• **FACT SHEET No. 12**

Neuropathic Mechanisms and Symptoms in Joint Pain: Impact on Assessment and Management

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Joint pain is frequently considered a pure nociceptive pain and a model for the assessment of analgesics dedicated to nociceptive pain such as NSAIDs and opioids. Recent studies suggest that patients frequently report neuropathic symptoms and that neuropathic mechanisms are involved in joint pain. This opens new approaches both for the assessment and management.

Neuropathic clinical characteristics in joint pain

Several papers suggest that patients with joint pain may exhibit neuropathic pain (NP) symptoms. In osteoarthritis (OA), some studies have demonstrated that quality of pain may exhibit some neuropathic characteristics (Cedraschi et al, 2013).

The diagnosis of NP is clinical and based on medical history, physical examination, and ancillary tests. Different clinical tests can be used to detect a neuropathic component: DN4, painDETECT, the LANNS Pain Scale, and others. The painDETECT test is a patient-reported questionnaire extensively validated for the diagnosis of NP in various chronic pain conditions (Freynhagen et al, 2006), with higher scores suggesting the likelihood of NP.

OA patients have been found to experience neuropathic pain (Hochman et al 2014), but NP has also been reported in such inflammatory disorders as rheumatoid arthritis (RA) (Ahmed et al., 2014). In musculoskeletal pain, several authors have also suggested that NP was frequent and underdiagnosed (Jespersen et al, 2010).

Neuropathic pain pathophysiology in joint pain

In joint pain, whatever the cause, the peripheral nociceptors may be sensitized by, for example, inflamed synovium and damaged subchondral bone (Mapp, 1995). Continuous and intense nociceptive input from the OA knee joint may drive central sensitization, which may arise from chronic nociceptor stimulation and subsequent modification of central pain-transmitting neurons and may be clinically associated with NP qualities.

Neuropathic pain peripheral mechanisms

There are probably both peripheral and central neuropathic mechanisms in joint pain at different stages—peripheral mechanisms more in the early stage and central mechanisms more in late and chronic stages. Interactions between central and peripheral systems suggest a general plasticity of the nociceptive system in osteoarthritis pain (Imamura et al, 2008). This plasticity may depend on different factors, including emotional factors.

Neuropathic central mechanisms and central sensitization

Pain has a complex pathophysiology, and recent findings have demonstrated the important role of central mechanisms in both OA and RA. In osteoarthritis, there is increasing evidence that central mechanisms play a role in pain sensation. When injecting a saline solution in the anterior tibialis muscle, patients with knee osteoarthritis experience more intense and more diffuse pain compared with normal controls (Arendt-Nielsen, 2010).

The most striking recent findings in OA pain have demonstrated brain activation and brain modifications in patients with pain related to OA. Some studies have analyzed brain activation and have demonstrated that OA pain, as is the cease in most chronic pain states, is associated with central sensitization (Graven-Nielsen et al, 2002). Clinically, central sensitization related to joint pain induces pain for stimuli that currently do not induce pain (allodynia), with larger areas of pain activation and a longer duration of pain. Central sensitization in OA has been confirmed both by quantitative sensory testing (QST) analyses

and functional MRI (Suokas et al, 2012). It could explain failures of therapeutic approaches, including joint replacement surgery.

Brain modifications

More-recent studies have analyzed brain volume, specifically in certain areas, and found some modifications in the gray matter: As in other chronic pain states, OA is associated with a decrease of gray matter, but this decrease my not be permanent, since gray matter is regenerated six to nine months after effective hip or knee surgery (Gwylin 2010).

In conclusion, NP can be observed in some conditions where nociceptive pain was mainly considered as the main mechanism, e.g., joint pain. This is frequently associated with chronic pain states and may explain some therapeutic failures, including pharmacological and surgical approaches. For the future, ineffective pain management and disability associated with joint pain herald changes in pain assessment and in treatment paradigms as well as new therapeutic approaches.

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