Reference fields in phantom tooth pain as a marker for remapping in the facial territory

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Summary

Six patients with chronic phantom tooth pain were studied for the presence of reference fields for their phantom sensation. In five of them, pain or dysesthesia in the affected oral structures was elicited by thermal or mechanical stimulation of areas that were well separate from these structures. However, a relation of topographical proximity between the stimulated areas and the areas of reference could be traced in the sensory maps. Therefore, denervation of small structures with coarse sensitivity can yield the plastic changes that have previously been described for larger deafferentations of areas endowed with finer discriminative capacity.

KEY WORDS: Adult plasticity, deafferentation, pain, referred sensation, somatotopic representation, trigeminal system.

Introduction

Phantom tooth pain (PTP), as first defined by Marbach (1), is a syndrome of persistent pain in teeth and other oral tissues, that may follow dental procedures such as pulpal extirpation (root canal therapy), apicectomy (root tip amputation), or tooth extraction. It can also occur when nerves are injured by physical trauma, or even after routine inferior alveolar nerve blocks, if the needle pierces the nerve sheath. PTP is also associated with infections and tumors that invade nerve tissue in the trigeminal system (2). In the case of tooth extraction, the site of pain corresponds to the edentate area, while after periodontal surgery pain or paresthesia is located in the gingiva. At the moment of diagnosis, physical and radiographic examination yield no pathological evidence. No dental procedures are effective in reducing pain, instead dental procedures frequently increase pain severity and distribution; the same is true of other interventions such as trigeminal rhizotomy and microvascular decompression. Therefore, successful treatment of acute dental pain can be the initiating factor for chronic pain. Campbell et al. (3) restrict the definition of PTP to cases in which pain was already present before the dental procedure(s), while proposing the definition “post traumatic dysesthesia” for the other cases.

PTP is persistent, allodynic (pain is caused by normally non-painful stimuli), frequently presents with delayed onset following dental procedures, and appears in only a small percentage of cases submitted to such treatments: according to Marbach et al. (4), it appears in 3%-6% of cases after endodontic treatments; Pöllmann (5) found PTP in 1.7% of an unselected population, in which, however, 2 620 out of 3 126 subjects had edentulous areas. The above characteristics, combined with the fact that the dental pulp with nerve endings has usually been amputated, suggest that a central mechanism plays a role in PTP. Central modifications could be triggered by abnormal impulses generated by an amputation neuroma at the root apex (6); experimentally, functional alterations in the properties of neurons in the trigeminal spinal tract have been described following tooth pulp deafferentation in the cat (7, 8).

In the present study, 6 PTP patients were examined for the presence and localization of reference fields (repeatedly taken as an index of reorganization of the central nervous system after amputations (9-12); see Ramachandran and Hirstein (13) for a review). Painful and non-painful sensations may be evoked within the phantom by stimulation of areas remote from, but topographically related to, the amputated body part. This relationship can often be predicted on the basis of contiguity as depicted in Penfield's maps. PTP occupies a special place in the field of referred pain, with formal experimental proof of reference of pain as a learned phenomenon in the dental territory dating back to the '40s. The basic observation was that during high-altitude flying some individuals suffered severe pain localized to the teeth (aerodontalgia). After every possible dental cause for the pain had been excluded, it was discovered that the pain stimulus was the expansion of air entrapped in the maxillary sinus in individuals with a high incidence of previous traumatic dental work on the side of reference (14). To test the hypothesis of habit reference of pain, Hutchins and Reynolds (15) performed fillings and extractions without block anesthesia; after several weeks, needle prick stimulation of the region of the maxillary sinus ostium produced pain that was referred to the previously stimulated teeth “whether or not any sensation was evoked from the site of the immediate stimulation”. Procaine
block anesthesia, on the other hand, was effective both in preventing referred pain, and in removing this sensation once established (16). Since then, sensitivity changes in the oral territory that are amenable to plastic modifications in the central nervous system have been repeatedly shown. For instance, Svensson et al. (17) recently showed that tonic painful stimulation of jaw muscles induces mechanical hyperesthesia of human facial skin, and considered such hyperexcitability changes as part of the pathophysiological mechanism involved in painful temporomandibular disorders.

Materials and methods

Subjects

The study was performed in 6 patients being treated by one of the authors (A.L.) for PTP. All but one were women; their ages ranged between 27 and 70 years. All the subjects gave their informed consent, and all the work was conducted in accordance with the ethical principles of the Declaration of Helsinki.

– FM, 70 years, has a typical history of PTP: a burning and throbbing pain had appeared 2 and half years before the study, in the gums adjacent to a bridge at the level of the 5\textsuperscript{th}-7\textsuperscript{th} upper left teeth. The bridge itself, and the extraction of the 6\textsuperscript{th} upper left tooth, dated back some 15 years. The patient underwent devitalization and then extraction of the above 5\textsuperscript{th} and 7\textsuperscript{th} teeth, followed by anesthetic block of the temporo-mandibular joint and thermorhizotomy of the left Gasserian ganglion, procedures that resulted solely in a painful hypoesthesia of the left hemiface. She is currently being treated with carbamazepine, amitriptyline and benzodiazepines.

– CR, 51 years, three years before the study and following prolonged exposure to the sun, experienced a “swollen head” sensation, followed by a sharp pain involving the zygomatic and lateronasal regions as well as the 5\textsuperscript{th} and 6\textsuperscript{th} upper right teeth. Devitalization did not resolve the pain, despite the absence of periapical lesions.

– MMR, 41 years, about two years before the study, began to experience toothache affecting the upper right 6\textsuperscript{th} tooth. After devitalization, the pain persisted and extended to the territory of the 2\textsuperscript{nd} and 3\textsuperscript{rd} trigeminal branches, provoking refractory to four further endodontic treatments and extraction of the affected tooth. She is currently being treated with amitriptyline and naproxen.

– RR, 48 years, 8 years before the study, started to experience a burning tongue sensation and “shaking” pain at the level of the 3\textsuperscript{rd} lower left tooth. No benefit was derived from analgesic or endodontic therapy.

– PP, 27 years, experienced a sudden pain affecting the 4\textsuperscript{th} lower right tooth 8 years before the study; since then the pain (which was tearing, tormenting and accompanied by a red-hot sensation) has persisted in spite of orthodontic and endodontic treatments, and ultimately extraction.

– ZF, the only man, 68 years, ten years before the study suffered a bilateral lesion of the mental nerves during a pre-prosthetic intervention (he is completely edentulous). Ever since he has experienced an area of painful hypoesthesia involving the lower lip and chin bilaterally. The pain is continuous, tormenting, sometimes throbbing, squeezing, and burning.

The patients’ characteristics are summarized in Table I.

Assessment of the topographic distribution of the phantom sensation

This study focused on the localization of areas (both inside and outside the mouth) where painful or painless sensations could be evoked in previously treated tooth/teeth, or in relative edentulous areas. The evaluation was based on both thermal and mechanical stimulation. Thermal stimulation was applied intraorally on teeth and gums, using gutta-percha at 60°C as warm stimulation, and melting ice (0°C) as cold stimulation. Mechanical stimulation was applied both intra- and extraorally. Superficial and deep digital pressure was used on soft tissues, while the handle of a dental mirror was used for percussion on tooth crowns. All the stimuli proved to be below the threshold for pain in normal controls; the
sensitivity of all the patients, as assessed at a standard clinical examination in extra-oral territories, was normal. The points of intraoral stimulation are listed in Table II. Extraoral mechanical stimulation was applied in selected areas of the three branches of the 5th nerve (temple, outer angle of the eye, zygomatic area, nasolabial sulcus, upper and lower lip, chin, emergence of the mental nerve, mandibular angle and margin), on both sides.

Questionnaires

The study of phantom topography was accompanied by two questionnaires. The first was designed to allow better qualification and quantification of pain, and included a modified version of the McGill Pain Questionnaire (MPQ) (18) and the Visual Analogue Scale (VAS) (19). The second was a personality test, the Bertolotti et al. (20) version of the Cognitive Behavioral Assessment (CBA). Each patient was studied separately in a single session. Four of them (FM, MMR, RR and PP) were re-examined for the topographic assessment of phantom pain sensations exactly two years following the first study, under exactly the same conditions.

Results

Questionnaires

PTP, as assessed by the modified MPQ, was described by most of the patients as continuous, throbbing, accompanied by thermal sensations from warm to red-hot, tormenting and influencing social life. Pain quantification according to the VAS (from 0 to 100%) varied: 10% (CR), 40% (PP), 50% (FM), 70% (MMR, RR, ZF). The CBA, according to internal indices (20), was unreliable in the case of ZF. All the other subjects displayed normal state anxiety. Trait anxiety, neuroticism, stress, phobias, depression, compulsions and obsessions were present in different cases.

Topographic assessment

Although the patients were instructed to report both painful and non-painful referred sensations, all the re-

Table II - Abnormal (painful or dysesthetic) responses to thermal stimulation (warm, gray rows; cold, white rows) of the intraoral structures listed in the first column.

<table>
<thead>
<tr>
<th>Affected tooth/teeth, hand gums, or gums of the free saddle</th>
<th>FM</th>
<th>CR</th>
<th>MMR</th>
<th>RR</th>
<th>PP</th>
<th>ZF</th>
</tr>
</thead>
<tbody>
<tr>
<td>“Delayed” allodynia</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>Dysesthesia</td>
<td>Allodynia</td>
</tr>
<tr>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>Alldynia</td>
<td>Alldynia</td>
<td>Alldynia</td>
<td></td>
</tr>
<tr>
<td>NO</td>
<td>NO</td>
<td>Referred allodynia</td>
<td>NO</td>
<td>NO</td>
<td>/</td>
<td></td>
</tr>
<tr>
<td>Dysesthesia</td>
<td>NO</td>
<td>Referred allodynia</td>
<td>NO</td>
<td>Alldynia</td>
<td>/</td>
<td></td>
</tr>
<tr>
<td>Referred allodynia</td>
<td>NO</td>
<td>Referred allodynia</td>
<td>NO</td>
<td>Alldynia</td>
<td>/</td>
<td></td>
</tr>
<tr>
<td>Gums of the adjacent teeth (mesially and distally)</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>Referred (“delayed”) allodynia</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>Referred allodynia</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>Dysesthesia</td>
<td>/</td>
</tr>
<tr>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>Alldynia</td>
<td>/</td>
</tr>
<tr>
<td>Controlateral tooth/teeth of the same arch</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>Dysesthesia</td>
<td>/</td>
</tr>
<tr>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>Alldynia</td>
<td>/</td>
</tr>
<tr>
<td>Controlateral gum of the same arch</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>Dysesthesia</td>
<td>NO</td>
</tr>
<tr>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>Alldynia</td>
<td>/</td>
</tr>
<tr>
<td>Teeth of the antagonistic arch</td>
<td>NO</td>
<td>NO</td>
<td>Referred allodynia</td>
<td>NO</td>
<td>Dysesthesia</td>
<td>/</td>
</tr>
<tr>
<td>NO</td>
<td>NO</td>
<td>Referred allodynia (slight)</td>
<td>NO</td>
<td>Dysesthesia</td>
<td>/</td>
<td></td>
</tr>
<tr>
<td>NO</td>
<td>NO</td>
<td>Referred allodynia</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td></td>
</tr>
<tr>
<td>NO</td>
<td>NO</td>
<td>Referred allodynia (strong)</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td></td>
</tr>
</tbody>
</table>

Referred allodynia means that stimulation of those structures produced a sensation that was localized to the affected tooth/teeth of the patient. Other sensations (allodynia, dysesthesia) were felt locally, i.e. within the stimulated structures.
ports were of painful or at least unpleasant (dysesthetic, paresthetic) sensations, in accordance with the characteristics of dental pulp, from which only painful sensations can be evoked. The patients' thermal stimulation and mechanical stimulation results are given in Tables II and III respectively. Altogether, five out of the six patients reported sensations which were referred to the previously treated (extracted or denervated) tooth or teeth. In these five cases, some sites of stimulation yielded sensations referred to the affected structures, while other sites yielded sensations attributed to the stimulated locations only (local). In all cases of referred sensation, the stimulation was perceived both locally with "normal", non-painful characteristics, and in the treated areas, with unpleasant or painful characteristics. Thermal stimulation of the teeth and gums adjacent to the treated ones produced referred allodynia in MMR, and both local and referred sensations in FM and PP. No referred, but only local sensations were elicited, in MMR and PP, by stimulation of the contralateral structures of the same dental arch. Instead, referred allodynia was evoked in both MMR and RR from the antagonistic arch, ipsilaterally; in MMR there was a modulation of referred pain upon cold stimulation, which was reported as slight and strong following stimulation of the teeth and gums respectively. Allodynia of the treated tooth or teeth was not in all the patients concomitant with sensations referred to these structures: for instance, such allodynia was absent in MMR, who showed evidence of referred pain, while it was present in CR, who did not report any referred sensation, or any other local allodynic phenomenon. Intraoral, superficial mechanical stimulation evoked local pain in four cases, while intraoral deep stimulation evoked referred pain in PP, local and referred pain in ZF, and only local sensations in three other cases. Extraoral superficial stimulation was effective in eliciting referred pain in three cases. In MMR, referred pain was elicited upon stimulation in the territory of the 1st and 3rd branch of the 5th nerve (the involved branch being the 2nd), while in RR stimulation of the cutaneous territory of the 2nd trigeminal branch was effective (the involved branch being the 3rd). A similar topographical relationship was present in ZF, who experienced referred pain in the territory of the denervated 3rd trigeminal branch upon stimulation of the 2nd. Local sensations were evoked in two other cases (as well as in RR). Finally, extraoral deep stimulation evoked local and referred pain in FM, only referred pain in RR (in both cases the referred sensations derived from the trigeminal branch involved in the treatment), referred pain in ZF (from the

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Table III - Abnormal (painful or dysesthetic) responses to mechanical stimulation, superficial and deep (including tooth percussion), in intraoral (gray columns) and extraoral structures (white columns). Unless otherwise specified, reference of sensation is intended to the affected structures, and other sensations (local, i.e., felt within the stimulated structures: allodynia, dysesthesia) are ipsilateral to the affected structures.

<table>
<thead>
<tr>
<th></th>
<th>SUPERFICIAL</th>
<th>DEEP</th>
</tr>
</thead>
<tbody>
<tr>
<td>FM</td>
<td>Alloodynia, antagonistic arch.</td>
<td>Alloodynia, temple and emergence of the mental nerve.</td>
</tr>
<tr>
<td>CR</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>MMR</td>
<td>Alloodynia, involved and adjacent teeth.</td>
<td>Referred allodynia, temple and mandibular angle.</td>
</tr>
<tr>
<td>RR</td>
<td>NO</td>
<td>Alloodynia, emergence of the contralateral mental nerve. Referred allodynia, upper lip at canine level bilaterally.</td>
</tr>
<tr>
<td>PP</td>
<td>Dysesthesia, involved and adjacent teeth.</td>
<td>Alloodynia, outer angle of the eye, nasolabial sulcus, inferior mandibular margin.</td>
</tr>
<tr>
<td>ZF</td>
<td>Alloodynia, emergence of the mental nerve bilaterally.</td>
<td>Referred paresthesia, lower lip and chin, upon stimulation of the upper lip at canine level bilaterally.</td>
</tr>
</tbody>
</table>
territory of the 2nd trigeminal branch, adjacent to the involved one), and local sensations in two other cases. Figure 1 displays a map of the areas in which local and referred pain was evoked in a typical case (MMR). When four of the patients were re-examined, two years after the first study, a referred sensation was still elicitable only in PP. In agreement with the first study (see Table II), pain was provoked near the affected tooth and with cold stimulation; but referred pain could no longer be elicited from the antagonistic arch (see Table III). In RR, a “shaking” pain could still be elicited from the affected tooth; as in the first study, exactly the same sensation could also be provoked by stimulation of the teeth and gums of the antagonistic arch (ipsilaterally), but this time without showing a clear topographical pattern of reference. Finally, in MMR, no procedure of the standard protocol succeeded in eliciting pain, but she reported still feeling a “direct” sensation of pain at the level of the affected tooth when happening to press or displace her nose with a finger. Local painful sensations appeared generally to be attenuated in the four cases.

**Discussion**

This study demonstrates that pain can be elicited in the territory of deafferented teeth by stimulating structures that are well separate from them, but show a rather regular pattern of topographical proximity in the sensory maps. Proximity on the body surface corresponds to proximity in the neural maps at cortical and subcortical level, therefore referred sensation in PTP may represent a further instance of neural plasticity. This result is novel insofar as it refers to dental sensitivity, which is not as topographically refined as that involving the hand or even the foot. That the result is reliable, despite the coarseness of dental sensitivity, is proven by the fact that the referred sensation was not in all cases evoked from the adjacent structures, while in some cases it was evoked only, or more strongly, from relatively remote structures. On the other hand, the presence in some cases of local allodynia, i.e., an exaggerated pain sensation that is localized to a site of stimulation that can be different from that affected by phantom sensations, may cast some doubts on this reliability.

One possible explanation of the local allodynia is simply that stimulation involves structures that are affected by other subclinical pathologies, probably in subjects with a particularly low pain threshold. An influence of premorbid personality should indeed be taken in account. Sicuteri et al. (21) found that idiopathic headache is a possible risk factor for PTP, and Pöllmann (5) described a high level of demoralization in PTP patients. We found different
personality disturbances in our cases; of course, we cannot say to what extent such disturbances are reactive to the chronic pain. However, the personality disturbances observed were considerably heterogeneous, and none seemed to be specific to PTP.

Another possibility is that in some cases PTP loses its topographic specificity, so that allodynic areas act as trigger points for a painful sensation that the patient has learned to feel without a precise localization and is now inclined to attribute to the actual area of stimulation. The second observation of case RR offers a clear instance of the passage from a localized to an unlocalized sensation. This kind of “generalization” of pain is antithetic to the precise localization of referred sensations, and suggests that a distinction should be made between reference fields of painful and non-painful sensations, which show a precise somatotopic relationship with amputated body segments, and trigger points for painful sensations, which may lack such a relationship. This distinction requires further studies and speculation. Multiple trigger points, even changing over time, can be observed in trigeminal neuralgia (22) as well as in other painful states. In fact, we found only pain, or at least dysesthetic sensations, in all our cases. This is in disagreement with the observations of Pöllmann (5, 23), that painless phantom phenomena coexist with painful phenomena after tooth removal, and that the painless phenomena are probably reported less frequently because patients tend not to complain of such sensations. Animal and human data, starting with the seminal electrophysiological studies by Merzenich and Kaas (24) right up to recent work on brain potentials (25) and cortical blood flow (26) in humans, suggest that referred sensations after deafferentation are due to the activation of a denervated cortical or subcortical territory by input from intact parts of the sensory periphery. Here, we refer briefly to just a couple of studies concerning the trigeminal system.

In the study of Hu et al. (7), following tooth pulp deafferentation in the cat, a decrease of trigeminal neurons having a receptive field within the mandibular or maxillary division was found, together with a parallel increase in the occurrence of neurons having a receptive field involving two or three trigeminal divisions.

An even larger remapping was described by Clarke et al. (27) in a patient who had the maxillary and mandibular parts of her trigeminal ganglion removed on one side, and experienced sensations referred to the denervated territory after stimulation of the ipsilateral hand and forehead. This study showed unequivocally that changes in somatosensory maps, without concurrent changes in motor maps, are sufficient to give a conscious experience of a phantom body part, as already suggested by the study on phantom breast by Aglioti et al. (11). We confirm this with more peripheral lesions. Clarke et al. (27) also showed that input from the primary sensory neurons is not necessary for the occurrence of referred sensations. Our observation that allodynia of the affected tooth/teeth does not always accompany referred sensations reinforces this point: local pain, a probable index of regeneration (neuroma?), can be found without referred sensations, which in turn may occur in the absence of local pain.

A final note concerns the time course of the observed phenomena. Both the above studies described a really short time course: Hu et al. (7) found a “return to control values from 7 to 15 days”, and Clarke et al. (27) reported “more realistic sensation 7 than 12 days after surgery”. In the present study we observed phenomena of much longer duration. Of course we do not know how soon after the original treatments they started, but we can testify to a clear reduction of the phenomena at the re-examination. 2 years following the first study.

In conclusion, PTP, as following deafferentation of other body parts, is accompanied by referred sensations that show a clear topographic relationship with the deafferented area. As is the case with other body parts, and actually even more than with other body parts - see Ramachandran and Hirstein (13) for comparison - referred sensations can be found in the large majority of cases selected for the presence of PTP. Therefore, denervation of even a very small territory can induce plastic changes in the CNS. Whether such changes happen in cortical or subcortical structures is unclear, particularly dealing with the largely unknown representation of pain (or at least unpleasant sensations). Also, we do not know the latency of the process; we can only be sure that its consequences last several years.

Acknowledgments

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Remapping of the face in phantom tooth pain

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