A "Dysfunctional" Pain Group in Addition to the "Neuropathic" and "Nociception/Inflammatory" Groups of Orofacial Pain Entities?

The knowledge recently acquired in the field of orofacial pain may contribute to the current debate regarding whether or not the term "dysfunction" should be removed from the definition of neuropathic pain.[1] Classical neuropathic pains are the direct consequence of a trauma or a disease affecting the peripheral or central nervous system. Neuropathic pain in the orofacial area may be due to surgical impairment of the inferior alveolar nerve or of the lingual nerve during orthognathic surgery or third molar removal. In these cases, neurological examination is generally abnormal and screening tools such as the DN4 questionnaire[2] may help identify such pain conditions as clearly neuropathic. Other neuropathic pains are not caused by a localized injury. This may be the case for some more diffuse nervous lesions related to a general disease such as diabetic polyneuropathies or HIV-induced pain. There are also examples of pains formally called "functional" in which evidence of non-traumatic degeneration of peripheral nerve fibers has been recently demonstrated. Stomatodynia, also called burning mouth syndrome, is a very homogeneous disease[3] characterized by spontaneous burning pain in the oral mucosa. Stomatodynia would not be classified as neuropathic by the above-mentioned tool (DN4), nor by current neurological examination because allodynia and anesthesia are lacking. However, four independent groups using lingual biopsies have recently described epithelial nerve fiber lesions.[4–7] Similar situations have also been suggested outside of the orofacial area. For example, two recent papers have shown nerve fiber degeneration in type I complex regional pain syndrome.[8,9] As underlined by Jänig and Baron[10] for complex regional pain syndrome, the neuropathy may be secondary to other factors since the cause of the degeneration is unknown. Indeed, one may hypothesize psychological disorders, a simultaneous participation of gonadal, adrenal, and neuroactive steroids and a genetic background, but the relationship between these different factors is far from being understood. Some other orofacial "functional" or "idiopathic" pain conditions such as atypical odontalgia or persistent idiopathic facial pain (atypical facial pain) have also been shown to share many neuropathic features,[11,12] although there are little clinical signs of anesthesia or allodynia.

Considering all these orofacial diseases together, it seems that a continuum exists from the purely neuropathic, post-traumatic nerve injury pain to atypical odontalgia. After a lesion of a large peripheral nerve, a neuropathic type of pain does not occur in all cases. A large inter-individual variability exists. The chance to develop such a pain probably depends in part on genetic predisposition of both, but the occurrence rate and the type of symptoms also depend on the size of the nerve being injured. This neuropathic continuum could be described in the following way: when cutting a large nerve, such as the lingual nerve or the inferior alveolar nerve, neuropathic pain will occur in a large fraction of the subjects. It will be accompanied by typical symptoms of anesthesia and allodynia. When cutting a smaller branch such as the mental nerve, the expectation for chronic pain is lower, and when cutting an even smaller nerve, such as an isolated tooth nerve, the chance to develop an atypical odontalgia is even smaller and generally no transient sign of anesthesia or allodynia is observed clinically. This line of thought could be summarized as follows: The smaller the nerve, the bigger must be the influence of genetic and hormonal imbalance factors to induce a neuropathy and the less the resulting chronic pain may be identified as "neuropathic" by screening tools such as the DN4.

At that point one may question the status of "functional" pain entities which, in many cases, may be the result of a neuropathic mechanism occurring after a diffuse nerve lesion or a lesion of a small nerve in predisposed subjects. Since there are also many other pain diseases such as migraine or tension-type headache in which other mechanisms are involved and which are neither purely neuropathic nor purely nociceptive/inflammatory, it appears that three terms are needed. A first one to cover the classical concept of pain by excess of stimulation, ie, nociception/inflammation, a second one for the pain characterized by symptoms such as

anesthesia and allodynia resulting from a clearly identified nerve injury or central lesion, and a third one for pain resulting from unclearly identified causes that may include dysfunction of the pain modulation system, a diffuse nerve lesion, or injury of a small nerve. It seems to be clear that a neuropathic continuum exists between the second and the third dysfunctional group or, to say it in another way, there are entities in which a purely neuropathic mechanism is mixed with a dysfunctional mechanism in a way similar to what is observed in cancer when neuropathic and inflammatory mechanisms are mixed.

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