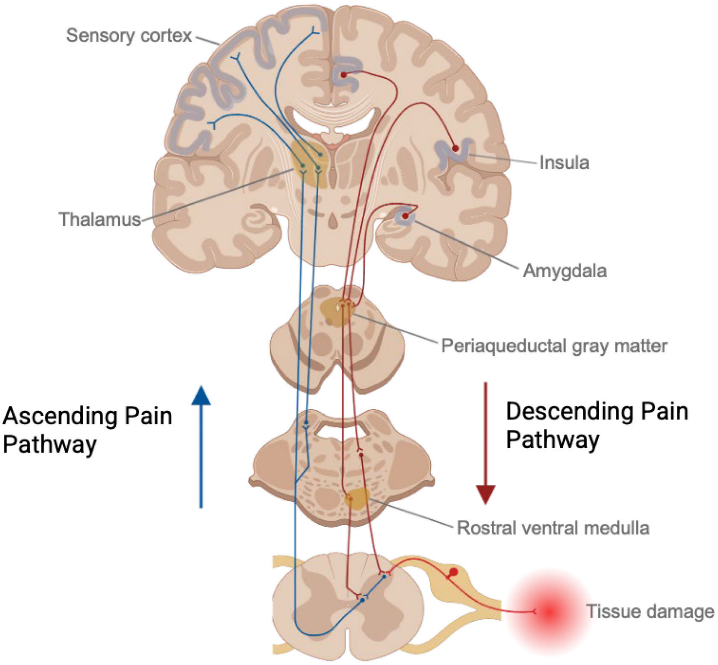

Figure 3. Ascending and descending pain pathways used to depict the transmission and modulation of nociceptive information in the nervous system.

But now picture another situation — you are fighting for your life. Despite injury, perhaps a sprained ankle or deep cut, you feel nothing. You keep running. Only later, when the threat is over, do you experience, or even notice, the pain. This reflects the body's built-in triage system — survival is prioritised. In such situations, the brain activates descending inhibition, releasing endogenous opioids to suppress pain so that escape and survival is possible.

When pain persists, this highly sophisticated physiological system may fail, to varying degrees. Pain transforms from being a protective signal into a persistent burden, no longer merely a messenger of danger, but now a source of dysfunction itself [86]. One of the systems that is most vulnerable to this type of transformation is the musculoskeletal system, whose primary role is to execute motor function. Motor function is fundamental to nearly every aspect of human life; breathing, eating, speaking, moving, and interacting with the world. This is essential not only for survival and daily life activities, but is also closely linked to long-term health and quality of life.

Motor Function

Motor function is not simply about movement per se, but an outcome of complex interactions between sensory input, motor planning, and muscular execution intertwined with continuous feedback [6; 97]. The musculoskeletal system functions through tightly regulated but still dynamic neural circuits that enable the coordination of muscles and muscle groups, with cerebellar contributions to timing and error correction, as well as stability, adaptability, and execution of movements [6; 85; 97]. Structures such as the motor cortex, basal ganglia, brainstem, and cerebellum work together to fine-tune and integrate these processes. These motor processes are not static: they are dynamically shaped by intention, context, experience, and sensory–motor feedback [1; 12; 92]. A clear example of this complex integration is jaw function [119]. Chewing, speech, and swallowing require exceptionally precise sensorimotor control and must be both finely tuned as well as powerful, often within the same movement sequence [59; 73; 119]. This control relies on comprehensive trigeminal sensory feedback from periodontal mechanoreceptors, oral mucosa, joint receptors, and jaw–muscle spindles, providing continuous updates to the nervous system on food texture, tooth load, and jaw position. These afferent signals are integrated with motor commands across brainstem circuits and higher motor networks, enabling rapid adjustment of bite force and movement trajectories through both feed-forward and feedback signalling [59; 111; 119].

This is particularly evident during chewing. Unlike movements that need to be consciously guided step by step, rhythmic chewing can continue even if attention is directed elsewhere. The central pattern generator (CPG) in the brainstem provides the basic rhythmic framework for this activity, while sensory feedback continuously adjusts motor output according to the mechanical properties of the food and the position of the jaw [59; 119]. If, during chewing, an unexpected hard object appears that may pose a threat to the teeth or oral tissues, sensory feedback can rapidly modify the motor output and engage higher order control mechanisms. Jaw function is therefore both highly automatic as well as continuously adaptable [59; 111].

Parafunction

When this finely tuned motor system functions well, the balance of load on the musculoskeletal structures is largely aligned with functional demands. However, motor activities are not always purely functional but may also be parafunctional.

Under certain conditions, such as stress, muscle activity may persist or increase without responding directly to an increased functional demand (Figure 4). Elevated stress levels can lead to increased muscle tension throughout the body [58; 60], including in small muscle groups such as those in the face [48]. A common example is involuntary eyelid twitching, i.e., myokymia, which, while not typically painful, illustrates how stress can activate muscles outside of conscious control [5; 11]. This type of subconscious muscle activity is especially relevant in the jaw motor system, which harbours stress-induced parafunctions such as teeth clenching and grinding; i.e., bruxism [16; 54].

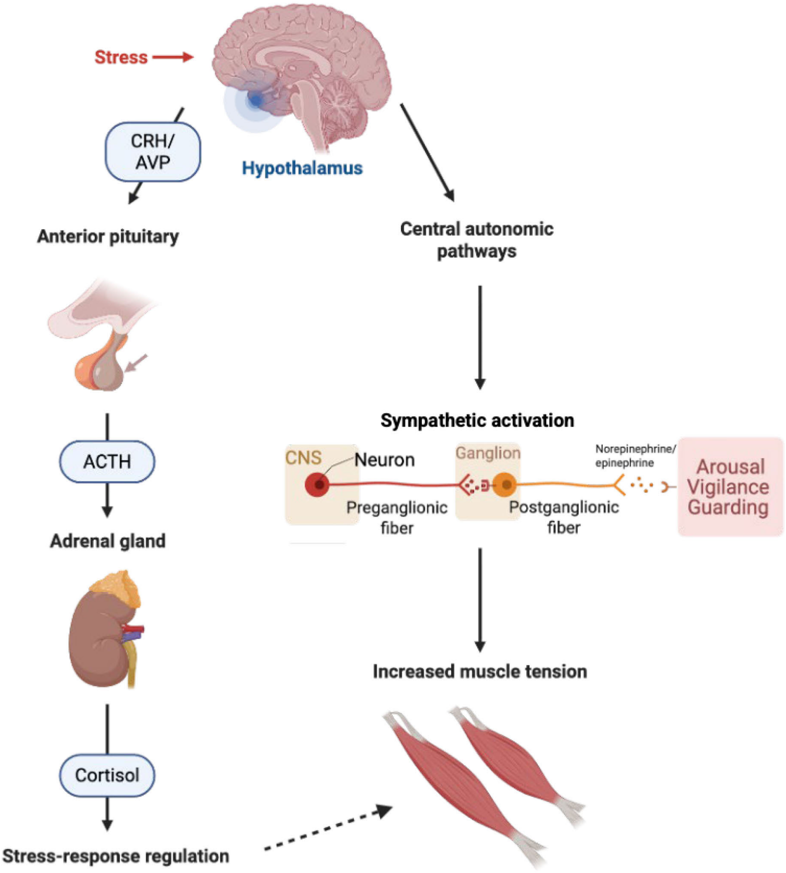

Figure 4. Stress-response pathways from the central nervous system (CNS) used to depict hypothalamic–pituitary–adrenal axis activation and sympathetic arousal regulation in the body involving release of corticotropin-releasing hormone (CRH), arginine vasopressin (AVP), and adrenocorticotropic hormone (ACTH).

Bruxism is considered a multifactorial behaviour situated at the intersection of motor control and emotional regulation, with possible consequences for neuroplasticity. It occurs in two forms depending on circadian rhythm: sleep bruxism, largely regulated by brainstem mechanisms and sleep-related micro-arousals, and awake bruxism, increasingly recognised as a behavioural manifestation of stress [4; 16; 50; 100; 114].

Awake bruxism is strongly linked to central stress systems, including the hypothalamic–pituitary–adrenal axis and sympathetic activation (Figure 4) [46]. Repeated or sustained stress can activate this axis, leading to cortisol release, sympathetic arousal, and increased vigilance. While this system is essential for short-term survival, chronic activation can lead to dysregulation [36]. In this context, awake bruxism can be viewed as a stress-related motor behaviour, but also deeply ingrained and centrally organised [55].

From Load to Overload

Parafunction does not automatically equal negative consequences. Behaviours such as bruxism may occur without necessarily causing any symptoms [117]. However, when the generated load becomes too frequent, too prolonged, or poorly tolerated by the musculoskeletal system, this balance can shift. When load exceeds the capacity for adaptation and recovery, parafunctional behaviour can result in overload of jaw muscles and joints. Bruxism may then contribute to local muscle ischemia and fatigue, stress on the temporomandibular joint, and ultimately pain and dysfunction [16].

Once pain develops it does not simply add to the problem — it becomes part of it. Pain can reduce the functional capacity of the musculoskeletal system, meaning that load which was previously tolerable may now exceed the system’s capacity. Overload triggers pain; pain reduces capacity; reduced capacity means that regular load becomes overload. What started as a stress-driven motor behaviour can thereby evolve into a self-sustaining parafunctional cycle.

Pain and Overload

When pain affects the musculoskeletal system, particularly when chronic, it does not merely overlay normal function; it reshapes it [39; 40]. One consistent finding in pain research is the redistribution of motor activity: a shift in how individual muscles and muscle groups are activated and coordinated during movement. Pain may lead to increased activity in some muscles and decreased activity in others, within or across muscle groups. These adjustments can not only reduce the load on the painful area, but can also change how mechanical load is distributed across the system, potentially generating new load patterns that over time can lead to overload elsewhere [38-40]. The redistributions can manifest as reduced, rigid, or guarded movements, or increased, unstable, and poorly coordinated movements. These changes tend to emerge more strongly in movements perceived as strenuous or threatening [108; 109]. Both these extremes carry risk: rigid movement can restrict function, while unstable movement may generate new sources of injury or strain [108].

Pain can alter motor behaviour by modifying movement patterns through feedback input and by influencing feed-forward motor planning at the cortical level [109]. In this way, chronic pain can influence not only movements, but also the motor system's ability to adapt, meaning that load which was previously tolerable may now transform into overload.

Initially, these motor adaptations are protective, aimed at minimising further harm. But if pain persists, they can become maladaptive. Movement strategies may outlast the original nociceptive input, sustained by fear-avoidance processes including kinesiophobia and central reorganisation, setting the stage for a pain–motor dysfunction cycle that is well-documented across the musculoskeletal system [98]. Stress and other psychosocial factors can compound this further, not only by creating parafunctional load but also by activating systems that lower the threshold at which input is perceived as painful, thereby driving central sensitisation [19; 72; 74]. Thus, physiology and psychology become entangled, each influencing and sustaining the other.

However, these parafunctional behaviours may go unnoticed, making them difficult for the individual to recognise and modify, while long-term stress may further contribute to heightened pain sensitivity and central sensitisation. This may be particularly relevant in the development or persistence of musculoskeletal overload and pain, including pain in the orofacial region.

Temporomandibular Disorders

If this pain–motor dysfunction cycle becomes ingrained in the jaw system, it may manifest clinically as temporomandibular disorders (TMDs), an umbrella term for pain and dysfunction in the masticatory muscles, temporomandibular joints, and related structures [32; 53]. TMDs are among the most common chronic musculoskeletal pain conditions [79; 96], and the clinical presentation reflects the full complexity of the cycle described above: local overload, altered motor behaviour, central sensitisation, and psychosocial amplification, often coexisting and reinforcing one another.

Because the jaw is in near-constant use for eating, speaking, and emotional expression, even small disruptions in motor function can accumulate into significant limitations in daily life [37]. TMD pain is frequently accompanied by reduced jaw opening capacity and kinesiophobia [35; 77]. In this way, TMD is not simply a condition of the jaw joint or muscle; it is a clinical expression of a broader musculoskeletal cycle in which pain reshapes movement, altered movement generates new load, and reduced capacity means that ordinary demands become overload. Parafunctional behaviour such as bruxism may both initiate and sustain this process, generating cumulative mechanical load while pain-related adaptations simultaneously reduce the system's ability to tolerate load over time.

Motor Training and Learning

In the management of musculoskeletal overload and pain, particularly within the biopsychosocial framework, descending inhibitory pathways are not only acknowledged but can also be targeted therapeutically [116]. Training interventions can induce a range of responses, including stimulation of low-threshold mechanoreceptors in the skin, joints, and muscles, including Aβ mediated cutaneous afferent input. Activation of afferent systems during training may not only support sensorimotor reintegration, but also modulate nociceptive processing, partly through segmental inhibitory mechanisms consistent with gate control theory [68], in which non-nociceptive Aβ input can inhibit transmission of nociceptive input from A-delta and C fibres, and partly through engagement of descending pain inhibitory pathways [24; 42; 52; 102]. In parallel, training may help modify maladaptive motor strategies, improve functional confidence, reduce kinesiophobia and pain-related hypervigilance, and enhance the capacity of the motor system to tolerate and recover from load. Through these interacting physiological, motor, and psychosocial mechanisms, training and exercise may help shift the nervous system from a facilitated toward a more inhibited and functionally adaptive pain state [8; 102].

Neuroplasticity

When movements are repeated, when sensory input changes, or when new demands are imposed by the environment, the response of neural circuits may adjust. Over time, these adjustments can result in more accurate, efficient, and stable motor output. In this sense, neuroplasticity is the biological basis for learning as well as for the continuous fine-tuning of motor behaviour [67; 91].

Within this framework, training becomes especially relevant. If pain and overload can promote maladaptive motor behaviour, training may provide a means for restoring adaptive sensorimotor responses. One relevant expression of this is training-induced neuroplasticity, i.e., the capacity of repeated sensorimotor activity to induce measurable changes in motor system responsiveness alongside changes in performance [62; 105]. This is particularly relevant in the context of chronic pain [80; 87], as pain has been associated with reduced excitability in motor cortex regions, altered intracortical inhibition, and impaired sensorimotor integration — changes that may compromise fine motor control, and delay movement onset [27; 43; 113]. This can provide a basis for evaluating how pain and overload-related behaviours relate to a baseline corticomotor state and to training-induced adaptation, and whether jaw training can modify both function and corticomotor excitability.

To study these neuroplastic changes in humans, advancements in the use of non-invasive neurophysiological tools have been essential. Transcranial Magnetic Stimulation (TMS) has become an important method for assessing cortical excitability, inhibition, and plasticity in vivo. By delivering brief magnetic pulses over the scalp, TMS can safely and painlessly stimulate targeted regions of the motor cortex. The evoked responses are then recorded with electromyography (EMG) from the corresponding muscle, making it possible to assess outcomes such as motor evoked potentials (MEPs), motor thresholds, stimulus–response curves, cortical silent periods, and paired-pulse indices of intracortical inhibition and facilitation.

RATIONALE FOR THE THESIS

Altered motor function is a common feature of musculoskeletal pain conditions. Because training is a central component of rehabilitation aimed to improve function, reduce pain, and support restoration of sensorimotor control, it is clinically important to understand how pain may influence training-related adaptation. However, knowledge about these relationships has largely been developed outside the jaw system, and it remains unclear to what extent current concepts are applicable to trigeminally innervated motor function.

The jaw motor system differs fundamentally from spinal motor systems through its trigeminal innervation, distinctive sensorimotor organisation, and frequent exposure to overload-related oral behaviours such as bruxism. This makes the jaw system a clinically relevant, but still insufficiently studied, model for understanding the interactions between pain, parafunction, and adaptive motor responses. Furthermore, parafunctional behaviours such as awake bruxism are difficult to quantify in daily life, as they are often intermittent, stress-related, and partly outside conscious awareness.

The rationale for this thesis was therefore to investigate these mechanisms in the jaw system by integrating evidence from existing knowledge, ecological real-world assessment of function and parafunction, as well as sensorimotor training and its relation to neuroplasticity in individuals with and without TMD pain.

AIMS

The overarching aim of this thesis was to examine how pain and parafunction interact with jaw function, muscle activity, training, and motor system plasticity.

Specific Aims

- To investigate the impact of acute and chronic pain on training-induced motor performance and neuroplasticity assessed by TMS (Study I).

- To investigate the relationship between self-reported awake bruxism using ecological momentary assessment (EMA) and jaw muscle activity registered by surface electromyography (sEMG), and differences between individuals with and without TMD pain (Study II).

- To investigate whether a jaw exercise programme can induce changes in masseter corticomotor excitability, assessed with TMS, and in jaw sensorimotor performance, and whether these responses are influenced by TMD pain and overload-related jaw behaviour (Study III).

MATERIAL AND METHODS

	Study I Systematic review	**Study II** Cross-sectional observational	**Study III** Case-control intervention
Sample	Included 17 studies: - 7 on experimentally induced acute pain in healthy - 10 in chronic pain conditions (low back pain, neck pain, hand arthritis, fibromyalgia, headache etc). - 258 pain participants, 248 controls.	70 adults (38♀, 32♂) Mean age 33 years (SD 6) - 48 participants w/o TMD pain - 22 cases with TMD pain Temporomandibular disorder (TMD) pain classified using 3Q/TMD and DC/TMD Symptom Questionnaire.	29 adults (22♀, 7♂) Mean age 25 years (SD 4) - 19 controls - 10 cases with TMD myalgia TMD confirmed clinically using brief DC/TMD after screening with DC/TMD Symptom Questionnaire.
Methods	Systematic review (PRISMA; PROSPERO). Search: PubMed, Web of Science, Cochrane until December 13, 2019. Included articles on short-term motor training in pain vs pain-free conditions, reporting Transcranial Magnetic Stimulation (TMS) outcomes (MEP amplitude, map measures, intracortical inhibition and facilitation).	Cross-sectional real-world design. 3-day EMA (≥12 prompts/day; five jaw states). Day 1: portable sEMG of masseter. Functional activities (eating/talking) excluded. Overload defined as activity >20% maximum voluntary contraction; duration and intensity/AUC. Baseline data included maximum jaw opening, PSS-10, and Numerical Rating Scale.	7-day jaw exercise programme: - jaw stretching (3/day) - thickness recognition (3mm-30mm blocks, once a day). Assessments at baseline, pre-training (after supervised introduction), and post-training. Outcomes: jaw opening replication and recognition; TMS stimulus–response curves with masseter (and FDI control) MEP.
Data analysis	Risk of bias assessed using a modified Newcastle-Ottawa Scale; TMS methodological quality evaluated with the Chipchase checklist. Narrative synthesis of the directions of effects.	Group comparisons: χ^2 and parametric/non-parametric tests. Spearman's correlation between EMA awake bruxism and EMG overload (duration and AUC). Stratified analyses by TMD status (and sex); within-group day effects: Friedman and Wilcoxon.	Baseline comparisons: Mann-Whitney U/Fishers exact tet. Behaviour: thickness-level tests and clustered models (Ratio/Odds ratio; Group × Time). TMS: within-group paired tests (Bonferroni); between-group change scores (Welch).
Ethical	Not applicable.	Approved by the Swedish Ethical Review Authority (Dnr 2022-06841-01/2024-05598-01). All participants provided written informed consent. Followed the Declaration of Helsinki.	Approved by the Danish Ethical Review Authority (case no. 1-10-72-141-24;). All participants provided written informed consent. Followed the Declaration of Helsinki.

AUC, Area Under Curve; DC/TMD, Diagnostic Criteria for Temporomandibular Disorders; EMA, Ecological Momentary Assessment; FDI, First Dorsal Interosseous; MEP, Motor Evoked Potential; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; PROSPERO, International Prospective Register of Systematic Reviews; PSS-10, Perceived Stress Scale-10; SD, Standard Deviation; sEMG, Surface Electromyography; 3Q/TMD, Three-Question Screening Tool for TMD; χ^2, Chi-Square.

STUDY I

Protocol Registration and Eligibility Criteria

This review followed a protocol pre-registered in the PROSPERO database (registration number: CRD42020168487) and adhered to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [71].

Inclusion and exclusion criteria were structured according to the PICO framework (Population, Intervention, Comparison, Outcome).

Studies were considered eligible if they met the following criteria:

- **Population**: Human participants with chronic pain conditions or experimentally induced acute pain.
- **Intervention**: Short-duration motor training performed during pain, defined as motor task training paradigms (voluntary active training) rather than long-term or professional training.
- **Comparison**: Pain-free control group performing equivalent training.
- **Outcome**:
    - **Primary** Assessment of neuroplasticity via TMS, targeting motor cortical regions corresponding to the trained muscles.
    - **Secondary** Measures related to motor behaviour and functional performance.

Studies were excluded if they:

- Included individuals with neurological or psychiatric disorders.
- Did not involve active motor training.
- Focused on long-term or professional training (e.g., athletes/musicians).
- Combined training with other therapeutic interventions.

Literature Search

A comprehensive electronic search was performed in PubMed, Web of Science, and the Cochrane Library, covering literature up to December 13, 2019. The search strategy, initially developed for PubMed using a combination of MeSH terms and free-text keywords, was created in collaboration with an experienced librarian and adapted for the other databases. The search strategy for PubMed is provided in Table 1. The objective was to identify studies evaluating the influence of acute or chronic pain on TMS-assessed training-induced neuroplasticity. In addition to the electronic database searches, reference lists of included articles were manually screened for relevant studies. Grey literature, editorial pieces, letters, and conference abstracts were excluded.

Table 1. PubMed search strategy used to identify studies on pain, motor training, and TMS-assessed neuroplasticity.

Search	Search Terms
1. Plasticity	("Sensorimotor Cortex"[Mesh] OR corticomotor plasticity[tiab] OR corticomotor control[tiab] OR corticomotor pathway*[tiab] OR sensorimotor cortex[tiab] OR neuroplasticity[tiab] OR "Neuronal Plasticity"[Mesh] OR cortical plasticity[tiab] OR cortical neuroplasticity[tiab] OR brain plasticity[tiab] OR Neuronal Plasticity[tiab])
2. TMS	(TMS[tiab] OR Transcranial Magnetic Stimulation[tiab] OR "Transcranial Magnetic Stimulation"[Mesh])
3. Exercise	(exercise[Mesh] OR rehabilitation[Mesh] OR rehabilitat*[tiab] OR exercis*[tiab] OR train*[tiab] OR physical therapy modalities[Mesh] OR physical therapists[Mesh] OR physiotherap*[tiab] OR physical therapy specialty[Mesh] OR kinesio*[tiab] OR learning[tiab] OR (physical[tiab] AND therap*[tiab]))
4. Pain	(Pain OR nociception)
5.Results	#1 AND #2 AND #3 AND #4

Study Selection

Titles and abstracts retrieved from the searches were independently reviewed by two authors (NS, BHH). Any study that was deemed potentially eligible by at least one reviewer was included for full-text evaluation. Full texts were then independently assessed by two authors (NS, BHH) against the predefined eligibility criteria. Disagreements regarding eligibility were resolved through discussion, with a third reviewer (MK) consulted when necessary.

Data Extraction

Two authors (NS, MK) independently extracted data from the included studies, and a third author (BHH) verified the extracted information. The following data were extracted: first author, publication year, study objectives, sample characteristics, research setting, study design, methodology, outcomes, and main findings.

Quality and Risk of Bias Assessment

The risk of bias was assessed using the Newcastle–Ottawa Scale (NOS) for case–control studies. This tool evaluates selection, comparability, and exposure using a star-based scoring system [106]. The methodological quality of the TMS procedures was evaluated using the TMS Quality Checklist [17]. This checklist covers participant characteristics, TMS methodology, and analysis-related aspects. Two authors (NS, YC) independently performed the quality assessments, resolving any disagreements through discussion, or involving a third reviewer (BHH) when necessary.

STUDY II

Study Design and Study Population

This observational, cross-sectional study combined EMA of jaw muscle behaviour with simultaneous portable sEMG registration in real-world settings. Participants were included if they were aged 18–65 years, used a smartphone daily, and were fluent in Swedish. Exclusion criteria included excessive facial hair or skin conditions interfering with electrode placement, or inability to wear the EMG device.

Sample size was estimated for a population prevalence of awake bruxism at 25.9% (95% CI: 22.2–29.9) [107], 95% confidence, and a 10% margin of error, resulting in a sample size of 70 participants.

Baseline Assessment

Participants completed a three-item TMD screening (3Q/TMD) and the Symptom Questionnaire for the Diagnostic Criteria for TMD (DC/TMD) [57; 94]. TMD pain was defined as facial pain (jaw, temple, ear, or in front of the ear) in the past 30 days, occurring at least weekly and aggravated by jaw function (e.g., chewing or talking). Participants also completed the Perceived Stress Scale (PSS-10) [20], rated average facial pain intensity using the Numeric Rating Scale (NRS, 0–10), and had maximal jaw opening measured before and after attachment of the sEMG device (Figure 5).

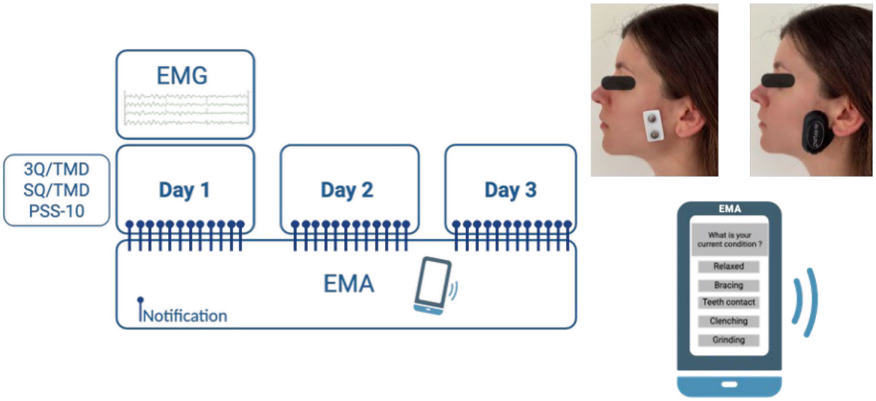

Figure 5. Study protocol combining electromyography (EMG) Day 1 and Ecological Momentary Assessment (EMA) Days 1–3 after baseline assessment of Temporomandibular disorders (TMD) with 3Q/TMD (Three-item TMD screening) and SQ/TMD (Symptom Questionnaire for TMD); and assessment of stress with PSS-10 (Perceived Stress Scale-10).

EMA and EMG Protocols

Participants were instructed to recognise five jaw muscle states related to the absence (relaxed) or presence of awake bruxism behaviour: light teeth contact; clenching; grinding; and mandible bracing. They used a smartphone-based EMA application (BruxApp, WMR srl, Italy) for three consecutive days, responding in real-time to at least 12 random prompts per day by selecting one of the five jaw muscle states.

On Day 1, the jaw muscle activity was simultaneously recorded with a portable sEMG device (dia-BRUXO, Biotech-Novations, Italy) attached over the left masseter muscle with Ag/AgCl electrodes (22 mm fixed inter-electrode distance). The signal was amplified, bandpass filtered (110–550 Hz), and root mean square integrated. Normalisation was performed for each participant by performing five seconds of maximum voluntary contraction (MVC) at baseline. Data were exported and converted to mean µV per second.

In addition to the EMA reporting, participants documented functional activities such as eating or prolonged talking in a diary with time stamps. These time periods were visually identified and removed to ensure that only non-functional muscle activity was included in the analysis.

Muscle overload, defined as EMG activity > 20% of MVC, was quantified as: i) duration (seconds); and ii) intensity, as area under the curve (AUC) (µV*s), reflecting both magnitude and duration.

Ethics

The study was approved by the Swedish Ethical Review Authority (Dnr 2022-06841-01/2024-05598-01). All participants provided written informed consent. All methods were performed in accordance with relevant guidelines and regulations.

STUDY III

Study Design and Study Population

In this case–control study with repeated assessments, participants were recruited via public advertisements and Aarhus University channels, including mailing lists, student platforms, and posted notices. Participants were screened for standard TMS contraindications and excluded for factors such as metal implants in the head/face, epilepsy history, pacemaker/medical pumps, or pregnancy, as well as regular analgesic use and relevant psychiatric/cognitive conditions.

The study included 19 pain-free controls and 10 individuals with TMD myalgia. All participants completed the TMD symptom questionnaire, and individuals reporting TMD pain underwent a clinical examination to confirm a TMD myalgia diagnosis according to the brief DC/TMD [31]. At baseline, participants also completed questionnaires on coping (BRCS-4) [103], perceived stress (PSS-10) [20], jaw function (JFLS-8) [82], and oral behaviours (OBC-21) [45]. JFLS-8 and OBC-21 were repeated at follow-up.

Intervention Exercise Program

Participants performed a seven-day exercise programme with two jaw sensorimotor tasks:

- Jaw stretching: 5 repetitions of maximal jaw opening, holding maximal opening 20 s each repetition; performed 3 times/day with at least four hours between sessions.
- Thickness recognition training performed once a day: nine rubber blocks (3, 4, 5, 10, 12, 15, 20, 25, and 30 mm) each placed between the central incisors for 10 seconds, progressing from smallest to largest, repeating the full sequence 3 times/session.

Adherence was assessed by participants completing a daily training diary; attendance at ≥70% (20 of 28) sessions was defined as compliance.

Jaw Sensorimotor Outcomes

Outcomes were assessed at three time points: (1) baseline; (2) pre-training, immediately after a supervised introductory training session; and (3) post-training at the seven-day follow-up (Figure 6).

At follow-up, two jaw sensorimotor tasks were performed while seated upright in a dental chair:

- Jaw opening replication: with eyes closed, participants reproduced target jaw openings corresponding to the test thicknesses, presented in random order with four repetitions per thickness. Jaw opening was measured manually using a metal ruler.
- Thickness identification (recognition): with eyes closed, participants identified block thicknesses presented in random order, with four repetitions per thickness.

Maximum jaw opening capacity, with and without pain, was measured at baseline and post-training.

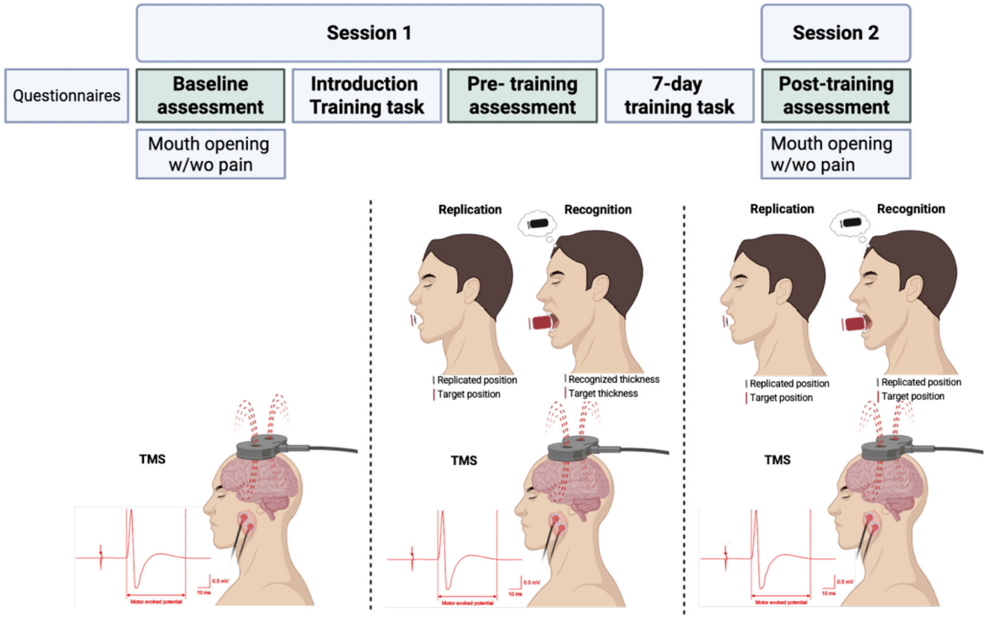

Figure 6. Experimental protocol across two sessions, including baseline assessment, training task, pre-training assessment, a seven-day jaw training period, and post-training assessment.

Transcranial Magnetic Stimulation (corticomotor excitability)

Single-pulse TMS was delivered using a Magstim 200 stimulator with a 5cm angled figure-of-eight coil. A fitted cap was positioned using International 10–20 landmarks, and the coil was oriented approximately 45° to the sagittal plane, generating a posterior–anterior induced current. Motor-evoked potentials (MEPs) were recorded from the right masseter (target muscle) and right first dorsal interosseous, (FDI, control muscle), while stimulating the left motor cortex. For each session, the optimal scalp location (“hotspot”) was identified as the site eliciting the largest and most consistent MEPs at the lowest stimulus intensity.

Active motor threshold (aMT) was defined as the lowest intensity evoking at least 4/10 discernible MEPs of at least 30μV. Expected latency ranges were used as plausibility checks for both masseter and FDI responses. Stimulus–response curves were obtained at 90%, 100%, 120%, 140%, and 160% of aMT, with 10 MEPs per intensity and an inter-stimulus interval of 8–12 seconds. MEP amplitude was quantified as peak-to-peak amplitude, defined as the voltage difference between the maximum positive and negative EMG deflections.

Ethics

Approved by De Videnskabsetiske Komitéer for Region Midtjylland (Central Denmark Region), case no. 1-10-72-141-24; written and oral informed consent obtained; conducted per Declaration of Helsinki.

STATISTICAL ANALYSIS

Study I

A narrative synthesis of the extracted data was performed. A meta-analysis was planned if TMS outcome variables and assessment time points were sufficiently homogeneous. In that case, a random-effects model would be used, and heterogeneity quantified using the I^2 statistic.

Study II

All variables were summarised using descriptive statistics. Continuous variables were tested for normality using the Shapiro–Wilk test, with independent samples t-tests or Mann–Whitney U tests as appropriate; categorical variables were compared with chi-square tests. EMA data were expressed as proportions and treated as continuous variables. Associations between EMA-reported awake bruxism, stress, and EMG overload were assessed with Spearman's rank correlation. Within-subject changes in EMA across days were tested with the Friedman and Wilcoxon signed-rank tests. All analyses were performed in Prism (v10.2.0, GraphPad), with statistical significance set at $p<0.05$.

Study III

Baseline group comparisons were performed using Mann–Whitney U tests for continuous variables and Fisher's exact test for sex. Replication performance was quantified as absolute error (mm) and percentage. Thickness-specific between-group comparisons were performed using Mann–Whitney U tests, and within-group pre–post comparisons using Wilcoxon signed-rank tests. To estimate overall training effects while accounting for repeated measurements across thicknesses, replication was also analysed using a clustered repeated-measures model with participant-level clustering, including Group, Time, Group × Time, and target thickness. Effects were reported as ratios with 95% confidence intervals (CI). Recognition performance was summarised as percent correct for each target thickness and time point. Thickness-specific between-group comparisons were performed using Mann–Whitney U tests, within-group pre–post comparisons using Wilcoxon signed-rank tests, and between-group differences in training response using Mann–Whitney U tests on change scores. To assess learning across all trials, each trial was coded as correct/incorrect and analysed using a clustered logistic model including Group, Time, target thickness, and Group × Time. Effects were reported as odds ratios with 95% confidence intervals.

Masseter MEP amplitude was analysed using a multivariable repeated-measures model including Group, Time, stimulation intensity (90%, 100%, 120%, 140%, 160% aMT), and their interaction terms, accounting for repeated observations within participants. When significant effects or interactions were observed, post hoc within-group paired t-test comparisons between time points were performed separately for each intensity with corrections for multiple testing. The FDI control muscle was analysed separately using a multivariable repeated-measures analysis across time. MEP latency was analysed using corresponding repeated-measures models for both the masseter and FDI muscles.

Spearman’s rank correlations were calculated between i) awake/sleep bruxism scores and active motor threshold; ii) bruxism scores and change in masseter MEP amplitude; and iii) change in masseter MEP amplitude and behavioural improvement in jaw-position replication/thickness recognition. For analyses involving MEP change, the mean change in masseter MEP amplitude from baseline to post-training across 100%–160% MSO was used. Statistical significance was set at $p < 0.05$.

RESULTS

STUDY I

The literature search identified 231 records. After removing duplicates, and screening of abstracts, 24 articles were assessed in full text for eligibility. Seven articles were excluded, and 17 studies published between 2007 and 2018 were included; 7 studies of experimentally induced acute pain [13; 25; 28; 29; 43; 66; 89] and 10 studies in chronic pain populations [3; 41; 63; 64; 69; 84; 88; 95; 113; 115] (Figure 7). In total, 258 participants with pain and 248 healthy controls were included.

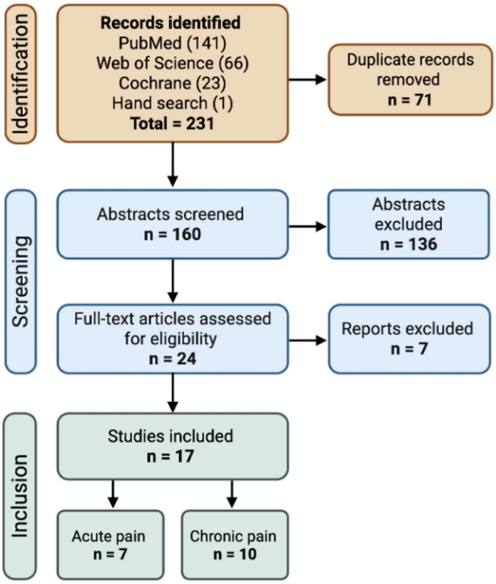

Figure 7. PRISMA flow chart showing number of included and excluded studies.

Among the seven acute pain studies, six reported attenuated or altered training-induced corticomotor plasticity in the pain condition compared with pain-free controls, whereas one study reported no such difference. Among the 10 chronic pain studies, five reported attenuated or altered training-induced corticomotor plasticity in the pain group compared with controls, whereas five reported no clear difference between groups (Table 2). In respect of functional outcomes, one acute and one chronic pain study reported reduced gain in motor performance in the pain condition compared with controls.

Table 2. Transcranial Magnetic Stimulation (TMS) evoked neuroplastic responses for the pain and control groups in the included studies on acute experimental pain (n = 7) and chronic pain conditions (n = 10).

First author, year	Pain group	Control group	Effect on neuroplasticity
Acute experimental pain studies			
Boudreau 2007	All TMS outcomes →	MEP ↑; rMT ↓	Impeded
Dancey 2019	All TMS outcomes →	IO slope ↑	Impeded
De Martino 2018a	Map volume + active sites ↓	Map volume + active sites →	Impeded
De Martino 2018b	Map volume: ↑ day 4; ↓ day 6	Map volume: ↑ day 4;↑ day 6	Impeded
Ingham 2011	Local pain: Muscle response ↓ Remote pain →	Muscle response ↓	No effect
Mavromatis 2017	MEP →; SICI →	MEP ↑↓; SICI →	Impeded
Rittig-Rasmussen 2014b	MEP ↓	MEP ↑	Impeded
Chronic pain studies			
Baarbe 2018	CBI remained inhibited	CBI disinhibited	Impeded
Hoeger Bement 2014	MEP ↓	MEP →	Impeded
Massé-Alarie 2016	aMT ↓; MEP ↓	aMT ↓; MEP →	Modified
Massé-Alarie 2017b	All TMS outcomes →	All TMS outcomes →	No effect
Mendonca 2016	All TMS outcomes →	All TMS outcomes →	No effect
Parker 2017	Post-training: twitch ↓	Post-training: twitch ↓	Not impeded
Rittig-Rasmussen 2014a	Neck pain: MEP ↓; Knee pain: MEP ↑	MEP →	Impeded (locally)
Schwenkreis 2011	MEP →; ICI ↑	MEP ↓;ICI ↓	Impeded
Tsao 2010	CoG shift; Map volume →	CoG → Map volume →	Not impeded
Vallence 2013	MEP →; rMT →	MEP ↑; rMT →	Impeded

↑ increase post-training ↓ decrease post-training → no significant change. MEP, Motor Evoked Potential; rMT, Resting Motor Threshold; AMT, Active Motor Threshold; IO, Input-Output; CBI, Cerebellar Inhibition; CoG, Centre of Gravity; ICI, Intracortical Inhibition; SICI, Short-Interval Intracortical Inhibition; SICF, Short-Interval Intracortical Facilitation.

The most common motor training involved hand or finger tasks (n = 6), and only one study investigated a cranially innervated motor system. This study evaluated a tongue-protrusion motor task during capsaicin-induced tongue pain, [13] and reported reduced improvement in task performance and reduced corticomotor plasticity in the pain condition compared with placebo.

STUDY II

EMA-reported awake bruxism on Day 1 was positively correlated with EMG overload duration (r = 0.62, p <0.001) and with overload intensity measured as AUC (r = 0.36, p = 0.002). When stratified by TMD pain status, the positive correlation between awake bruxism and overload duration was significant in both groups. For overload intensity (AUC), the correlation was significant in the TMD pain group but not in the No TMD pain group (Figure 8).

Participants with TMD pain had longer EMG overload duration than participants without pain (21 vs 15 min; p <0.001). They also reported higher awake bruxism activity on Day 1 (23% vs 13%; p <0.001) and across Days 1–3 (22% vs 11%; p <0.001), as well as higher PSS-10 scores (p <0.001). Jaw opening capacity and MVC were lower in the TMD pain group than in the No TMD pain group (both p <0.001).

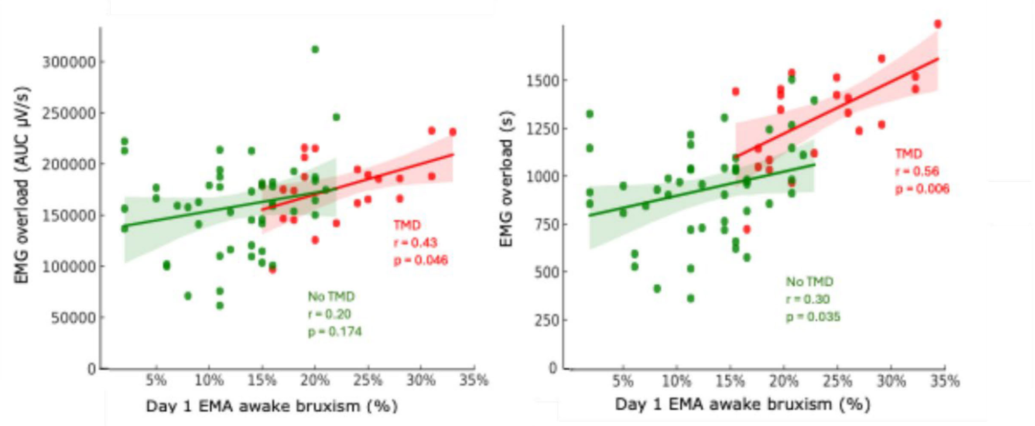

Figure 8. Associations (Spearman's correlation) between Ecological Momentary Assessment (EMA) of awake bruxism on Day 1 and surface Electromyography (EMG) of muscle overload assessed by area under curve (AUC) stratified by Temporomandibular disorder (TMD) pain status.

EMG overload duration by MVC intensity range differed between groups; the TMD pain group spent significantly more time in the 20%–39% MVC ranges, and less time in the 60%–79% MVC ranges. No significant group differences were reported for the other MVC ranges (Table 3). A schematic illustration of this is shown in Figure 9.

There was a significant day-to-day variation in awake bruxism activity across the three EMA days in the overall sample ($p = 0.001$) and in the group without pain ($p < 0.001$), but not in the TMD pain group ($p = 0.097$).

Table 3. EMG overload presented as duration (minutes/seconds) and intensity expressed as area under curve (AUC) together with duration for different intensity ranges for individuals with and without Temporomandibular disorder (TMD) pain.

Variable	**No TMD pain** (n = 48)	**TMD pain** (n = 22)	**p-value**
Duration, minutes (SD)	15 (4)	21 (4)	**<0.001[1]**
Intensity µV×min -AUC (SD)	2692.7 (774.5)	3018.3 (551.1)	0.084[1]
Duration by % maximum voluntary contraction (MVC) intensity range (s)			
20%–29%	197.7	438.9	**<0.001[1]**
30%–39%	211.0	340.5	**<0.001[1]**
40%–49%	197.7	226.3	0.021[1]
50%–59%	135.7	138.6	0.717[1]
60%–69%	90.4	76.2	**0.005[1]**
70%–79%	53.8	37.9	**<0.001[1]**
80%–89%	5.5	3.8	0.039[2]
90%–100%	5.1	3.4	0.087[2]

[1]Independent samples t-test, [2]Mann–Whitney U test was applied to each row based on the Shapiro–Wilk normality check. p-values adjusted for multiple comparisons using Bonferroni correction ($\alpha = 0.00625$). Significant p-values are in bold.

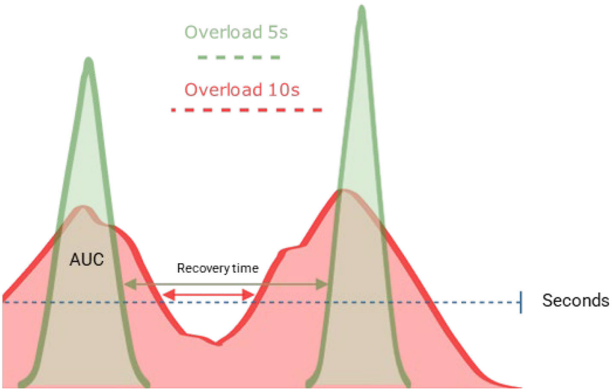

Figure 9. Schematic illustration of electromyography (EMG) activity as percentage of maximum voluntary contraction (MVC) displayed as area under curve (AUC) in individuals with (red) and without (green) pain. Note that despite group differences in duration of overload (≥20% MVC, 5s vs. 10s) both groups exhibit comparable AUC overload values.

STUDY III

There were no significant baseline differences between individuals with TMD pain and pain-free controls in age, sex distribution, or maximal jaw opening. The pain group reported more jaw functional limitations, whereas no significant differences were found for the remaining questionnaire measures.

In the jaw opening replication task, the TMD pain group showed larger errors than controls before training at 10mm–12mm and 30mm, and after training across 10mm–30mm. Both groups improved from pre- to post-training, mainly at the larger target thicknesses, while controls also improved at the smallest targets (3mm–4mm). In the repeated-measures model, absolute replication error decreased significantly in controls (post vs pre ratio = 0.59; $p < 0.001$) (Figure 10A), whereas improvement was smaller in the TMD pain group (Group × Time ratio = 1.25; $p = 0.002$).

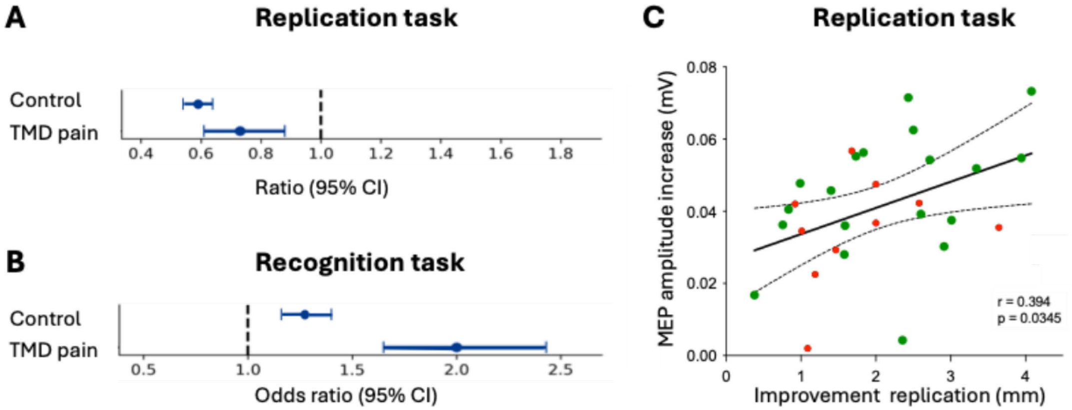

Figure 10. Forest plots of the repeated-measures analyses of behavioural outcomes after the seven-day jaw training programme showing changes in A) jaw opening replication error (ratios with 95% confidence intervals); and B) thickness recognition accuracy (odds ratios with 95% confidence intervals). The dashed vertical lines indicate no change. Values to the left of 1 in the replication task indicate reduced error after training, whereas values to the right of 1 in the recognition task indicate improved correct identification. The scatter plot C) illustrates the relationship between improvement in the replication task and increase in masseter motor evoked potential (MEP) amplitude from baseline to post-training across 100%–160% MSO for controls (green) and participants with TMD pain (red). The fitted line indicates the overall association for all participants.

In the thickness recognition task, there were no significant group differences before training. Both groups improved with training, with significant gains at 3mm in controls and at 3mm – 5mm in the TMD pain group. At 5mm, the improvement was significantly greater in the TMD group than in controls. In the repeated-measures model, recognition accuracy improved in both groups, with a larger improvement in the TMD group (Group × Time OR = 1.57; $p < 0.001$) than in controls (OR = 1.27; $p < 0.001$) (Figure 10B).

Masseter MEP amplitudes increased over time in both groups, but with different patterns across stimulation intensities (Figure 11). The repeated-measures model showed significant effects of time and intensity, as well as significant Time × Intensity and Group × Time × Intensity interactions ($p = 0.013$), indicating that the temporal pattern of corticomotor modulation across the stimulus–response curve differed between groups. For masseter MEP latency, there was no significant main effect of time or TMD status, but there was a significant effect of intensity and a significant Group × Time × Intensity interaction ($p = 0.023$). No significant time effect was observed for amplitude or latency in the FDI control muscle ($p = 0.521$).

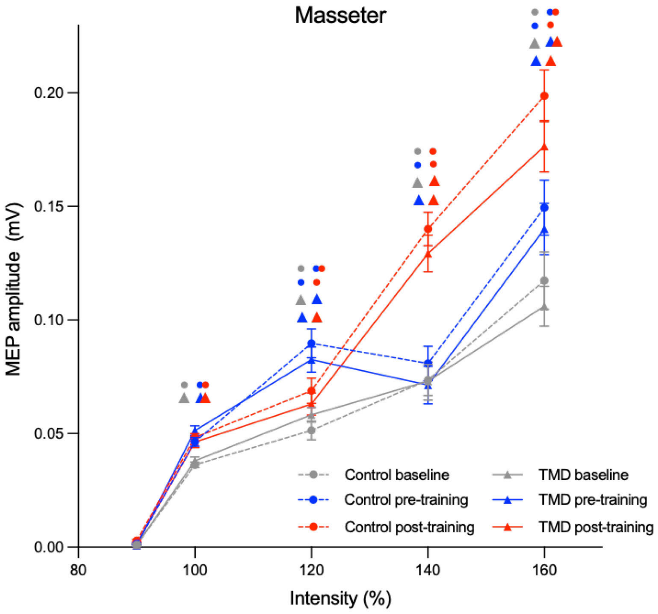

Figure 11. Stimulus-response curves showing masseter motor evoked potential (MEP) amplitudes at baseline, pre-training, and post-training across stimulation intensities (100%–160% active motor threshold, aMT) in controls and participants with TMD pain. Error bars indicate standard error of the mean. The figure illustrates corticomotor excitability and response patterns across the stimulus-response curve.

Improvement in jaw-position replication was positively correlated with the average increase in masseter MEP amplitude from baseline to post-training across 100–160% MSO (Figure 10C), whereas no significant correlation was found between MEP amplitude change and improvement in recognition accuracy. Both sleep and awake bruxism scores were positively correlated with active motor threshold and negatively correlated with the change in masseter MEP amplitude from pre- to post-training (Figure 12).

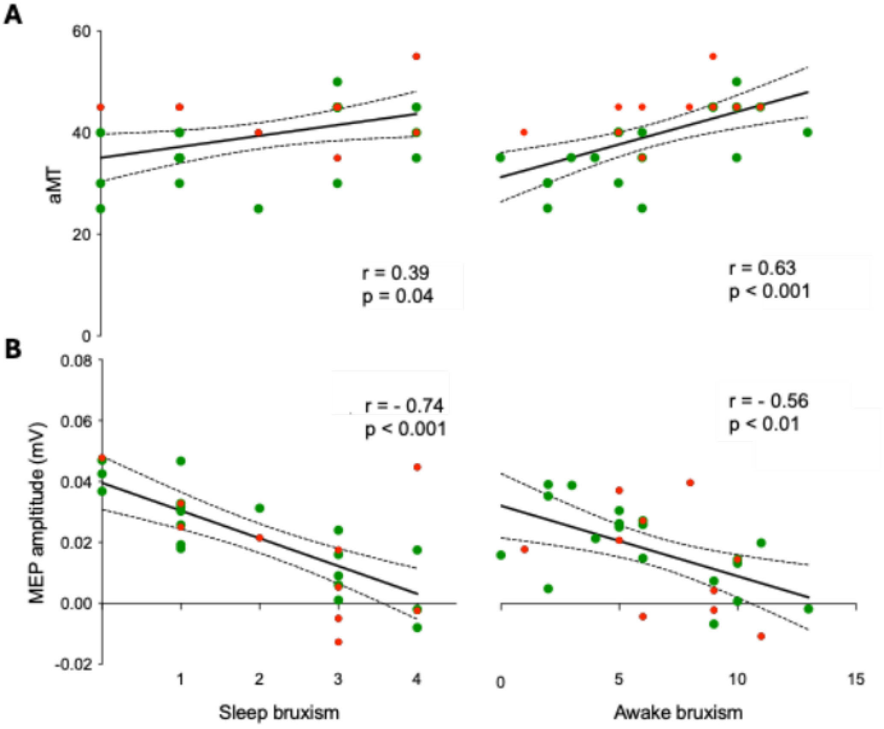

Figure 12. Scatter plots showing the associations (Spearman's correlation) between self-reported sleep and awake bruxism and A) active motor threshold (aMT); and B) change in masseter motor evoked potential (MEP) amplitude from pre- to post-training for controls (green) and participants with TMD pain (red).

DISCUSSION

The overarching aim of this thesis was to examine how pain and parafunction interact with jaw function, muscle activity, training, and motor system plasticity. First, the evidence base for pain-related modulation of training-induced neuroplasticity assessed with TMS was synthesised (Study I). Second, an ecological approach was used to evaluate jaw behaviour and muscle activity by combining EMA of awake bruxism with portable sEMG (Study II). Third, we tested whether a jaw training programme can affect jaw sensorimotor performance and corticomotor excitability, and whether pain and overload-related parafunction influence this training response (Study III). Taken together, the findings support that pain may alter training-related neuroplasticity; that awake bruxism relates to cumulative muscle load in daily life; and that training can improve jaw sensorimotor performance with accompanying changes in motor system responsiveness, within a framework where pain and overload may shape capacity for adaptation.

Function, Parafunction and Pain

Motor systems and behaviour can be modulated not only by pain, but also by other sensory and mechanical input [7; 47; 65], such as overload [9]. It is therefore relevant to consider whether parafunctional behaviours, such as bruxism, can influence the functional state of the jaw motor system. Awake bruxism is common in the general population, with a higher prevalence in individuals with orofacial pain [107]. However, as such parafunctional behaviours are often brief, intermittent, and partly outside awareness, they can be difficult to quantify using retrospective questionnaires or clinic-based observations. In Study II, this challenge was addressed by combining EMA, which captures behaviour in real time and in a natural environment, with simultaneous portable sEMG. This approach linked self-reported awake bruxism to registered masseter muscle activity to provide an ecologically valid way of quantifying behaviour and at the same time evaluating its relationship to physiological load.

Key findings emerged that can improve our understanding of the relationship between parafunctional behaviour, overload and pain. First, self-reported parafunctional behaviour by EMA aligned with registered muscle activity by sEMG, indicating that real-time self-reporting can capture behaviourally meaningful jaw muscle activity. Second, TMD pain was associated with a distinct load phenotype characterised by sustained low-intensity activity over longer periods. In contrast, pain-free individuals reported higher overload intensity but with shorter durations. This pattern is clinically relevant as sustained muscle activity over longer periods will reduce recovery time for the musculoskeletal system. In this context, consequences of overload may be driven less by short high-intensity contractions and more by the cumulative duration of low-level activity.

Participants with TMD pain reported substantially more perceived stress, and in both groups, stress was associated with AUC, indicating a relationship with the overall overload burden. This is in line with studies suggesting that perceived stress can be associated with increased muscle tension and sustained muscle activity in the neck/shoulder region, as well as with headache-related muscle tenderness and altered muscle properties [2; 44; 83; 104].

The finding that the pain-free group, but not the pain group, showed a reduction in awake bruxism across the EMA days, suggests that self-monitoring increases awareness and modifies behaviour in pain-free individuals, but that for individuals with TMD pain, overload-related jaw behaviour may be a manifestation of a more rigid or “overtrained” state, in which repetitive behaviours such as bruxism are less consciously regulated [9; 10].

Capacity and Overload

Overload is not determined by load alone, but also by the relationship between load and capacity; i.e., the system’s ability to tolerate and recover from that load. Capacity is dynamic and can be reduced by pain-related motor adaptations, such as guarding, reduced range of movement, and altered muscle coordination, as well as by psychosocial factors. The lower MVC in the TMD pain group compared to the pain-free group may reflect such reduced capacity, meaning that similar load can generate proportionally greater demand on the musculoskeletal system. From this perspective, the sustained low-intensity activity pattern observed in TMD pain may be clinically relevant not only because it increases cumulative load, but because it occurs in a context where capacity may already be reduced. Thus, in a clinical setting, a patient with sustained low-level jaw muscle overload, elevated stress, and reduced capacity, particularly in the presence of ongoing pain, would enter a training programme with a jaw motor system already operating under constraint. The capacity for training-induced corticomotor plasticity may therefore be established before the first session begins.

Pain and Training-induced Neuroplasticity

Acute and chronic pain conditions

Study I showed that the presence of pain during motor training can disrupt training-induced neuroplastic response. This was particularly evident in acute pain conditions, whereas the studies in chronic pain conditions showed more variability. One explanation for this could be that acute pain serves a biologically protective function, prioritising tissue protection over motor training [40]. In this framework, suppression of training-related plasticity may represent an adaptive response, as the nervous system is, in a sense, actively suppressing motor adaptation in favour of protection [33]. In line with this, neuroimaging studies of acute orofacial pain have shown a transient increase in primary motor cortex activity during muscle pain, followed by a more prolonged decrease in M1 signal outlasting the period of perceived pain [75]. This suggests that acute pain initially evoke protective motor responses before shifting the motor system towards limitation of movement. Chronic pain, however, may have lost this protective role. Without the same inhibitory mechanisms, the motor system may retain its capacity to adapt to training, which could explain some of the variability seen in the chronic pain studies. This variability may also reflect heterogeneity across chronic pain conditions as different central mechanisms may be involved in different conditions. In the trigeminal region, thalamic abnormalities have been reported in trigeminal neuropathic pain but not in TMDs, suggesting that different chronic pain conditions may involve partly different central processes [34; 122].

An additional consideration relates to the behavioural meaning, or salience, of the training task. Participants with chronic pain may approach exercise with a cognitive incentive; for example that training is associated with expected relief, recovery, or improved function. In acute pain, on the other hand, the same task may be experienced more as interference, or even as a potential threat, reducing engagement with adaptive motor learning processes. This may help explain why acute pain more consistently suppressed training-induced neuroplasticity, whereas chronic pain produced more variable findings.

The effect on training-induced neuroplasticity may depend not only on whether pain is present, but also on whether it is in the anatomically relevant region for the trained motor task. This was shown by Rittig-Rasmussen et al (2014); neck training reduced trapezius MEP amplitudes in patients with neck pain, but increased short-term MEP amplitudes in patients with knee pain [88]. This finding suggests that pain may interfere more with training-induced neuroplasticity when it is located within the trained motor region. In contrast, in more widespread pain conditions [41; 95], or in disorders such as low back pain where exercise may not be confined to a single symptomatic structure [63; 113], the influence of pain on training responses may be more diffuse and less anatomically specific.

The variability across chronic pain studies may also reflect individual differences in baseline cortical state. In a recent study on prolonged jaw pain induced by intramuscular nerve growth factor (NGF), two cortical biomarkers—slower baseline electroencephalogram (EEG) rhythm and an early reduction in jaw motor excitability—predicted whether individuals were classified as having high or low pain sensitivity, based on pain trajectories during chewing and yawning [18]. This demonstrates that motor responses to pain are not necessarily uniform, and that baseline cortical state may influence how strongly pain interferes with training-induced neuroplasticity.

Differences in training protocols, study populations and pain conditions

In the included primary studies in Study I, the most frequently reported perturbations in training responses were reduced or absent MEP facilitation, together with alterations in other cortical excitability measures. However, experimental pain models, chronic pain conditions, and training protocols varied considerably between studies. Thus, both within and between the acute and chronic pain groups, there were differences in pain induction, time course, task complexity, and the degree to which training protocols induced fatigue. These differences are relevant as the amount of training, task complexity, and whether training protocols induced fatigue, are all factors that independently can influence the degree of neuroplastic changes. When pain appears to attenuate training-induced neuroplasticity, it is difficult to determine whether this reflects a direct effect on the motor system, or an indirect effect mediated by altered task performance. Pain may influence neuroplasticity both by changing corticomotor excitability and by modifying the task behaviour. This includes changes in movement strategy as well as cognitive attention and motivation for engagement with training protocols. Clinically, this is relevant, as it suggests that the presence of pain does not necessarily equate to a need for avoidance of training, but that optimising training conditions may facilitate adaptive cortico-motor processes as well as clinical outcomes.

Cranially and spinally innervated regions

Most evidence in Study I was based on studies in spinally innervated limb muscles, with only one study targeting a cranially innervated motor system. Differences between the jaw and limb motor systems are also reflected in TMS methodology. In contrast to limb muscles, where motor thresholds are commonly determined at rest, jaw muscle thresholds often need to be assessed during a slight contraction, such as light tooth contact, as stable responses can be difficult to elicit at rest. These neuroanatomical differences limit how the findings from Study I can be generalised to jaw motor control as the jaw system is organised differently from the limb system, with more bilateral cortical control and stronger integration with brainstem circuits. [18; 22; 90].

There is however emerging research in the trigeminal region that can provide the necessary context for interpreting pain-plasticity relationships in the jaw motor system [10; 22]. Experimental jaw pain models using NGF, which induces a prolonged muscle pain state through sensitisation of nociceptive pathways, have demonstrated inhibitory corticomotor effects on the masseter muscle. This supports the concept that nociceptive input can suppress jaw motor system excitability in a protective manner [10]. Jaw motor plasticity also appears to be sensitive to mechanical and sensory context. For example, in patients with obstructive sleep apnéa, short-term use of a mandibular advancement device increased masseter and tongue MEP amplitudes and enlarged corticomotor map volume. This suggests that altering the position of the mandible, and thereby orofacial sensory input, may modulate the corticomotor organisation of the jaw motor system [65].

In summary, the findings from Study I suggested that more studies incorporating pain and training in the jaw motor system are needed to build an evidence base relevant to trigeminally innervated regions, as the jaw motor system is not necessarily a straightforward extension of spinally innervated motor systems.

Training in the Jaw System: Behavioural Changes

In Study III we investigated whether short-term jaw sensorimotor training could modify jaw motor behaviour and corticomotor excitability, and whether pain and overload-related parafunctions influenced these effects. Both TMD pain and controls improved with training, but in different ways: controls showed larger gains in jaw-position replication, whereas individuals with TMD pain showed larger gains in thickness recognition. Masseter corticomotor excitability changed over time in both groups, but with different patterns across the stimulus–response range. Self-reported bruxism, regardless of the presence of pain, was also associated with higher aMT at baseline and smaller corticomotor changes after training. Together, these findings support that pain and overload-related behaviour shape the degree and dimensions of training-induced improvement of jaw sensorimotor function.

The finding of task-related differences in improvement between the TMD pain and control group suggests that the two tasks relied on partly different sensorimotor processes. Replication required reproducing a target jaw opening without an external reference and therefore depended more on "internal" estimation of jaw position, proprioceptive integration, and the ability to update sensorimotor representations through practice. In contrast, thickness recognition was supported by contact with a physical object and therefore by more salient external somatosensory input, particularly from periodontal and other trigeminal mechanoreceptive input [110; 112]. From this perspective, pain may constrain internally guided recalibration more than cue-supported perceptual learning. This interpretation is consistent with observations that painful TMD may affect somatosensory function in a region- and task-dependent manner, with reduced tactile acuity reported in extraoral trigeminal regions, but preserved or even enhanced performance in certain intraoral perceptual tasks such as occlusal tactile acuity [14; 49; 56].

This interpretation is strengthened by the finding that improvement in jaw-position replication, but not in thickness recognition, was positively correlated with the training-induced increase in masseter MEP amplitude. This suggests that the corticomotor changes captured by TMS were behaviourally relevant, but mainly for the aspects of learning that depended on internally generated jaw motor calibration, i.e. the proprioceptive integration. The absence of a correlation for recognition supports the view that recognition could improve through partly different mechanisms, such as repeated sensory exposure, perceptual learning, or more efficient use of tactile reference cues during tooth contact, without requiring the same degree of corticomotor facilitation in the masseter pathway. This distinction suggests jaw sensorimotor outcomes may rely on different combinations of sensory and motor plasticity, and that pain may affect these in a varied manner.

Training in the Jaw System: Neurophysiological Adaptation

The intensity-dependent changes over time in masseter MEP amplitudes together with the significant group interaction indicates that the training response across the stimulus–response range was affected by pain. This finding suggests group differences in recruitment profiles of the corticomotor pathway after training. In both groups, some of the lower stimulation intensities showed elevated amplitudes at the pre-training session compared with baseline, whereas the clearest post-training increases were seen at the higher intensities. This pattern suggests that near-threshold responses were more influenced by session-related factors such as arousal, attention, or minor changes in background activation, whereas the higher-intensity portion of the range more likely reflected genuine training-induced changes in recruitment. This is consistent with the known properties of the stimulus-response curve, where near-threshold intensities recruit only a small and variable pool of corticomotor neurons, making responses more susceptible to fluctuations in cortical state, whereas higher suprathreshold intensities recruit a larger portion of the pathway and generally provide more stable estimates of corticomotor output [26; 101]. Thus, the jaw motor system appears capable of expressing short-term neurophysiological adaptation, but in painful conditions, that adaptation may emerge in a different configuration rather than simply being absent [70].

Training Responsiveness in Relation to Parafunction

For both groups, higher awake and sleep bruxism scores were associated with higher aMT and smaller masseter MEP changes after training. The aMT finding reflects the baseline dimension: overload-related behaviour was linked to a less readily recruitable corticomotor state. The MEP changes reflect the responsiveness dimension with less neurophysiological change in response to the same training dose. Together, these observations suggest that repetitive parafunctional jaw activities such as bruxism may be associated with a motor system operating in a more rigid and less adaptable control state. One possible interpretation is that such behaviour may come to resemble an overlearned or overtrained motor pattern, in which repeated jaw motor activity becomes increasingly automated through repetition, leaving less scope for additional short-term facilitation.

Prior work has shown reduced training-related corticomotor facilitation in individuals with sleep bruxism, with attenuated excitability changes following experimental masseter sensitisation [10]. The present findings extend this by suggesting that this relationship apply not only to sleep bruxism but also to awake bruxism, and that overload-related behaviour may influence both the baseline recruitment threshold and the magnitude of training-related change.

Whereas Study II documented a distinct overload phenotype in TMD pain characterised by sustained low-intensity muscle activity, Study III suggests that parafunctional behaviour may be associated with a less responsive corticomotor baseline. In this perspective, pain may reorganise how plasticity is expressed at the level of motor output, whereas overload-related behaviour may precondition the baseline state from which plasticity develops.

Strengths and Limitations

Study I was the first systematic review to examine the effect of pain on training-induced plasticity assessed by TMS. The pre-registered protocol and adherence to guidelines strengthened transparency and reproducibility. Another strength is the coverage of both acute and chronic pain states, making it possible to identify consistent patterns despite heterogeneity. This heterogeneity represents a limitation: the included studies varied in pain models, motor tasks, and TMS protocols. This made direct comparisons difficult, and it was not deemed appropriate to perform a meta-analysis. Only one study involved the trigeminal system, meaning that in relation to the jaw system, most conclusions are extrapolated from spinal or limb muscles.

Study II introduced combined EMA and sEMG in natural settings. The high compliance rate ensures that the data have strong ecological validity. The concurrent sEMG recording provided objective validation of the EMA, showing that self-reported awake bruxism behaviour corresponded meaningfully to recorded muscle activity. This alignment strengthens confidence in EMA as a useful measure of jaw overload behaviour. Another strength is that overload was quantified in two ways: both duration and AUC which allowed detection of a pattern of sustained low-intensity activity in individuals with pain. Still, the chosen 20% MVC threshold may have overlooked more subtle degrees of overload. In addition, the sample was based on relatively young individuals, which may reduce generalisability to older populations. Furthermore, both EMA prompts and EMG device wear may have influenced behaviour. However, given the short duration of the recording period and the fact that self-reported activity levels were in accordance with those in previous EMA studies, a substantial influence on the overall findings is considered unlikely.

Study III combined assessment of corticomotor excitability and behavioural jaw sensorimotor performance, allowing training effects to be evaluated at both neurophysiological and functional levels. The use of a standardised, short-duration jaw training programme with repeated assessments strengthened internal validity, and the inclusion of an FDI control measure helped interpret whether excitability changes were specific to the jaw motor system. However, the sample size, particularly in the TMD pain group, was modest, which limits statistical power and generalisability. The intervention period was short, so persistence of training effects could not be evaluated. In addition, behavioural tasks may be influenced by training effects as well as measurement errors. Markers of bruxism and overload were mainly self-reported, which may introduce uncertainty regarding categorisations. Finally, TMS assessment of cranial muscles has methodological challenges, including variability and dependence on background activation, which may reduce sensitivity in detecting subtle between-group differences.

Ethical Considerations

This thesis comprises different study designs, which relates to different ethical considerations. Study I did not involve the collection of new data or direct participant exposure. Therefore, the primary ethical responsibility concerns research integrity, transparent protocol registration, unbiased study selection, and appropriate risk-of-bias assessment, to avoid misleading conclusions that could influence future research as well as clinical practice. More broadly, systematic reviews have ethical benefits. Avoiding research waste is an important ethical consideration, particularly when new studies unnecessarily duplicate existing evidence [15]. By mapping the existing evidence base and identifying knowledge gaps, Study I contributes to the justification of the subsequent studies in this thesis, rather than simply adding to an already crowded literature.

Both Study II and Study III involved primary data collection and therefore raised ethical issues related to autonomy, safety, burden, and data protection. Both studies included participants with chronic pain, a population that may be more vulnerable to therapeutic misconception, where the boundary between research participation and treatment can become blurred. Specific care was taken to ensure that participants understood that the studies were designed to generate knowledge, not to provide individualised treatment, and that withdrawal at any point carried no consequences. Both studies were approved by ethics committees and conducted in accordance with the Declaration of Helsinki.

Study III raises additional considerations specific to exercise interventions in pain populations: the question of dosage and individual appropriateness. Training is not uniformly beneficial, and a specific intervention and dose that may be insufficient for some individuals may be excessive for others. This is especially relevant when pain and reduced capacity alter the system's ability to respond and recover. The findings of this thesis, which show that pain and overload shape training responses, underscore the importance of individually adapted approaches in clinical settings rather than standardised protocols applied uniformly.

Finally, across all studies, data management plans were implemented to ensure GDPR-compliant handling of sensitive health and behavioural data, including pseudonymisation, secure storage, restricted access, and defined retention periods, as well as procedures for archiving and deleting data.

Clinical Implications

The results of this thesis point to several clinical implications and knowledge gaps.

First, EMA provides a more comprehensive collecting of information compared to traditional single-point measures such as questionnaires or interviews. Questionnaires rely on recall and awareness, whereas EMA can collect longitudinal data during daily life and capture fluctuations in symptoms such as pain intensity, as well as episodes of jaw overload that the individual may not notice. EMA can also be extended to include psychosocial factors such as stress or mood, making it possible to link behaviour, physiology, and context in a way that cross-sectional tools cannot. When combined with sEMG, this approach offers a more valid and dynamic picture of how overload develops and is maintained. One important consideration is that repeated prompting, inherent to EMA, may in itself influence behaviour by increasing awareness. EMA therefore has the potential to function as a behavioural intervention, an effect sometimes referred to as ecological momentary intervention. This should be acknowledged both as a possible confounder in research settings and as a potential opportunity in the clinic.

Second, the findings highlight the importance of sustained low-level muscle activity. This pattern was more common in participants with pain and may, over time, contribute to overload and pain in the jaw system. Activities such as jaw bracing without tooth contact may remain outside conscious awareness, possibly because it does not create the same sensory signalling as clenching and grinding. Over time, such behaviours may also become automated. Clinicians should therefore not only focus on clenching or grinding, but also consider prolonged, low-intensity bracing of the jaw, which may be clinically relevant even if it goes unnoticed by the patient and does not result in traditional clinical signs such as tooth wear.

Third, the results show that pain itself influences how the motor system functions and adapts. When pain is present, the capacity for training-induced neuroplastic change may be reduced or altered, which may limit the effect of training and behavioural retraining. Patients with pain may respond differently to training programmes compared to pain-free participants, as pain reorganises the conditions under which motor learning occurs. This has a practical implication—adequate pain management may be a prerequisite for maximising training-related gains.

Finally, the results from this thesis reinforce the importance of a biopsychosocial perspective in the management of TMD pain. Perceived stress was associated with higher levels of awake bruxism and jaw muscle overload, suggesting that psychosocial factors are not merely background variables but active contributors to the load placed on the jaw system. Management of TMD pain should therefore include strategies for stress reduction, behavioural self-monitoring, and coping. The interaction between biological, psychological, and social factors means that no single intervention is likely to be sufficient, and that treatment responses will vary considerably between individuals depending on their overload profile, pain state, and psychosocial context.

FUTURE PERSPECTIVES

- **Identify predictors of response to jaw training**

Future studies could combine EMA and portable sEMG to quantify daily jaw overload and evaluate whether these measures predict behavioural and neurophysiological responses to training. This may help identify which individuals are more or less likely to benefit from a given intervention.

- **Ecological approaches into real-time interventions**

The combined EMA//sEMG approach makes it possible to detect overload-related jaw behaviour in everyday life. A logical next step is to investigate whether this system can be expanded into a real-time feedback intervention; for example, by alerting individuals when overload occurs, and whether such feedback can reduce jaw overloading and improve symptoms.

- **Longitudinal designs to capture change over time**

Short-term pre-post studies cannot determine whether training effects persist, or how overload and pain interact over longer periods. Repeated longitudinal assessments combining TMS, EMA, and sEMG may clarify how the jaw system changes over time and help identify early markers of poor response or sustained improvement.

SUMMARY OF FINDINGS

- Self-reported awake bruxism in real time correlated with registered masseter muscle activity both in terms of duration and intensity of overload.

- Participants with TMD pain exhibited more awake bruxism and stress, as well as longer duration of overload, especially for low-intensity muscle activity.

- Published literature shows an effect of pain on training-induced corticomotor plasticity. This effect was more consistent in acute pain compared to chronic pain conditions. Functional outcomes showed more variable findings.

- Pain-related perturbations in training responses were observed across multiple neurophysiological measures, including corticospinal excitability, intracortical circuits, and cortico-cerebellar connectivity, suggesting that the effects of pain on neuroplasticity are not confined to a single mechanism.

- Sensorimotor training improved performance in both jaw opening replication and thickness recognition tasks. The improvement was larger among controls for the replication task, and larger among individuals with TMD pain for the recognition task.

- Higher bruxism scores were associated with higher active motor threshold and smaller training-related changes in MEP amplitude.

CONCLUSIONS

- Awake bruxism is reflected in physiological jaw muscle overload in daily life as evidenced by the correlations between EMA-based reports of awake bruxism and sEMG-defined overload.

- Individuals with TMD pain show a higher overall burden in regard to overload duration, stress and self-reported awake bruxism, together with a higher propensity for sustained low-intensity loading.

- Both acute and chronic pain may perturb training-induced corticomotor neuroplasticity, although the evidence is more consistent in acute pain.

- The impact of pain on training-induced neuroplasticity is complex and cannot be fully understood from a single neurophysiological measure, which has implications for how training responses should be assessed in clinical and research settings.

- Short-term jaw training may induce both sensorimotor and corticomotor adaptation, but TMD pain influences response patterns.

- Parafunctional behaviours may influence the pain-training-plasticity relationship. Self-reported bruxism appears to shape baseline motor excitability or the degree of training-related change, supporting a model where pain and parafunction jointly influence capacity, loading, and adaptive potential of the jaw system.

AUTHOR CONTRIBUTIONS

The contributions by the author of the present thesis to the individual studies is outlined in Table 4.

Table 4. The author’s contribution to the individual studies included in the thesis.

Study I	Study II	Study III
Conceptualisation Study design Protocol registration Literature search strategy Abstract screening Full-text assessment Data extraction Quality assessment and risk-of-bias assessment Interpretation of findings Writing of the original draft Critical revision and editing of the manuscript All journal correspondence	Conceptualisation Study design Ethical application Data management plan Participant recruitment Data collection Data curation Statistical analysis Visualisation Interpretation of findings Writing of the original draft Critical revision and editing of the manuscript All journal correspondence	Conceptualisation Study design Ethical application Data management plan Participant recruitment Data collection Data curation Statistical analysis Visualisation Interpretation of findings Writing of the original draft Critical revision and editing of the manuscript

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