LETTER TO THE EDITOR

Small fibre neuropathy, fibromyalgia and dorsal root ganglia sodium channels

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Sir,

In their elegant study, Üçeyler et al. (2013) provide objective evidence of small fibre neuropathy in patients with fibromyalgia. They conclude that fibromyalgia may be a neuropathic pain syndrome (Üçeyler et al., 2013). Small fibre neuropathy is a disorder of the peripheral nerves resulting in sensory changes and sympathetic dysfunction.

For years, we have proposed that fibromyalgia is a neuropathic pain syndrome based on the following three arguments: (i) fibromyalgia is a stimulus-independent pain state. There is no structural damage that could explain the pain intensity; (ii) the presence of allodynia as an essential feature of fibromyalgia; and (iii) the presence of paraesthesias as a distinctive feature of fibromyalgia (Martinez-Lavin et al., 2003). It seems difficult to ascribe an aetiology other than neuropathic pain to a syndrome with such characteristics.

Among neuropathic pain syndromes, we proposed that fibromyalgia pain is sympathetically maintained based on the following issues: (i) the high frequency of physical or psychological trauma as a triggering event; (ii) diverse heart rate variability studies showing that patients with fibromyalgia have changes consistent with ongoing sympathetic hyperactivity (Lerma et al., 2011); and (iii) a double-blind study showing that norepinephrine injections rekindle fibromyalgia pain (Martinez-Lavin et al., 2002).

Based on animal models of sympathetic pain, we focused our attention on dorsal root ganglia as potential sympathetic–nociceptive short-circuit sites in cases of fibromyalgia. Dorsal root ganglia contain the sensory fibres cell bodies. Trauma and/or infection trigger sympathetic sprouting within dorsal root ganglia through nerve growth factor over-expression. Such aberrant neuroplasticity enables catecholamines and sympathetic traffic to induce sensory neuron firing. Sodium channels play a pivotal role in this hyperexcitability. A sodium channel isoform (NaV1.7) encoded in gene SCN9A of chromosome 2q24.3 is predominantly expressed in the dorsal root ganglia pain-sensing neurons and sympathetic ganglia neurons and their fine-diameter axons.

In a pilot study, we described a particular SCN9A sodium channel gene variant (rs6754031 GG genotype) associated with severe fibromyalgia (Vargas-Alarcon et al., 2012). On the other hand, Faber et al. (2012) reported that a gain of function mutations in sodium channel NaV1.7, which render dorsal root ganglion neurons hyperexcitable, are present in a substantial proportion (28.6%; 8 of 28) of patients meeting strict criteria for small fibre neuropathy (Faber et al., 2012). This preliminary information raises the possibility that some cases of fibromyalgia and small fibre neuropathy may have underlying dorsal root ganglia sodium channelopathy.

The Üçeyler et al. (2013) study reinforces our proposal of fibromyalgia as sympathetically maintained neuropathic pain syndrome. Sympathetic dysfunction provides a coherent explanation for the multiple non-pain related fibromyalgia symptoms (Martinez-Lavin, 2012).

References

