Excitability of the central masticatory pathways in patients with painful temporomandibular disorders

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Abstract

Much is unclear about the pathophysiological mechanisms underlying painful temporomandibular disorders. In addition to various other theories, masticatory muscle dysfunction and pain have also been attributed to primary central nervous system hyperactivity. We assessed this possibility in a study using recent neurophysiological techniques. From among outpatients whose diagnosis of temporomandibular disorders had been obtained in stomatognathic facilities, we studied 10 patients with bilateral pain and 15 patients with unilateral pain, in whom electromyographic examination of the trigeminal reflexes disclosed normal findings except for absence or amplitude asymmetry of the jaw jerk. Transcranial magnetic stimulation yielded masseter motor evoked potentials of normal latency and amplitude, but five patients had to exert a near-maximum contraction to obtain their responses. The masseter silent periods elicited by the double-shock technique recovered normally. Because these tests measure the excitability of the masticatory system (including motor cortex, corticobulbar and corticoreticular connections, reticular interneurones and lower motoneurones), the lack of facilitation in these patients’ responses excluded central hyperactivity as the primary cause of their masticatory dysfunction and pain.

Keywords: Temporomandibular disorder; Masseter muscle; Electromyography; Transcranial magnetic stimulation; Jaw reflexes; Masseter silent periods

1. Introduction

In using the term temporomandibular disorder (TMD), also called craniomandibular dysfunction, we refer here to TMD and its related pain conditions, regardless of the primary cause. Nosographic classifications of TMD vary widely because the syndrome has various possible underlying mechanisms and its causative agent is often unknown. Many of the hypotheses proposed to explain its etiology and pathophysiological mechanisms remain substantially unproved (Fricton and Dubner, 1995; Sessle et al., 1995). Yet the temporomandibular region and masticatory muscles are among the most common sources of chronic pain (Fricton and Schiffman, 1995). Epidemiological surveys have estimated a high incidence (up to 70% of a normal population) (Helkimo, 1974). Efforts to clarify the problem currently involve physiological and clinical experts in this field (Fricton and Dubner, 1995; Sessle et al., 1995).

Electromyographic (EMG) abnormalities of the voluntary or reflex activity in the masticatory muscle have often been found in association with TMD. Despite abundant research, EMG studies have nonetheless led neither to reliable diagnostic criteria nor to a breakthrough in our understanding of the pathophysiology of this controversial syndrome. The more recent neurophysiological techniques should help to verify at least one theory.

Instead of a primary derangement of dental occlusion or joint as the cause of TMD, one of the main theories proposed a state of central nervous system (CNS) hyperactivity...
(Griffin and Munro, 1971; see references in De Laat, 1987). The currently most cited factor that might favour central hyperactivity is psychological stress (McCrea et al., 1991; Maixner et al., 1995; Rudy et al., 1995). Although previous studies have disproved a muscle hyperactivity (see references in Lund et al., 1990), none has directly measured central nervous system (CNS) excitability.

The excitability of the central masticatory pathways can now be studied in the intact human subject by recording the motor potentials evoked in the masseter muscles after transcranial magnetic stimulation and by measuring the recovery of the masseter silent periods elicited by the double-shock technique. In this study we used these neurophysiological investigations to seek evidence of abnormal CNS excitability in patients with TMD. Besides a group of TMD patients with pain and muscle tenderness on both sides of the face, we also studied a group of patients who had strictly unilateral pain. The latter group allowed us to examine intraindividual side differences thus increasing the sensitivity of our tests.

2. Patients and methods

2.1. Patients

Many patients with a diagnosis of TMD are referred by odontologists and maxillofacial surgeons of the University Hospital to our outpatient pain clinic, to exclude possible inapparent neurological disease as the source of facial pain. From among referrals we selected for study two groups of patients. Ten patients, eight women and two men aged 29–62 years (mean age 42 years), had a clinical history of bilateral pain in the masticatory muscles or the TM joint; some also had masticatory muscle tenderness. Fifteen patients, 11 women and four men aged 24–56 years (mean 33 years), had strictly unilateral pain and, if present, masticatory muscle tenderness on one side only. All patients had normal clinical neurological findings, and neurophysiological evidence of normal latency trigeminal reflexes (blink reflex in response to supraorbital nerve stimulation, masseter inhibitory reflex after stimulation of the maxillary and mandibular divisions, and jaw jerk reflex (Ongerboer de Visser and Cruccu, 1993). Patients who had asymmetry in the jaw jerk amplitude, or an absent jaw jerk were included. Some patients underwent magnetic resonance imaging (MRI) of the skull. No patient suffered from bruxism. Although none of the controls underwent examination for a possible malocclusion or temporomandibular joint abnormalities, none reported head, face or neck pain.

2.3. Jaw jerk

The subject sat in the upright position on a dentist’s chair, with the head leaning against the headrest. The jaw jerk was obtained by tapping the patient’s chin with a reflex hammer fitted with a microswitch that triggered the sweep of the recording apparatus (Ongerboer de Visser and Cruccu, 1993). The patient kept the mandible in its resting postural position with the muscles completely relaxed (“postural”), or very slightly clenched, with the teeth in full intercuspal occlusion (“occlusal”). EMG signals were recorded (filters 10–2000 Hz) through surface electrodes from the right and left masseter muscles, simultaneously. The active electrode was placed over the lower third of the muscle belly and the reference electrode just below the mandible; the distance between the electrodes was about 4–5 cm. The onset latency and peak-to-peak amplitude of the jaw jerk were averaged over six trials for each of the two (postural and occlusal) positions.

2.4. Transcranial magnetic stimulation

Motor evoked potentials (MEPs) were recorded with the same recording electrodes and filters used for the jaw jerk. Transcranial stimuli were delivered by a MagStim 200 device (Novametrix) connected to a round coil (outer diameter 10 cm), generating magnetic fields of up to 2 T (100% output). The intensity of stimulation was expressed as a percentage of the maximum power output. The magnetic coil was placed flat over the scalp; the optimal stimulating position was on the midline, with the centre of the coil slightly anterior to the vertex. This position produced the largest MEPs in the masseter muscles of both sides, without apparently directly exciting the trigeminal root on either side. MEPs were induced with clockwise and anticlockwise currents. Single magnetic shocks (40–100% output) were delivered with the target muscles at rest and while subjects exerted a slight voluntary contraction (approximately 30% maximum) of the muscles on both sides. The onset latency and peak-to-peak amplitude were measured over six trials (Cruccu et al., 1991b).

2.5. Recovery of masseter silent periods to double shocks

EMG signals were recorded through the same electrodes used for the investigations above, amplified (bandwidth 50–5000 Hz), full-wave rectified, and stored by a biopotential analyser. The subjects were instructed to clench their teeth in central occlusion and as hard as possible, for periods of 2 s, with the aid of auditory feedback. After resting for 10–20 s, the subject repeated the contraction. Electrical stimuli (0.2 ms, 10–50 mA) were delivered to the mental nerve...
through surface electrodes during the ‘clench phase’. The stimulus intensity was adjusted to 2.5-fold the reflex threshold and maintained throughout the recording session. This intensity yielded the best evidence of the early (SP1) and late (SP2) silent periods, and evoked a painful sensation that the subject could bear without undue discomfort. Onset and end of the SPs were taken at the intersection of the rectified and averaged signal and a line indicating 80% of the background EMG level, and the area of the SPs was automatically computed. The recovery cycle was studied by delivering double shocks at an interstimulus time interval of 250 ms (Fig. 1). A series of 8–16 trials was repeated. To prevent fatigue and habituation, we delivered the double shocks at a low rate, during the ‘clench’ phases described above. Recovery was measured as the area of the response to the second shock (test) in percentage of the area of the response to the first shock (conditioning) (Cruccu et al., 1984; Ongerboer de Visser and Cruccu, 1993).

2.6. Statistical analysis

Descriptive data are given as mean ± 1 SD. Intraindividual side differences were evaluated by Student’s t-test for paired data, and differences between groups by analysis of variance (ANOVA) with Bonferroni multiple comparisons test. Side-differences in amplitude were also normalised: in the control group (to obtain the maximum possible mean asymmetry), higher-minus lower-amplitude side in percentage of the higher-amplitude value; in the TMD patients with laterised pain, painful side minus contralateral side in percentage of the contralateral side value.

P-values less than 0.01 were considered to indicate statistical significance.

3. Results

3.1. Jaw jerk

The mean onset latency of the jaw jerk in the TMD patients with bilateral pain (6.9 ± 0.7 ms) and in those with unilateral pain (painful side 7.2 ± 0.9 ms, and non-painful side 7 ± 0.8 ms) was similar to values commonly found in normal subjects (Ongerboer de Visser and Cruccu, 1993; Kimura et al., 1994).

Of the patients with bilateral pain, one had a bilaterally absent jaw jerk in postural and two in occlusal recordings. Of the patients with unilateral pain, three had an absent jaw jerk on the painful side in postural and four in occlusal recordings (Fig. 1). The patients with a unilaterally absent jaw jerk had normal MRI of the brain.

The jaw jerk elicited in the occlusal position had a smaller mean amplitude in the TMD patients than in controls (Table 1). The significance of the difference between the three groups, however, was weak \((P = 0.047)\), and no individual group differed significantly from the others \((P > 0.05)\).

3.2. Motor evoked potentials

Motor evoked potentials (MEPs) were absent in the painful side during slight clenching, but became normal and symmetrical during strong clenching. In (C) the test silent periods, evoked by the second shock, recover to 48% of the conditioning responses on the painful side and to 45% on the non-painful side. In (A) the jaw jerk is smaller and absent in the occlusal position, on the painful side. In (B) although the motor evoked potential is absent on the painful side during slight clenching, it becomes normal and symmetrical during strong clenching. In (C) the test silent periods, evoked by the second shock, recover to 48% of the conditioning responses on the painful side and to 45% on the non-painful side. In (A) and (B), two averages of six trials each are superimposed; calibration is 10 ms, 1 mV. In (C) each trace is the average of 12 trials; calibration is 100 ms, 200 \(\mu\)V.
Neurophysiological findings in patients with bilateral or unilateral TMD pain and controls

<table>
<thead>
<tr>
<th>Jaw jerk amplitude (mV)</th>
<th>Recovery cycle (area %)</th>
<th>Motor evoked potentials</th>
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<tbody>
<tr>
<td></td>
<td>Postural</td>
<td>Occlusal</td>
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<tr>
<td>Controls</td>
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<tr>
<td>1.2 ± 0.7 (40)</td>
<td>1.43 ± 1.2 (40)</td>
<td>90 ± 12 (40)</td>
</tr>
<tr>
<td>Patients with bilateral pain (values refer to right and left sides)</td>
<td>0.93 ± 0.9 (18)</td>
<td>0.88 ± 0.9 (16)</td>
</tr>
<tr>
<td>Patients with unilateral pain (values refer to painful sides)</td>
<td>0.97 ± 0.5 (12)</td>
<td>0.65 ± 0.4 (11)</td>
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Comparison between groups: absolute values

<table>
<thead>
<tr>
<th></th>
<th>NS</th>
<th>P = 0.047</th>
<th>NS</th>
<th>NS</th>
<th>NS</th>
<th>NS</th>
</tr>
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<tbody>
<tr>
<td>Painful side minus non-painful side</td>
<td>-0.53 ± 0.70 (12)</td>
<td>-0.82 ± 0.76 (11)</td>
<td>2 ± 11 (15)</td>
<td>-0.7 ± 10.4 (15)</td>
<td>-0.05 ± 0.18 (11)</td>
<td>-0.14 ± 0.61 (11)</td>
</tr>
<tr>
<td>Normalised (%) side difference in amplitude</td>
<td>29 ± 34 (12)</td>
<td>49 ± 36 (11)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>10 ± 41 (11)</td>
</tr>
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</table>

Significance between sides (t-test for paired data) | P < 0.01 | P < 0.001 | NS       | NS       | NS       | NS |

Results are given as mean ± SD (n); NS, not significant.

Bonferroni. In the TMD patients with unilateral pain, the jaw jerk elicited in the postural position was significantly smaller on the painful than on the contralateral side (P < 0.01); in the occlusal position the asymmetry increased (P < 0.001) (Table 1). None of the control patients had an absent jaw jerk and the mean absolute amplitude side asymmetry (right side minus left side) approached zero (2 μV). But the wide intraindividual asymmetry present even in many controls yielded a large standard deviation (0.33 mV). In the control group, normalising the side difference resulted in a significant asymmetry of 19.4 ± 20% (P < 0.001). In the unilateral TMD group, normalising the side difference resulted in a lower amplitude on the painful side (29 ± 34% lower in the postural position; 49 ± 36% in the occlusal position) (Table 1). The asymmetry was significantly greater than in controls (P < 0.01).

3.2. Transcranial magnetic stimulation

As commonly found in normal subjects, transcranial stimuli evoked no response in relaxed muscles, but normal MEPs in contracted muscles (Cruccu et al., 1989b; Ongerboer de Visser and Cruccu, 1993). But some TMD patients had to exert a near-maximum contraction to obtain responses on the painful side (Fig. 1). With slight clenching, MEPs were absent bilaterally in one patient with bilateral pain (this patient also had a bilaterally absent jaw jerk) and absent on the painful side in four patients with unilateral pain (three of whom had an absent jaw jerk in occlusal position). With strong clenching all these subjects had normal MEPs: in the patient with bilateral pain the latency and amplitude were 6.1 ms and 1.6 mV on the right side and 6.1 ms and 1.6 mV on the left side; in the four patients with unilateral pain the latency was 6.0 ± 0.2 ms on the painful side and 5.9 ± 0.2 ms on the contralateral; the amplitude was 1.63 ± 0.6 mV on the painful side and 1.64 ± 0.6 mV on the contralateral side. All these values were similar to those of controls and between sides.

In the remaining subjects, slight clenching yielded MEPs of similar latency and amplitude in patients and controls, and negligible differences between painful and non-painful sides (Table 1).

3.3. Recovery of the masseter silent periods to double shock

At an interstimulus interval of 250 ms, SP1 recovered to about 90% and SP2 to about 50% of the unconditioned responses in the TMD patients, as they do in normal subjects (Cruccu et al., 1991; Ongerboer de Visser and Cruccu, 1993). No significant differences were found between patients and controls, nor did the intraindividual differences between painful and non-painful sides reach significance (Table 1).

4. Discussion

Six of our TMD patients had an absent jaw jerk and those with unilateral pain had a smaller jaw jerk on the painful side. Five patients had absent masseter MEPs to transcranial stimulation (during slight clenching). When they provided a sufficient level of background contraction, all patients had normal MEPs. All patients also had normal recovery of masseter silent periods elicited by the double-shock techni-
4.1. Diagnostic value of EMG studies

Reports over the years have described an array of neurophysiological abnormalities in patients with TMD. Several investigators using surface EMG have described excessive masseter and temporal muscle activity, lending support to the ‘vicious cycle’ hypothesis that hyperactive muscles cause pain, which then reinforces muscle hyperactivity (see references in Stohler, 1995). Conversely, others found reduced EMG activity and bite force, or a shift in the power spectrum to lower frequencies (Molin, 1972; Naeije and Hansson, 1986). Yet others found no difference between EMG measures on painful and non-painful muscles in patients with unilateral temporal muscle pain (Majewski and Gale, 1984; Dolan and Keefe, 1988) and fibromyalgia (Zidar et al., 1990). In a recent review, Stohler (1995) comments that studies of EMG activity in sore muscles have provided conflicting results and that the literature about EMG changes in TMD is inconclusive.

Numerous studies have noted that in patients with TMD the chin tap elicits long-lasting silent periods that shorten again to normal range after occlusal therapy (see references in De Laat, 1987). Others have questioned these results because of the large intraindividual variabilities and various methodological problems (Hellsing and Klineberg, 1983; Lavigne et al., 1983). A study evaluating the silent period in a long-term follow-up found no difference between patients who achieved complete, partial, or no relief of the symptoms (Strychański et al., 1984).

Equally contradictory results emerge from jaw jerk studies in TMD. Few have reported an increased side asymmetry of the amplitude or latency (Murray and Klineberg, 1984; Buchner et al., 1989; Cruccu et al., 1992). Hence we agree with the view that EMG studies currently have uncertain diagnostic value and that their use may yield false-positive diagnoses (Mohl, 1995).

Despite this proviso, the side asymmetry in amplitude of the jaw jerk, confirmed in our group of TMD patients with unilateral pain, merits discussion. The jaw jerk was consistently smaller on the painful side, and the asymmetry worsened in the ‘occlusal’ position (Table 1). This is a common finding in our experience. The most immediate explanation would be that the noxious input causes motoneuronal inhibition. This theory opposes the classical ‘vicious cycle’ hypothesis in TMD and receives support from experimental pain studies in animals and humans (Lund et al., 1990; Stohler and Lund, 1994; Schwartz and Lund, 1995; Svensson et al., 1995). Although injection of algogenic substances into the TM joint region increases EMG activity in the ipsilateral masseter muscle in rats (Sessle, 1995; Yu et al., 1995; Yu et al., 1996), a common theory has been proposed, the pain-adaptation model (Lund et al., 1990; Lund and Sessle, 1994). According to this model, activity in nociceptive afferents leads to facilitation of inhibitory pathways when the muscle acts as an agonist and facilitation of excitatory pathways when the muscle acts as an antagonist.

Pathophysiological mechanisms apart, in clinical practice the finding of a jaw jerk asymmetry in a given patient by no means leads to a diagnosis of TMD. Owing to the influence of dental occlusion and bite force (Molin, 1972; Ongerboer de Visser and Cruccu, 1993), jaw jerk amplitudes and side asymmetries vary widely even in normal subjects. For this reason, the special committee of the International Federation of Clinical Neurophysiology appointed to review technical standards and normal values for reflex responses refrained from indicating a normal range for amplitude asymmetry in the jaw jerk (Kimura et al., 1994). But they deemed the unilateral absence of the jaw jerk a sign of a trigeminal (peripheral or central) lesion. Yet in this study we found a unilaterally absent jaw jerk in TMD patients in whom neurological disease could be excluded. From a diagnostic point of view our findings therefore provide information more useful to a neurological centre. They show that in a patient with no other trigeminal abnormality, the unilateral absence of the jaw jerk may be a functional impairment. It does not necessarily imply damage to the nerve fibres or brainstem, and should warrant stomatognathic investigations.

4.2. Excitability of the motor cortex and corticobulbar connections

Transcranial magnetic stimulation activates the primary motor cortex mainly by exciting the facilitatory interneuronal fibres that project onto the pyramidal cells, thereby giving rise to a short train of action potentials (indirect waves, I waves). High-intensity magnetic shocks also directly excite the axon hillock of the pyramidal cells thus giving rise to a mixed volley comprising a direct action potential (D wave) and some I waves (Rothwell et al., 1991). Stimulation of the facial motor cortex elicits a descending volley that travels along the corticobulbar tract and reaches the trigeminal and facial motoneurones. Whereas the comparatively long synaptic delay estimated for the facial motoneurones allows for a multisynaptic connection, the connection for the masseteric motoneurones is most probably monosynaptic and almost completely contralateral. It is therefore similar to the corticospinal projection onto hand muscle motoneurones (Cruccu et al., 1989b; Rothwell et al., 1991).

Peculiar to the corticotrigeminal system is the need for pre-innervation: even with high-intensity magnetic shocks, no motor potential can be evoked without contraction of the target muscles. During contraction, the masseter MEPs appear as short-latency, short-duration, and synchronous responses, which reach an amplitude corresponding to about 30% of the direct motor response after supramaximal stimulation of the masseteric nerve. The motoneuronal acti-
A wealth of literature confirms that mechanical or electrical stimuli delivered anywhere within the mouth or on the facial skin of the maxillary and mandibular trigeminal divisions evoke a reflex inhibition in the jaw-closing muscles. These reflexes probably play a role in the reflex control of mastication, by preventing the intraoral damage that could be caused by uncontrolled contraction of jaw closing muscles, and in the control of jaw movements during speech. Evoked by electrical stimulation of the mental nerve, the masseter silent periods, also called inhibitory periods or silent phases (Bogue, 1958), are considered normal excitability of the jaw-closing muscles. The recovery of brainstem reflexes to double shocks is thought to depend on the level of excitability of the reticular interneurons: the higher the excitability, the quicker the recovery and greater the response to the second shock (test) (Cruccu et al., 1984; Kimura, 1989; Ongerboer de Visser and Cruccu, 1993). The reflex values are influenced by the effectiveness of the input, the excitability of the interneurons, and the excitability of motoneurons. Previous studies eliciting masseter silent periods with chin-tap (see Section 4.1), tooth-tap (De Laat et al., 1985), tooth (Sharav et al., 1982) and cutaneous electrical stimulation (Hussein and McCall, 1983), have reported conflicting results in TMD, possibly owing to the quality of the input, dental occlusion, or bite force, which can affect silent periods (Molin, 1972). Because the double-shock technique ensures equal input and output for the two responses, the recovery cycle provides a measure of the excitability of the interneurons alone (Ongerboer de Visser and Cruccu, 1993).

In patients with extrapyramidal disorders, such as Parkinson’s disease, generalised dystonia, oromandibular dystonia, or blepharospasm, the recovery of the masseter SP2 is greatly enhanced; at the 250-ms interstimulus interval the test SP2 reaches 80–100%, in normal subjects no more than 50–60%. This facilitation has been attributed to hyperactivity of the corticoreticular drive (Cruccu et al., 1991; Ongerboer de Visser and Cruccu, 1993). The reflex values are influenced by the effectiveness of the input, the excitability of the interneurons, and the excitability of motoneurons. Previous studies eliciting masseter silent periods with chin-tap (see Section 4.1), tooth-tap (De Laat et al., 1985), tooth (Sharav et al., 1982) and cutaneous electrical stimulation (Hussein and McCall, 1983), have reported conflicting results in TMD, possibly owing to the quality of the input, dental occlusion, or bite force, which can affect silent periods (Molin, 1972). Because the double-shock technique ensures equal input and output for the two responses, the recovery cycle provides a measure of the excitability of the interneurons alone (Ongerboer de Visser and Cruccu, 1993).
A 'central' etiological model proposed that a primary CNS hyperexcitability created chronic muscle strain, pain and jaw dysfunction. In the 1970s, this central hyperexcitability was attributed either to an unknown mechanism that produced hyperactivity of the reticular formation (Griffin and Munro, 1971) or, more commonly, to psychological factors (De Laat, 1987). Possibly, multifactorial problems are at play.

Our study clarifies one pathophysiological question. In our TMD patients the responses to transcranial cortical stimulation neither had a longer latency nor an increased amplitude, nor was the recovery of the masseter silent periods enhanced. In TMD, therefore, neither the motor cortex nor the reticular formation are hyperexcitable. This conclusion contrasts with the hyperexcitability of the motor cortex (Ikoma et al., 1996) and the reticular formation (Cruccu et al., 1991) previously observed in oromandibular dystonia and other extrapyramidal disorders that induce masseter hyperactivity and pain. Interestingly in oromandibular dystonia and hemimasticatory spasm, muscle and joint pain is the result, not the cause, of the abnormal muscle activity. Because central hyperactivity continues to be quoted as a likely cause of pain in patients with TMD, we consider it useful to dispense with an erroneous theory.

Far less clear is whether this finding weakens the psychogenic theory (McCready et al., 1991; Maixner et al., 1995; Rady et al., 1995). Yet by proving that TMD patients with bilateral or unilateral pain have neither central masticatory system nor masticatory muscle hyperactivity, it undeniably breaks the chain 'stress - central hyperactivity - muscle hyperactivity - pain'. Stress, or psychological factors in general, may lead to pain through a different route.

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References


