Neuropathic Pain in Temporomandibular Joint Disorders: Case-Control Analysis by MR Imaging

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BACKGROUND AND PURPOSE: Temporomandibular joint disorders (TMJ-D) may be associated with the onset of neuropathic pain. The purpose of this study was to prospectively assess if, at the open-mouth position, the distance between the temporomandibular joint (TMJ) disk and the mandibular nerve is shorter in patients with TMJ-D and neuropathic pain vs patients with TMJ-D without neuropathic pain or in healthy people.

MATERIALS AND METHODS: After ethical committee approval, we evaluated by MR imaging 16 TMJs with TMJ-D and neuropathic pain, 16 TMJs with TMJ-D without neuropathic pain, and 16 TMJs of healthy volunteers. All of the subjects were informed about the study procedure. We evaluated the distance between the TMJ disk and the mandibular nerve at the oval foramen level. Furthermore, the presence within the TMJs of internal derangement, osteoarthrosis, joint effusion, and bone marrow edema was evaluated.

RESULTS: At the maximal open-mouth position, the distance between the TMJ disk and the mandibular nerve is shorter in patients with TMJ-D and neuropathic pain than in patients with TMJ-D without neuropathic pain or in healthy volunteers (P < .05). The imaging findings of TMJ internal derangement, effusion, osteoarthrosis, and bone marrow edema were present both in patients with TMJ-D without neuropathic pain and in patients with TMJ-D and neuropathic pain.

CONCLUSIONS: We suggest that a closer proximity between the TMJ disk and the mandibular nerve could be one of the causes of the onset of neuropathic pain in patients with TMJ-D and neuropathic pain.

Subjects

From January 2007 to February 2008, a group of 82 consecutive patients with TMJ-D (164 TMJs) came to see us for observation. All of the subjects were informed about the study procedure, and informed consent was received. The local ethical committee’s approval was given.

Materials and Methods

Subjects

From January 2007 to February 2008, a group of 82 consecutive patients with TMJ-D (164 TMJs) came to see us for observation. All of the subjects were informed about the study procedure, and informed consent was received. The local ethical committee’s approval was given.
After a clinical examination, we set up 1 study group (group A) and 2 control groups (groups B and C). Study group A consisted of 13 patients who showed the simultaneous presence of TMJ-D and neuropathic pain with a total of 16 TMJs because 3 patients showed the bilateral presence of neuropathic pain. Control group B consisted of 16 patients with monolateral TMJ-D without neuropathic pain. Control group C consisted of both the TMJs of 8 healthy volunteers.

The term TMJ-D was used in accordance to the classification of temporomandibular disorders proposed by Oakeson (approved by the American Dental Association). In particular, only the patients with a clinical diagnosis of TMJ degenerative joint disease or with a clinical diagnosis of TMJ disk displacement with reduction or with a clinical diagnosis of TMJ disk displacement without reduction were included. The clinical diagnosis of TMJ-D was achieved by the “Clinical Diagnostic Criteria for TMD” proposed by Truelove et al. The TMJ degenerative joint disease subgroup was defined as having hard grating or crepitus during mandibular range of motion. The TMJ disk displacement with reduction subgroup included patients who were experiencing a click of the TMJ during vertical mandibular range of motion, with or without clicking in lateral or protrusive excursion and in normal closing. The TMJ disk displacement without reduction subgroup was composed of patients with sudden reduction in mandibular opening, with unassisted mandibular opening less than 35 mm, and with a mandibular opening with assistance increased by 3 mm or less than an unassisted opening.

Patients with myofascial pain dysfunction and a diagnosis of myalgia were excluded. Myalgia was diagnosed in all of the patients who showed a clear and reproducible reaction by the use of the bilateral manual palpation technique produced a clear reaction from the patient. This sensation should be reproducible by repeated palpation of the muscle sites.

Instead, we assessed the presence of neuropathic pain using the “Neuropathic Pain Diagnostic Questionnaire (DN4)” proposed by Bouhassira et al. This test consists of a clinician-administered 10-item questionnaire based on the evaluation of both sensory descriptors and signs. The patients were asked about the presence of burning, painful cold, electric shocks, tingling, pins and needles, numbness, itching, hypoesthesia to touch, hypoesthesia to prick, and increase in pain after brushing. According to Bouhassira et al, the total score was calculated as the sum of the 10 items (1 point corresponds to each positive answer), and the cutoff value for the diagnosis of neuropathic pain was a total score of 4/10 or more. Patients with a total score higher than 3 were included in our study group A, whereas the patients with a total score lower than 4 were included in our control group B.

Patients who showed the simultaneous presence of TMJ-D and other possible causes of neuropathic pain not correlated with TMJ structures (eg, patients with multiple sclerosis; meningitis; neoplasia of the meninges; tumors of the head, neck, and the cerebellopontine angle; trauma; vascular diseases; intrasellar carotid aneurysms; inflammation of the orbit, nasal, and paranasal sinuses) were excluded from study group A.

The criteria for inclusion of a healthy volunteer in the control group C were the presence of a normal mandibular excursion, the absence of TMJ-D, and neuropathic pain (DN4 = 0). Volunteers with a previous trauma to the head and with dental or ear diseases were excluded from control group C.

The mean age of group A was $34 \pm 8$ years (range, 17–65 years); for group B, $34 \pm 1$ year (range, 24–54 years); and for group C, $34 \pm 6$ years (range, 19–60 years). To avoid sex-related bias, study group A consisted of 11 women and 2 men, group B was composed of 14 women and 2 men, and group C was composed of 7 women and 1 man.

**MR Imaging Analysis**

We performed MR imaging analysis in patients in our study group A and those in control groups B and C. All images were obtained with a 1.5T whole-body MR imaging scanner (Gyroscan; Philips Medical Systems, Best, the Netherlands) and a dedicated surface round coil. The data were collected on a $256 \times 256$ matrix with a FOV of 160 mm. Images were acquired with the patients in the supine position.

With each subject in the closed-mouth position, we obtained bilateral sagittal proton attenuation (PD−)-weighted (gradient-echo, flip angle (FA), 90°; TR, 1500 ms; TE, 30 ms; section thickness, 2 mm) and T2-weighted images (gradient-echo, FA, 20°; TR, 23 ms; TE 450 ms; section thickness, 2 mm). Furthermore, we performed a bilateral dynamic examination (ie, with the patients both in the closed-mouth and at the open-mouth positions) of the mandibular motion on a sagittal plane (gradient-echo, FA, 20°; TR, 13 ms; TE, 65 ms; section thickness, 2 mm).

Finally, with the patients in the maximal open-mouth position, we carried out paracoronal scans to gain the visualization of the disk and the oval foramen on the same section (gradient-echo, FA, 20°; TR, 13 ms; TE, 313 ms; section thickness 2 mm). For this reason, an axial scout that passes through the condyle was selected on a previous sagittal scout. We chose the right orientation of the paracoronal plane after identification on that axial scout view of the oval foramen and the articulare eminence; in fact, the disk is located just below the articular eminence at the open-mouth position. To achieve the maximal open-mouth position, we used a nonferromagnetic bite block.

We first investigated the relationship of the disk with the mandibular nerve at the oval foramen level. The distance of these 2 structures was identified on paracoronal sections at the maximal open-mouth position. It was measured as the distance between the more medial portion of the TMJ disk and the lateral edge of the oval foramen (Figs 1–3). The interpretation of the MR imaging findings of the TMJs was completed by the observation of the presence of internal derangement, osteoarthrosis, joint effusion, and bone marrow edema.

Internal derangement (ie, the abnormal positional relationship...
between the articular disk, the mandibular condyle, the glenoid fossa, and the articular eminence) was identified on sagittal planes on the dynamic sequences. We defined a normal disk in which its posterior band lies over the superior surface of the condyle at the 12 o’clock position. We defined a displaced disk in which its posterior band was not in normal position.1,3 Osteoarthrosis was diagnosed on PD and dynamic sequences as the presence of flattening of the articular surfaces, subchondral sclerosis, osteophytes, and condylar erosions.3,12 Finally, we investigated joint effusion and bone marrow edema on T2 images. Joint effusion was identified as an area of high signal intensity on T2-weighted images in the region of the joint space. When more than 1 line of high signal intensity was evident in at least 2 consecutive sections, it was considered positive for TMJ effusion. Bone marrow edema was defined as the presence on T2-weighted images of a hyperintense signal intensity within the bone.1,3,12,13

Statistical Analysis
First, we performed a Student $t$ test to assess the absence in the 3 groups of age-related bias. There were no statistically significant age-related differences among the 3 groups ($P > .05$). All MR images were independently evaluated by 3 observers who were blinded to the clinical examination. We evaluated interobserver reliability using interclass correlation. Differences among the observers in the evaluation of the data gained by MR imaging were resolved by consensus.

The 3 observers measured the distance (at the maximal open-mouth position) between the TMJ disk and the oval foramen and assessed the eventual presence within the TMJ of internal derangement, osteoarthrosis, joint effusion, and bone marrow edema.

Each value obtained by the blinded evaluation was successively associated with the corresponding patient or healthy volunteer. Data were collected in a software spreadsheet (Excel 2007; Microsoft, Redmond, Wash), and a Student $t$ test was performed to assess if the distance between the disk and the oval foramen was statistically different between the study group and the 2 control groups. A $P$ value of less than .05 was considered statistically significant.

Results
Results of our prospective study are summarized in on-line Tables 1–3 and in Fig 4. The prevalence of joint internal derangement was 93.7% in the TMJs with TMJ-D and neuropathic pain, 75% in the TMJs with TMJ-D without neuropathic pain, and 6.2% in the TMJs of the healthy volunteers. The prevalence of osteoarthrosis was 56.2%, 75%, and 6.2%, respectively. The prevalence of effusion in those 3 groups was 81.2%, 62.5%, and 18.7%, respectively, and the prevalence of bone marrow edema was 18.7%, 18.7%, and 0%, respectively.

The mean distance at the maximal open-mouth position between the disk and the mandibular nerve was 6.25 mm (SD, 2.01 mm) in group A (Fig 1), 8.18 mm (SD, 1.83 mm) in group B (Fig 2), and 9.43 mm (SD, 1.82 mm) in group C (Fig 3; on-line Tables 1–3; Fig 4).

Two TMJs in study group A showed a close proximity of the disk to the oval foramen but no signs of effusion, osteoarthrosis, and bone marrow edema (on-line Table 1, number: 8, 14); 3 TMJs of study group A showed the presence of effusion and osteoarthrosis but no proximity between the disk and the mandibular nerve (on-line Table 1, number: 1, 4, 7); 2 TMJs of control group B showed a proximity of the disk to the oval foramen and signs of osteoarthrosis and internal derangement (on-line Table 2, number: 8, 15).

The Student $t$ test (cutoff value, 0.05) demonstrated that distance between the disk and the oval foramen was significantly different between group A and group B ($t$ test, 0.01), and between groups A and C ($t$ test, 0.00005), whereas there was no significant difference between the 2 control groups B and C ($t$ test, 0.062).
Discussion

Recognition of possible causes of the onset of neuropathic pain (in particular, trigeminal pain) in patients with a history of TMJ-D is controversial.1,2 In 1934, Costen3 described how many neuropathic symptoms in TMJ-D could be caused by nerve compression, but with time, the hypothesis of nerve impingement was disfavored because it was never possible to provide convincing evidence.4,5 In a cadaveric study on 18 TMJ autopsy specimens, Johansson et al6 re-proposed the theory of mechanical influence on the bundles of the mandibular nerve suggesting that in certain circumstances (ie, disk displacement or the presence of anatomic variations), compression of these nervous fibers during jaw movement could be anatomically possible.6 Moreover, they noticed that the distance between the oval foramen and the medial pole of the condyle, when seated underneath the articular eminence, was 5 to 10 mm. Unfortunately, because their study was on cadaveric specimens, they were not able to provide any clinical examinations of any subjects nor any evidence of history of neuropathic pain. Furthermore, it is reasonable to speculate that in vivo movement of the jaw might be slightly different from that of cadavers because of different trophism of the tissues and ligaments.

The results of our study show that in vivo at the maximal open-mouth position, the distance between the disk and the mandibular nerve and/or its branches at the oval foramen level is significantly shorter in patients with TMJ-D and neuropathic pain than in patients with TMJ-D without neuropathic pain as in healthy volunteers (P < .05; Figs 1–4; on-line Tables 1–3).

We suggest that in many patients with TMJ-D and neuropathic pain, the medially displaced disk during jaw-opening movement may directly damage the mandibular nerve or its branches at the oval foramen level by exerting intermittent compression, traction, or friction. The mechanical influence of the disk could, in fact, alter the nerve bundles causing neuromas (so-called ephapses) and cross-talking phenomena. These “false synapses” may fire and elicit—continuously and antidromically—the trigeminal spinal nucleus of the brain stem and might be a reasonable explanation of the neuropathic pain and sensory symptoms that affect some patients with TMJ-D (eg, headache, cervicalgia, toothache, ear sounds, painful cold, electric shocks, tingling, pins and needles, numbness, itching, hypoesthesia to touch, etc).14–17

It is reported in the literature that, at the level of the brain stem, sensory neurons from the mandibular nerve share the same neuron pool as neurons from the maxillary, ophthalmic, and upper cervical nerves (cervical nerves I–III). This convergence of nerve fibers could explain how pain may be referred in different regions than in the dermatomal distribution of the mandibular nerve.9

Almost all of the patients with neuropathic pain showed short values of the distance between the disk and the mandibular nerve. In 2 TMJs with TMJ-D and neuropathic pain (12.5% of our study group), there were no signs of effusion, osteoarthrosis, or bone marrow edema but only a close proximity of the disk to the nerve (on-line Table 1, TMJ: 8, 14). Proximity of the disk to the oval foramen was observed also in 2 TMJs (12.5% of our control group B) with TMJ-D but without neuropathic pain (on-line Table 2, TMJ: 8, 15). However, because nerve impingement requires time to create damage to the nerve sheaths, it is possible that in those 2 patients there was not enough time.

One possible limitation of our study was the absence of a statistical correction for the amount of mouth opening. The MR imaging evaluation of the distance between the disk and the mandibular nerve at various degrees of mouth opening (10, 20, 30, and 40 mm) would have created new perspectives in the comprehension of the pathophysiology of TMJ-D, but, unfortunately, patients with neuropathic pain were able to stay in the open-mouth position for only few minutes because of increase in symptoms. To avoid this inconvenience, we chose to carry out only 1 MR imaging para-coronal sequence with the patient in the maximal open-mouth position; nevertheless, in 2 patients from group A, the pain was so unpleasant that we had to temporarily interrupt the imaging investigation.

The marked increase in neuropathic pain in these patients while they are in the maximal open-mouth position during imaging could be consistent with the hypothesis of a nerve impingement. A closer look at our data (on-line Tables 1–3) suggests that nerve compression might not be the only factor to define the occurrence of TMJ neuropathic pain in TMJ-D. In fact, in 3 cases (on-line Table 1, TMJs 1, 4, and 7), the distance of the disk from the oval foramen was wider than we expected. The patient with TMJ labeled “1” of the study group showed imaging signs of effusion and osteoarthrosis, and in patients with TMJ labeled “4” and “7” (group A), imaging signs of internal joint derangement, effusion, and osteoarthrosis were present (on-line Table 1). The prevalence of osteoarthrosis was higher in group B than in groups A or C. The prevalence of the imaging findings of internal joint derangement and effusion was higher in the patients from group A than in patients from groups B and C.

In our opinion, the role of imaging findings of internal joint derangement, effusion, osteoarthrosis, and bone marrow edema in the onset of neuropathic pain is not clear (on-line Tables 1–3). In fact, these findings are present both in patients with TMJ-D without neuropathic pain (on-line Table 2)3,5,12 and in patients with TMJ-D and neuropathic pain (on-line Table 1).

Conclusions

With the patient in the open-mouth position, the distance between the disk and the mandibular nerve and/or its branches at the oval foramen level is shorter in patients with TMJ-D and neuropathic pain than in patients with TMJ-D without neuropathic pain as well as in healthy volunteers. It is possible that in many patients with TMJ-D and neuropathic pain, the disk may directly damage the mandibular nerve and/or its branches by exerting intermittent compression, traction, or friction during the jaw-opening movement. The onset of neuropathic pain could be a direct consequence of lesions of the mandibular nerve fibers.

Additional clinical, surgical, and radiologic studies with larger samples are needed to confirm these data and clarify if these observations may have important implications in the therapeutic management (both conservative and surgical) of patients with TMJ-D and neuropathic pain.

References