

Masticatory Muscle Pain. Causes, Consequences, and Diagnosis
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Masticatory muscle pain is known as myogenous temporomandibular disorder (TMD) pain. It has a prevalence of approximately 10% in the general population and affects women more than men. It is usually characterized by a dull, aching pain, which aggravates on function. The etiology of TMD pain is still not clear, and multiple factors are considered to play role. Oral parafunctions, like the habit of chewing gum or bruxism (i.e., clenching and/or grinding of the teeth), are thought to play a pivotal role in the initiation and perpetuation of TMD pain, even though this has not yet been verified unequivocally by epidemiological and experimental studies. At the same time, the effects of TMD pain on the masticatory sensory-motor function are not fully understood either. Two models, the vicious cycle model and the pain adaptation model, have been proposed to explain these effects the best, although neither of them is able to fully explain the effects that are present in TMD-pain patients. In everyday clinical practice, for the establishment of a TMD-pain diagnosis, palpation and dynamic/static tests are commonly used, however without having full insight into the factors that influence the responses of these tests. To further clarify the above-outlined gaps in the current knowledge, this thesis includes five studies. Chapters 2, 4, and 5 describe studies on the role of experimental parafunctions in the provocation of TMD pain and on the effects of this pain on masticatory muscle function. Chapter 3 is a methodological paper about the recording of the jaw-stretch reflex (i.e., the short-latency response of the jaw-closing muscles after a sudden stretch), which is an important descriptor of motor function. Chapter 6 deals with the factors influencing the outcome of clinical diagnostic tests for TMD pain.

The aim of the first study of this thesis (Chapter 2) was to assess the effects of an intense chewing exercise on the masticatory sensory-motor system. It has been proven that nociceptive substances, injected into the masseter muscle, induce pain and facilitate the jaw-stretch reflex. In this study, it was hypothesized that intense and prolonged chewing would provoke similar effects. Fourteen men gave their informed consent and agreed to participate in the study. They performed 20 bouts of 5-minute chewing exercises. After each bout, 20 minutes, and 24 hours after the exercise, all participants were examined for signs and symptoms of TMD. In addition, data were collected regarding muscle fatigue and pain, the normalized reflex amplitude from the left masseter muscle, and pressure-pain thresholds. Fatigue and pain scores had increased during the exercise ($P<0.001$), but the reflex amplitude did not ($P=0.123$). Twenty minutes after the exercise, 12 participants showed signs of myofascial pain or arthralgia. Pressure pain thresholds were decreased 20 minutes after the exercises ($P=0.009$) but also 24 hours afterwards ($P=0.049$). Based on the results of this study, it can be concluded the intense and prolonged chewing exercises can induce fatigue, pain, and decreased pressure-pain thresholds in the masticatory muscles, but that it does not influence the jaw-stretch reflex.

In the second study of this thesis (Chapter 3), it was tested whether normalization of the jaw-stretch reflex amplitude with respect to the pre-stimulus electromyographic (EMG) activity will make the amplitude more independent of the location of the surface electrodes over the masseter muscle. A 5×6 electrode grid was used to record the jaw-stretch reflex from 25 sites over the right masseter muscle of fifteen healthy men. Results showed that there was a significant site dependency of the pre-stimulus EMG activity and the reflex amplitude. High cross-correlation coefficients were found between the spatial distribution of mean pre-stimulus EMG activities and reflex amplitude. When the reflex amplitude was normalized with respect to the pre-stimulus EMG activity, however, no site dependency was found. In conclusion, normalization of the jaw-stretch reflex amplitude by the pre-stimulus EMG activity strongly reduces its spatial dependency.

In the third study of this thesis (Chapter 4), it was aimed to construct an apparatus that can impose intense eccentric contractions to the jaw-closing muscles, and to test the hypothesis that eccentric contractions can provoke symptoms of delayed-onset muscle soreness (DOMS) in these muscles. The provocation apparatus consisted of two tungsten arms, connected by a hinge axis on one end. Participants bite with their anterior teeth on biting plates located on the other end. Each time the experimenter gradually released the compression force of the apparatus' rubber tubings, the mouth was forced open, during which the jaw-closing muscles performed an eccentric contraction. Six male participants thus performed sequences of concentric and eccentric contractions of

their jaw-closing muscles in six sets of exercises, each lasting 5 minutes, and with one minute of rest in between. Each set consisted of 60 open-close movements. Before and after the exercises, and after 24 hours, 48 hours, and one week, feelings of fatigue and pain, the maximum mouth opening without pain, the muscles' tenderness to palpation, and the maximum voluntary bite force were recorded. After 24 hours and 48 hours, the levels of fatigue and pain were elevated, the maximum mouth opening without pain decreased, and five of the six participants reported tenderness to palpation. The maximum voluntary bite force also decreased after 24 hours. These findings indicate that this novel apparatus is successful in inducing DOMS in the jaw-closing muscles.

In the fourth study of this thesis (Chapter 5), the possible role of overuse of the jaw muscles in the pathogenesis of jaw-muscle pain was studied. A protocol involving concentric and eccentric muscle contractions was used to provoke a state of DOMS in the jaw-closing muscles of healthy individuals. It was tested whether the accompanying signs and symptoms would yield the temporary diagnosis of myofascial pain according to the research diagnostic criteria for temporomandibular disorders (RDC/TMD) in these individuals. Forty participants (mean age \pm SD = 27.7 \pm 7.5 years) performed six, 5-minute bouts of eccentric and concentric jaw-muscle contractions. Before and immediately after the exercise, and 24 hours, 48 hours, and one week later, self-reported muscle fatigue and pain, pain-free maximum mouth opening, pressure-pain thresholds, and the number of painful jaw-muscle palpation sites were recorded. Significant signs and symptoms of DOMS in the jaw-closing muscles were found, which all had resolved after one week. In 31 (77.5%) of the participants, these signs and symptoms also gave rise to a temporary diagnosis of myofascial pain according to the RDC/TMD. Within the limits of the study, it was shown that an experimental protocol involving concentric and eccentric muscle contractions can provoke DOMS in the jaw-closing muscles and can yield a temporary diagnosis of myofascial pain according to the RDC/TMD. This strengthens the supposition that the myofascial pain in TMD patients may be a manifestation of DOMS in the jaw muscles.

The aim of the last study of this thesis (Chapter 6) was to investigate whether diagnostic tests for TMD pain are influenced by the presence of comorbid conditions, and to determine whether this influence decreases when the presence of "familiar pain" is used as outcome measure. In total, 117 patients (35 males, 82 females; 75 TMD-pain patients, 42 pain-free patients; mean age \pm SD = 42.9 \pm 14.2 years) were examined with palpation tests and dynamic/static tests. After each test, they were asked whether any pain was provoked and whether this pain response was familiar or not. For four clinical outcome measures (pain on palpation, familiar pain on palpation, pain on dynamic/static tests, and familiar pain on dynamic/static tests), multiple logistic regression analyses were performed, with the presence of TMD pain as the primary predictor and regional (neck/shoulder) pain, widespread pain, depression, and somatization as comorbid factors. Pain on palpation was not associated with the primary predictor but with regional pain ($P=0.02$, OR=4.6) and somatization ($P=0.011$, OR=8.5), whereas familiar pain on palpation was associated with the primary predictor ($P=0.003$, OR=5.2) but also with widespread pain ($P=0.001$, OR=2.0). Pain on dynamic/static tests was associated with the primary predictor ($P<0.001$, OR=11.1) but also with somatization ($P=0.037$, OR=4.5), whereas familiar pain on dynamic/static tests was only associated with the primary predictor ($P<0.001$, OR=32.4). In conclusion, diagnostic tests are negatively influenced by the presence of comorbidity. This influence decreases when the presence of familiar pain is used as outcome measure.